ASX Release

21 October 2020

Opthea Announces Closing of Initial Public Offering in the United States

Melbourne, Australia; 21 October 2020 – Opthea Limited (ASX:OPT; Nasdaq:OPT), a clinical stage biopharmaceutical company developing a novel therapy to treat highly prevalent and progressive retinal diseases, today announces the closing of its previously announced initial public offering in the United States (the "**Offering**") of 8,563,300 American Depositary Shares ("**ADS**"), representing 68,506,400 ordinary shares, at an initial public offering price of US$13.50 per ADS, and pre-funded warrants to purchase 936,700 ADSs at a public offering price of US$13.49999 per pre-funded warrant. The aggregate gross proceeds of the Offering were approximately US$128.2 million. The Company has also granted the underwriters a 30-day option to purchase up to an additional 1,425,000 ADSs at the initial public offering price per ADS less underwriting discounts. All of the ADSs in the Offering were offered by Opthea Limited.

Opthea Limited's ordinary shares are listed on the Australian Stock Exchange and its ADSs are listed on the Nasdaq Global Select Market, each under the symbol "OPT." The ADSs began trading on the Nasdaq Global Select Market on October 16, 2020.

Citigroup and SVB Leerink acted as joint book-running managers for the Offering. Oppenheimer & Co. and Truist Securities acted as lead managers.

A registration statement relating to these securities has been declared effective by the U.S. Securities and Exchange Commission (the "**SEC**") on October 16, 2020. The Offering was made only by means of a prospectus. A copy of the final prospectus relating to and describing the terms of the Offering is attached to this announcement and may also be obtained from Citigroup Global Markets Inc., c/o Broadridge Financial Solutions, 1155 Long Island Avenue, Edgewood, NY 11717, telephone: 1-800-831-9146; or SVB Leerink LLC, Attention: Syndicate Department, One Federal Street, 37th Floor, Boston, MA 02110; by telephone at (800) 808-7525, ext. 6132; or email: syndicate@svbleerink.com.

This press release does not constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction, and shall not constitute an offer, solicitation or sale in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of that jurisdiction.

About Opthea

Opthea (ASX:OPT) is a biopharmaceutical company developing a novel therapy to address the unmet need in the treatment of highly prevalent and progressive retinal diseases, including wet age-related macular degeneration (wet AMD) and diabetic macular edema (DME). Opthea's lead product candidate OPT-302 is being developed for use in combination with anti-VEGF-A monotherapies to achieve broader inhibition of the VEGF family, with the goal of improving overall efficacy and demonstrating superior vision gains over that which can be achieved by inhibiting VEGF-A alone.

Inherent risks of Investment in Biotechnology Companies

There are a number of inherent risks associated with the development of pharmaceutical products to a marketable stage. The lengthy clinical trial process is designed to assess the safety and efficacy of a drug prior to commercialization and a significant proportion of drugs fail one or both of these criteria. Other risks include uncertainty of patent protection and proprietary rights, whether patent applications and issued patents will offer adequate protection to enable product development, the obtaining of necessary drug regulatory authority approvals and difficulties caused by the rapid advancements in technology. Companies such as Opthea are dependent on the success of their research and development projects and on the ability to attract funding to support these activities. Investment in research and development projects cannot be assessed on the same fundamentals as trading and manufacturing enterprises. Therefore, investment in companies specializing in drug development must be regarded as highly speculative. Opthea strongly recommends that professional investment advice be sought prior to such investments.

Forward-looking Statements

Certain statements in this announcement may contain forward-looking statements, including within the meaning of the U.S. Private Securities Litigation Reform Act of 1995, regarding the Company's business as well as the proposed Offering. Any statement describing Company goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, including market conditions, the satisfaction of customary closing conditions relating to the Offering and the impact of general economic, industry or political conditions in Australia, the United States or internationally. These and other risks and uncertainties are described more fully in the section titled "Risk Factors" in the final prospectus related to the Offering to be filed with the SEC. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise, except as required under applicable law. You should not place undue reliance on these forward-looking statements as predictions of future events, which statements apply only as of the date of this announcement. Actual results could differ materially from those discussed in this ASX announcement.

Authorized for release to ASX by Megan Baldwin, CEO & Managing Director

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PROSPECTUS

8,563,300 American Depositary Shares
Pre-Funded Warrants to Purchase 936,700 American Depositary Shares representing 76,000,000 Ordinary Shares

This is the initial public offering of 8,563,300 American depositary shares, or ADSs, in the United States, representing 68,506,400 ordinary shares of Opthea Limited. Each ADS represents eight ordinary shares, no par value, deposited with The Bank of New York Mellon, as depositary.

We are also offering to a certain purchaser pre-funded warrants to purchase 936,700 ADSs, representing 7,493,600 ordinary shares of Opthea Limited, in lieu of ADSs. Each pre-funded warrant will be exercisable for one ADS. The purchase price of each pre-funded warrant will be equal to the price at which an ADS is sold to the public in this offering, minus US$0.00001, and the exercise price of each pre-funded warrant will be US$0.00001 per ADS. The pre-funded warrants will be immediately exercisable and may be exercised at any time until all of the pre-funded warrants are exercised in full, subject to certain conditions under Australian law set forth under "Description of Pre-Funded Warrants." This offering also relates to the ADSs (and ordinary shares underlying the ADSs) issuable upon exercise of the pre-funded warrants sold in this offering.

We have granted the underwriters an option to purchase up to an additional 1,425,000 ADSs to cover over-allotments, if any.

Prior to this offering, there has been no public market for the ADSs. The ADSs have been approved for listing on the Nasdaq Global Select Market under the symbol "OPT." There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. In addition, we do not intend to apply for a listing of the pre-funded warrants on any national securities exchange or other nationally recognized trading system.

Our ordinary shares are listed on the Australian Securities Exchange under the symbol "OPT." On October 16, 2020, the last reported sale price of our ordinary shares on the Australian Securities Exchange was A$2.78 per ordinary share, equivalent to a price of US$15.73 per ADS, after giving effect to the Australian dollar/U.S. dollar exchange rate of A$1.4134 to US$1.00 as of October 16, 2020, and an ADS-to-ordinary share ratio of 1-to-8.

Investing in our securities involves a high degree of risk. See "Risk Factors" beginning on page 12 of this prospectus.

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company reporting requirements.

Neither the U.S. Securities and Exchange Commission nor any U.S. state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per ADS	Per Pre-funded Warrant	Total
Public offering price	US$13.50000	US$13.49999	US$128,249,991
Underwriting discounts and commissions	US$ 0.94500	US$ 0.94500	US$ 8,977,499
Proceeds, before expenses, to Opthea Limited[1]	US$12.55500	US$12.55499	US$119,272,491

(1) We have agreed to reimburse the underwriters for certain expenses. See "Underwriting."

The underwriters expect to deliver the ADSs and the pre-funded warrants to purchasers on or about October 20, 2020.

Joint Book-Running Managers

Citigroup **SVB Leerink**

Lead Managers

Oppenheimer & Co. **Truist Securities**

October 16, 2020.

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We are responsible for the information contained in this prospectus and any free writing prospectus we prepare or authorize. We and the underwriters have not authorized anyone to provide you with different information. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information others may give you. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in this prospectus is accurate as of any date other than its date.

For investors outside the United States: neither we nor any of the underwriters have done anything that would permit this offering or possession or distribution of this prospectus or any free writing prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus or any free writing prospectus must inform themselves about, and observe any restrictions relating to, the offering of the ADSs and the distribution of this prospectus and any free writing prospectus outside the United States.

We are incorporated under the laws of Australia, and a majority of our outstanding ordinary shares are owned by non-U.S. residents. Under the rules of the U.S. Securities and Exchange Commission, or the SEC, we are eligible for treatment as a "foreign private issuer." As a foreign private issuer, we will not be required to file periodic reports and financial statements with the SEC as frequently or as promptly as domestic registrants whose securities are registered under the Securities Exchange Act of 1934, as amended, or the Exchange Act.

Our reporting and functional currency is the Australian dollar, and our financial statements included elsewhere in this prospectus are presented in Australian dollars. The consolidated financial statements and related notes included elsewhere in this prospectus have been prepared under the International Financial Reporting Standards, or IFRS, as issued by the International Accounting Standards Board, or IASB, which differs in certain significant respects from U.S. Generally Accepted Accounting Principles, or GAAP.

All references in this prospectus to "US$," "U.S. dollars," and "dollars" mean U.S. dollars and all references to "A$" mean Australian dollars, unless otherwise noted. Throughout this prospectus, all references to "ADSs" mean American depositary shares, each of which represents eight of our ordinary shares, no par value, and all references to "ADRs" mean the American depositary receipts that evidence the ADSs.

This prospectus contains translations of some Australian dollar amounts into U.S. dollars. Except as otherwise stated in this prospectus, all translations from Australian dollars to U.S. dollars are based on the rate published by the Reserve Bank of Australia as of October 16, 2020. No representation is made that the Australian dollar amounts referred to in this prospectus could have been or could be converted into U.S. dollars at such rate.

"Opthea," the Opthea logo and other trademarks or service marks of Opthea appearing in this prospectus are the property of Opthea or its subsidiary. Solely for convenience, the trademarks, service marks and trade names referred to in this prospectus are listed without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their right thereto. All other trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our securities. You should read this entire prospectus, and the registration statement of which this prospectus is a part, including "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations," and our consolidated financial statements and the related notes included elsewhere in this prospectus, before making an investment decision. Unless otherwise indicated or the context otherwise requires, "Opthea," the "Company," "our company," "we," "us" and "our" refer to Opthea Limited and its consolidated subsidiary, taken as a whole.

Overview

We are a clinical stage biopharmaceutical company developing a novel therapy for the treatment of highly prevalent and progressive retinal diseases. We are developing our Phase 3-ready product candidate, OPT-302, a biologic designed to inhibit VEGF-C and VEGF-D, to complement VEGF-A inhibitors for the treatment of ophthalmic diseases. Anti-VEGF-A therapies represent the standard of care for wet age-related macular degeneration, or AMD, and other retinal diseases; however, there remains a significant unmet medical need as many patients do not adequately respond to these treatments. As the only biologic inhibitor of VEGF-C and VEGF-D in clinical development, OPT-302 differs from standard of care therapies and when administered in combination with a VEGF-A inhibitor, is designed to achieve broader inhibition of the vascular endothelial growth factor, or VEGF, family and target a mechanism of clinical resistance to improve visual acuity. Our lead indication for OPT-302 combination therapy is wet AMD, a chronic, progressive disease and the leading cause of vision loss for individuals over the age of 50. In a 366-patient Phase 2b clinical trial for the treatment of wet AMD, 2.0 mg OPT-302, in combination with a standard of care anti-VEGF-A therapy, ranibizumab (Lucentis), met the primary endpoint of a statistically significant superior mean gain in visual acuity over ranibizumab monotherapy at week 24. We intend to initiate two pivotal Phase 3 clinical trials in treatment-naive patients with wet AMD to evaluate the efficacy and safety of OPT-302 in combination with anti-VEGF-A therapies compared to anti-VEGF-A monotherapy in the first half of 2021. We expect to report topline data from these Phase 3 clinical trials in 2023. In addition to our clinical trials in wet AMD, we have observed evidence of improved clinical outcomes in a Phase 1b/2a clinical trial of OPT-302 in combination with another standard of care anti-VEGF-A therapy, aflibercept (Eylea), in patients with treatment-refractory diabetic macular edema, or DME. We retain worldwide rights to develop and commercialize OPT-302 for the treatment of wet AMD and DME and believe that the novel treatment mechanism of OPT-302 has the potential to provide therapeutic benefit for other progressive eye diseases.

Wet AMD is a rapidly progressing disease with loss of central vision developing over a period of weeks to months in which abnormal new blood vessels form in the back of the eye in a process called choroidal neovascularization. These newly formed vessels are highly permeable, leaking exudate leading to fluid accumulation and retinal lesion formation. This, in turn, adversely affects sensory cells in the retina and if left untreated, results in rapid loss of visual acuity.

Wet AMD affects approximately one million people in the United States and 2.5 million people in Europe. The standard of care for wet AMD and other ocular neovascular diseases is the administration of monotherapies that primarily inhibit VEGF-A. These therapeutic agents, which include ranibizumab and aflibercept, prevent VEGF-A molecules from binding to, and activating, VEGF receptors and thereby inhibit the formation and permeability of blood vessels. As the risk of developing wet AMD increases with age, it is predicted that the overall aging of the population will result in a significant increase in the number of wet AMD cases, both in the United States and worldwide. Many wet AMD patients also experience suboptimal clinical responses despite

receiving one or both of the leading standard of care treatments, ranibizumab and aflibercept, which had combined annual worldwide sales of over US$11.9 billion in 2019. In addition, nearly half of wet AMD patients are treated with off-label bevacizumab as a lower cost alternative anti-VEGF-A therapy. As a result, we believe there is a significant and expanding market opportunity for novel therapies that can improve vision in patients with wet AMD, which has the potential to lead to sales greater than the combined annual sales of ranibizumab and aflibercept.

OPT-302 is designed to address a deficiency in the treatment paradigm for wet AMD and other retinal diseases, such as DME, by targeting alternate members of the VEGF family, namely VEGF-C and VEGF-D, which are not targeted by current standard of care therapies. VEGF-C and VEGF-D function in parallel with VEGF-A to drive neovascularization and vascular leakage, which are key hallmarks of both wet AMD and DME. In addition, treatment with VEGF-A inhibitors leads to upregulation of VEGF-C and VEGF-D to compensate for VEGF-A inhibition, which may represent an important mechanism of clinical resistance to anti-VEGF-A monotherapy. We are developing OPT-302 to be used in combination with standard of care anti-VEGF-A monotherapies to achieve broader inhibition of the VEGF family, with the goal of improving overall efficacy and demonstrating superior vision gains over that which can be achieved by inhibiting VEGF-A alone.

In our completed Phase 2b wet AMD clinical trial, 2.0 mg OPT-302 in combination with ranibizumab met the primary endpoint of a statistically significant superior mean gain in visual acuity at week 24 compared to patients treated with ranibizumab with a sham injection, which we refer to as ranibizumab monotherapy. The trial was an international, multi-center, double-masked trial in 366 treatment-naive patients with wet AMD. Patients were randomized into three groups and received intravitreal injections every four weeks of either 0.5 mg or 2.0 mg OPT-302 in combination with 0.5 mg ranibizumab or 0.5 mg ranibizumab monotherapy. Secondary endpoints in the trial included changes in retinal thickness and change in intraretinal and subretinal fluid. Results from such measures were generally consistent with the visual acuity gains observed in the trial. Our clinical experience to date, which includes administration of over 1,800 doses of OPT-302 to 399 patients with retinal disease for treatment periods of up to 24 weeks, indicates that OPT-302 intravitreal injections are well tolerated, with the incidence of treatment-emergent adverse events, or TEAEs, comparable to anti-VEGF-A monotherapy in our clinical trials. In the Phase 2b wet AMD clinical trial, OPT-302 was well tolerated with a very low incidence of ocular inflammation and no safety issues identified with addition of OPT-302 to ranibizumab intravitreal therapy. The incidence of ocular TEAEs was similar in OPT-302 combination groups compared to the ranibizumab monotherapy group. Three patients treated with OPT-302 combination therapy had potentially treatment-related serious adverse events, or SAEs: one case each of vitritis, endophthalmitis and myocardial infarction.

We are planning to initiate two concurrent pivotal Phase 3 clinical trials for the treatment of wet AMD. These double-masked, sham-controlled Phase 3 clinical trials will enroll treatment-naive patients and assess the efficacy and safety of 2.0 mg of OPT-302 in combination with ranibizumab (Lucentis) (referred to as the ShORe trial) or aflibercept (Eylea) (referred to as the COAST trial), compared to ranibizumab or aflibercept monotherapy in each respective trial. In addition, to understand the durability of OPT-302 treatment effect with less frequent dosing, each trial will compare the clinical efficacy of OPT-302 administered in combination with the applicable VEGF-A inhibitor on an every four-week and every eight-week dosing regimen. For consistency, the ShORe and COAST Phase 3 trials build upon and maintain key features of our Phase 2b clinical trial of OPT-302 combination therapy for the treatment of wet AMD, while evaluating the administration of OPT-302 combination therapy over a longer treatment period and in a greater number of patients. We expect to initiate the trials in the first half of 2021 and to report topline data in 2023. If the results at the completion of the primary efficacy phase at week 52 of the Phase 3 clinical trials are favorable, we intend to file for marketing approval for OPT-302 for the treatment of wet AMD in the United States, European Union and other territories.

In addition to our planned pivotal Phase 3 clinical trials, we plan to develop a co-formulation of OPT-302 with an approved and/or biosimilar anti-VEGF-A therapy designed to achieve VEGF-A, VEGF-C and VEGF-D inhibition following the administration of a single intravitreal injection of the co-formulated product. OPT-302 is

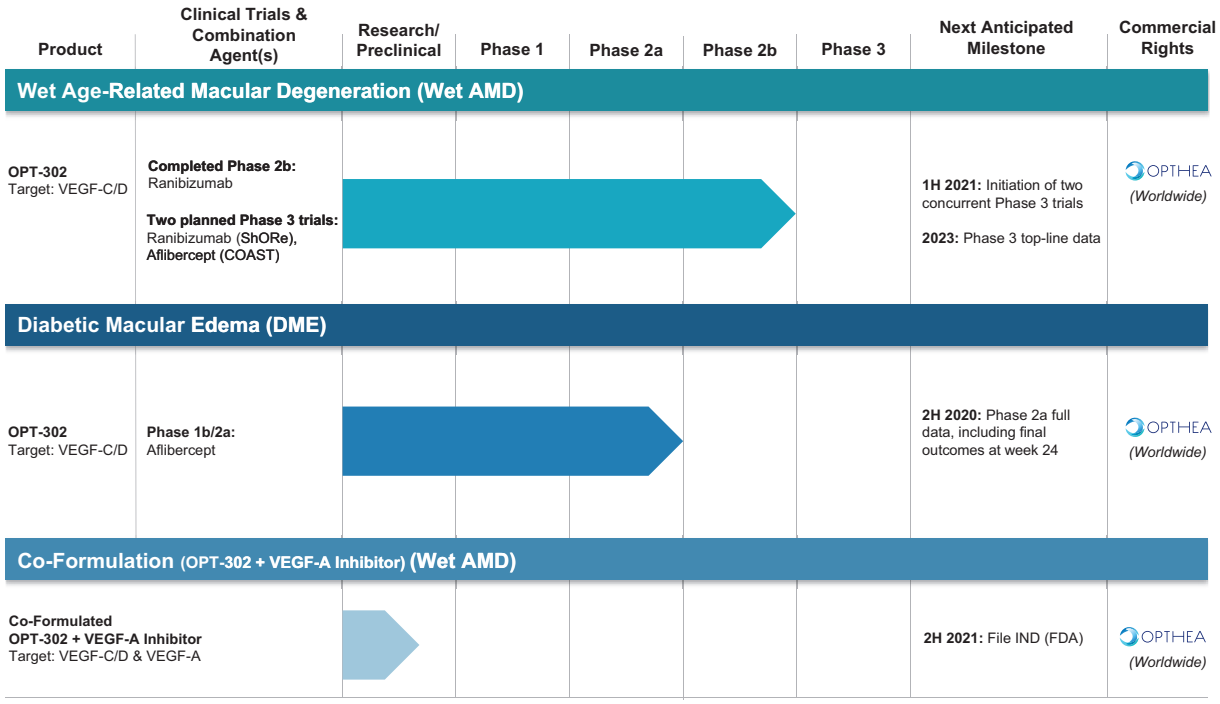
currently administered as a combination therapy consisting of a sequential injection of OPT-302 following intravitreal administration of a VEGF-A inhibitor. We believe that a co-formulated OPT-302 and VEGF-A inhibitor product could provide flexibility of treatment options for physicians and reduce the frequency and number of injections for patients. We expect to file an investigative new drug application, or IND, for the co-formulated product in the second half of 2021 and subsequently investigate the co-formulated product in a Phase 1 clinical trial for the treatment of wet AMD.

We are also investigating the therapeutic potential of OPT-302 for DME. DME is a progressive eye disease and a complication of diabetic retinopathy, or DR, a condition caused by chronically elevated glucose levels in diabetics that damages the retina. DME can cause blurred vision, severe vision loss and blindness. Wet AMD and DME share a similar underlying pathophysiology, including retinal neovascularization and increased vascular permeability, and as a result, VEGF-A inhibitors are also considered the standard of care treatment for DME. Based on its mechanism of action and clinical results to date, we believe that OPT-302 also has the potential to deliver therapeutic benefit in DME patients. In our Phase 1b/2a clinical trial of OPT-302 in combination with aflibercept in patients with treatment-refractory DME, we observed evidence of improved clinical outcomes following OPT-302 combination therapy in this indication, as OPT-302 combination therapy met the primary efficacy endpoint based on the proportion of patients achieving a ≥5 letter gain in visual acuity at week 12 compared to baseline. OPT-302 combination therapy was also well tolerated in this trial. The most common TEAEs were mainly related to the intravitreal injection procedure, and TEAEs did not lead to discontinuation of the trial for any patient. There was only one potentially treatment-related SAE of cerebrovascular accident, or stroke, resulting in one patient discontinuing treatment and withdrawing from the trial.

We also believe that our novel treatment mechanism has the potential to provide therapeutic benefit for other progressive retinal diseases beyond wet AMD and DME. We may further investigate the efficacy of OPT-302 to improve clinical outcomes in patients with polypoidal choroidal vasculopathy, a form of wet AMD that is highly prevalent in Asian populations and less responsive to anti-VEGF-A therapy than other wet AMD subtypes. Beyond wet AMD and DME, we may explore applications of OPT-302 in other retinal diseases in which a VEGF-C or VEGF-D inhibitor could have therapeutic potential, such as retinal vein occlusion.

Our Pipeline

The following table summarizes the stage of clinical development and status of our product candidate, OPT-302.



Our Strategy

Our goal is to become a leader in developing and commercializing therapeutics for the treatment of retinal diseases. The key elements of our strategy are to:

- Advance OPT-302 through two concurrent Phase 3 trials for the treatment of wet AMD.
- Optimize OPT-302 administration and develop a co-formulation to reduce injection burden for patients and provide treatment flexibility.
- Expand clinical development of OPT-302 in wet AMD, DME and other retinal diseases.
- Maximize the commercial potential of OPT-302 through commercialization independently and opportunistic collaborations with third parties.

Certain Preliminary Financial Information

As of September 30, 2020, we had estimated cash and cash equivalents of approximately A$54.1 million (or approximately US$38.5 million, based on the Australian dollar/U.S. dollar exchange rate of A$1.4068 to US$1.00 as of September 30, 2020). This estimate of our cash and cash equivalents is preliminary and subject to completion, including the completion of customary financial statement closing and review procedures for the three months ended September 30, 2020. As a result, the unaudited preliminary cash and cash equivalents set forth above reflects our preliminary estimate with respect to such information, based on information currently available to management, and may vary from our actual financial position as of September 30, 2020. Further, this

preliminary estimate is not a comprehensive statement or estimate of our financial results or financial condition as of and for the three months ended September 30, 2020. The unaudited preliminary cash and cash equivalents included herein has been prepared by, and is the responsibility of, management. Deloitte Touche Tohmatsu, our independent registered public accounting firm, has not audited, reviewed, compiled or performed any procedures with respect to the unaudited preliminary cash and cash equivalents set forth above. Accordingly, Deloitte Touche Tohmatsu does not express an opinion or any other form of assurance with respect thereto and assumes no responsibility for, and disclaims any association with, the unaudited preliminary cash and cash equivalents set forth above. This estimate should not be viewed as a substitute for financial statements prepared in accordance with IFRS and is not necessarily indicative of the results to be achieved in any future period. Accordingly, you should not place undue reliance on this preliminary estimate.

Risks Associated with Our Business

Our business is subject to numerous risks and uncertainties, including those described in "Risk Factors" and elsewhere in this prospectus. You should carefully consider these risks before making an investment. These risks include, among others, the following:

- We are a clinical stage biopharmaceutical company with no products approved for commercial sale. We have incurred net losses since our inception, we expect to incur significant losses and increasing operating losses for the foreseeable future, and we may never be profitable.
- We currently have no source of product revenue and may never become profitable.
- We will require substantial additional capital to finance our operations, which may not be available to us on acceptable terms, or at all. As a result, we may not complete the development and commercialization of OPT-302 or develop new product candidates.
- Our business substantially depends on the success of OPT-302, our only product candidate under clinical development, which has not completed a pivotal Phase 3 clinical trial. If we are unable to obtain regulatory approval for and successfully commercialize OPT-302 or any future product candidates, or we experience significant delays in doing so, our business will be harmed.
- Clinical drug development involves a lengthy and expensive process with uncertain timelines and uncertain outcomes. Our clinical trials may fail to adequately demonstrate the safety and efficacy of OPT-302 or any future product candidates.
- If we experience delays in clinical testing, our commercial prospects will be harmed, our costs may increase and our business may be harmed.
- If we encounter difficulties in enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise negatively affected.
- OPT-302 and any future product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval or limit the commercial profile of an approved label.
- Even if we complete the necessary Phase 3 pivotal clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us or any future collaboration partners from obtaining approvals for the commercialization of OPT-302 for the treatment of wet AMD or any other indication as well as for any other product candidate we develop.
- OPT-302 and any future product candidates may not achieve adequate market acceptance among physicians, patients, healthcare payors and others in the medical community necessary for commercial success.
- Lack of efficacy, adverse events or undesirable side effects may emerge in clinical trials conducted by third parties with product candidates for wet AMD or DME, which could negatively affect our stock price, our ability to attract additional capital and our development program.

- The results of completed clinical trials may not be predictive of future results. Data from our clinical trials to date may not be indicative of results obtained when these trials are completed or in later stage trials.
- Interim, topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.
- We may face substantial competition, which may result in others discovering, developing or commercializing competing products before or more successfully than us.
- Our business could be negatively affected by the effects of health epidemics, including the evolving effects of the COVID-19 pandemic, in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of clinical trial sites or other business operations.
- We have relied on, and expect to continue to rely on, third-party manufacturers to produce OPT-302 or any future product candidates.
- Our success depends upon our ability to obtain and maintain intellectual property protection for our products and technologies.
- There has been no prior market for the ADSs and an active and liquid market for our securities may fail to develop, which could harm the market price of the ADSs.
- If we fail to implement and maintain an effective system of internal controls to remediate our material weaknesses over financial reporting, we may be unable to accurately report our results of operations, meet our reporting obligations or prevent fraud, and investor confidence in our company and the market price of the ADSs may be negatively impacted.

If we are unable to adequately address these and other risks we face, our business may be harmed.

Corporate Information

We were incorporated under the laws of Australia in 1984 under the name Circadian Technologies Limited. In 1985, we completed an initial public offering of our ordinary shares and the listing of our ordinary shares on the Australian Securities Exchange, or the ASX. In December 2015, we changed the name of our company to Opthea Limited. Our headquarters and registered offices are located at Suite 0403, Level 4, 650 Chapel Street, South Yarra, VIC 3141, Australia. Our telephone number is +61 3 9826 0399. Our agent for service of process in the United States is Corporation Service Company, located at 1180 Avenue of the Americas, Suite 210, New York, NY 10036. Our website address is www.opthea.com. The reference to our website is an inactive textual reference only and information contained in, or that can be assessed through, our website is not part of this prospectus.

Implications of Being an Emerging Growth Company

As a company with less than $1.07 billion in revenue during our last fiscal year, we qualify as an "emerging growth company" as defined in the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- exemption from the auditor attestation requirement of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, in the assessment of our internal controls over financial reporting; and
- to the extent that we no longer qualify as a foreign private issuer, (i) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and (ii) exemptions from

the requirements of holding a non-binding advisory vote on executive compensation, including golden parachute compensation.

We may take advantage of these exemptions until such time that we are no longer an emerging growth company. Accordingly, the information that we provide shareholders and holders of the ADSs may be different than you might obtain from other public companies. We will cease to be an emerging growth company upon the earliest to occur of (i) the last day of the fiscal year in which we have more than $1.07 billion in annual revenue; (ii) the last day of the fiscal year in which we qualify as a "large accelerated filer"; (iii) the date on which we have, during the previous three-year period, issued more than $1.0 billion in non-convertible debt securities; and (iv) the last day of the fiscal year in which the fifth anniversary of this offering occurs.

In addition, Section 107 of the JOBS Act provides that an emerging growth company can use the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Given that we currently report and expect to continue to report under IFRS, as issued by the IASB, we have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required by the IASB.

Implications of Being a Foreign Private Issuer

We are also considered a "foreign private issuer" under U.S. securities laws. In our capacity as a foreign private issuer, we are exempt from certain rules under the Exchange Act that impose certain disclosure obligations and procedural requirements for proxy solicitations under Section 14 of the Exchange Act. In addition, our senior management, the members of our board of directors and our principal shareholders are exempt from the reporting and "short-swing" profit recovery provisions of Section 16 of the Exchange Act and the rules under the Exchange Act with respect to their purchases and sales of our securities. Moreover, we are not required to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. companies whose securities are registered under the Exchange Act. In addition, we are not required to comply with Regulation FD, which restricts the selective disclosure of material information.

We may take advantage of these exemptions until such time as we are no longer a foreign private issuer. We will remain a foreign private issuer until such time that 50% or more of our outstanding voting securities are held by U.S. residents and any of the following three circumstances applies: (i) the majority of the members of board of directors or our senior management are U.S. citizens or residents; (ii) more than 50% of our assets are located in the United States; or (iii) our business is administered principally in the United States.

We have taken advantage of certain reduced reporting and other requirements in this prospectus. Accordingly, the information contained herein may be different from the information you receive from other public companies.

THE OFFERING

ADSs offered by us	8,563,300 ADSs.
Pre-funded warrants offered by us	We are also offering to a certain purchaser pre-funded warrants to purchase 936,700 ADSs in lieu of ADSs. Each pre-funded warrant will be exercisable for one ADS. The purchase price of each pre-funded warrant will be equal to the price at which an ADS is being sold to the public in this offering, minus US$0.00001, and the exercise price of each pre-funded warrant will be US$0.00001 per ADS. The pre-funded warrants will be exercisable immediately and may be exercised at any time until all of the pre-funded warrants are exercised in full, subject to certain conditions under Australian law set forth under "Description of pre-funded warrants." This offering also relates to the ADSs (and ordinary shares underlying the ADSs) issuable upon exercise of any pre-funded warrants sold in this offering.
Option to purchase additional ADSs	The underwriters have an option for a period of 30 days from the date of this prospectus to purchase up to 1,425,000 additional ADSs.
Ordinary shares to be outstanding after this offering, including shares underlying ADSs	337,664,169 shares (or 349,064,169 shares if the underwriters exercise their option to purchase 1,425,000 additional ADSs in full), in each case assuming no exercise of any pre-funded warrants offered and sold by us.
American depositary shares	Each ADS represents eight ordinary shares, no par value. The ADSs are issued by the depositary. You will have the rights of an ADS holder as provided in the deposit agreement among us, the depositary and all owners and holders of ADSs issued thereunder. The depositary, through its custodian, will be the holder of the ordinary shares underlying the ADSs. You may surrender your ADSs to the depositary for cancellation to receive the ordinary shares underlying your ADSs. The depositary will charge you a fee for such a cancellation. We may amend or terminate the deposit agreement for any reason without your consent. Any amendment that imposes or increases fees or charges or which materially prejudices any substantial existing right you have as an ADS holder will not become effective as to outstanding ADSs until 30 days after notice of the amendment is given to ADS holders. If an amendment becomes effective, you will be bound by the deposit agreement as amended if you continue to hold your ADSs. To better understand the terms of the ADSs, you should carefully read the section titled "Description of American Depositary Shares." We also encourage you to read the deposit agreement, which is filed as an exhibit to the registration statement of which this prospectus forms a part.

Depositary	The Bank of New York Mellon.
Use of proceeds	We estimate that the net proceeds from the sale of the ADSs and pre-funded warrants that we are selling in this offering will be approximately US$116.4 million (or approximately US$134.3 million if the underwriters' option to purchase additional ADSs is exercised in full), based upon an initial public offering price of US$13.50 per ADS and US$13.49999 per pre-funded warrant, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering, together with our existing cash and cash equivalents, to advance the clinical development of OPT-302 for the treatment of wet AMD, including the initiation of and reporting of topline data from two pivotal Phase 3 clinical trials, to advance the development of, and non-clinical studies for, a co-formulation of OPT-302 with an approved and/or biosimilar anti-VEGF-A therapy, and to fund other research and development activities for OPT-302 in potential additional indications, including DME, and for working capital and other general corporate purposes. See "Use of Proceeds" for additional information.
Risk factors	See "Risk Factors" and the other information included in this prospectus for a discussion of the risks you should carefully consider before investing in our securities.
Nasdaq Global Select Market symbol for the ADSs	"OPT". We do not intend to list the pre-funded warrants on any securities exchange or nationally recognized trading system.
Australian Securities Exchange symbol for our ordinary shares	"OPT"

The number of ordinary shares (including ordinary shares underlying ADSs) that will be outstanding after this offering is based on 269,157,769 ordinary shares outstanding as of June 30, 2020, and excludes:

- 18,044,000 ordinary shares issuable upon the exercise of outstanding options as of June 30, 2020 with a weighted-average exercise price of A$0.68 per ordinary share under our equity incentive plans;
- 4,000,000 ordinary shares issuable upon the exercise of outstanding options granted under our non-executive director share and option plan to certain of our non-employee directors subsequent to June 30, 2020, of which an option to purchase 2,000,000 ordinary shares has an exercise price of A$2.99 per ordinary share and an option to purchase 2,000,000 ordinary shares has an exercise price of A$4.49 per ordinary share;
- 3,000,000 ordinary shares issuable upon the exercise of an option to be granted to one of our non-employee directors upon approval by our shareholders at a future meeting of shareholders following the closing of this offering (see "Management—Remuneration of Non-Employee Directors"); and
- 12,446,777 ordinary shares reserved for future issuance under our Long Term Incentive Plan.

In addition, unless we specifically state otherwise, all information in this prospectus assumes (i) no exercise by the underwriters of their option to purchase up to 1,425,000 additional ADSs, (ii) no exercise of outstanding options to purchase ordinary shares and (iii) no exercise of any pre-funded warrants offered and sold by us.

SUMMARY CONSOLIDATED FINANCIAL DATA

The following tables summarize our consolidated financial and other data. The summary consolidated statement of profit or loss and other comprehensive income data for the years ended June 30, 2019 and 2020 have been derived from our audited consolidated financial statements included elsewhere in this prospectus. Our audited consolidated financial statements have been prepared in accordance with IFRS, as issued by the IASB, as of and for the years ended June 30, 2019 and 2020.

You should read the consolidated financial and other data set forth below in conjunction with our consolidated financial statements and the accompanying notes, the information in "Selected Consolidated Financial and Other Data" and the information in "Management's Discussion and Analysis of Financial Condition and Results of Operations" contained elsewhere in this prospectus.

Consolidated Statement of Profit or Loss and Other Comprehensive Income Data

	Year Ended June 30,	
	2019	2020
	(in thousands, except per share data)	
Revenue	A$ 159	A$ 87
Other income[1]	837	784
Research and development expenses	(31,348)	(17,954)
Patent expenses	(161)	(429)
Intellectual property costs	(113)	(114)
Administrative expenses	(5,175)	(7,001)
Occupancy expenses	(109)	(34)
Net foreign exchange gain (loss)	363	(401)
Loss before income tax	(35,547)	(25,062)
Income tax benefit	14,637	8,533
Loss for the year	(20,910)	(16,529)
Other comprehensive income:		
Items that will not be reclassified subsequently to profit or loss:		
Fair value gains on investments in financial assets	260	59
Other comprehensive income for the period, net of tax	260	59
Total comprehensive loss for the year	A$(20,650)	A$(16,470)
Total comprehensive loss for the year is attributable to:		
Owners of the Company	(20,650)	(16,470)
	A$(20,650)	A$(16,470)
Loss per share attributable to Owners of the Company – basic and diluted (in cents)	A$ (8.98)	A$ (6.34)

(1) Other income primarily comprises finance income from interest on bank deposits, funding under a one-time Australian government grant from the Commonwealth Scientific and Industrial Research Organization during the year ended June 30, 2019, and funding under a one-time government grant from the Australian Tax Office during the year ended June 30, 2020.

Consolidated Statement of Financial Position Data

	As of June 30, 2020	
	Actual	As Adjusted[1]
	(in thousands)	
Cash and cash equivalents	A$ 62,020	A$ 226,501
Working capital[2]	64,398	228,879
Total assets	71,887	236,368
Total liabilities	7,079	7,079
Accumulated losses	(102,589)	(102,589)
Total equity	64,808	229,289

(1) The as adjusted statement of financial position data give effect to our receipt of net proceeds from the issuance and sale of 8,563,300 ADSs and pre-funded warrants to purchase 936,700 ADSs at the initial offering price of US$13.50 per ADS and US$13.49999 per pre-funded warrant, after deducting underwriting commissions and estimated offering expenses payable by us.

(2) Working capital is defined as current assets less current liabilities.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should consider and read carefully all of the risks and uncertainties described below, as well as other information included in this prospectus, including our consolidated financial statements and related notes included elsewhere in this prospectus, before making an investment decision. If any of the following risks actually occur, it could harm our business, prospects, results of operations and financial condition. In such event, the trading price of the ADSs could decline and you might lose all or part of your investment.

Risks Related to Our Financial Position and Need for Capital

We are a clinical stage biopharmaceutical company with no products approved for commercial sale. We have incurred net losses since our inception, we expect to incur significant losses and increasing operating losses for the foreseeable future, and we may never be profitable.

We are a clinical stage biopharmaceutical company with no products approved for commercial sale. To date, our operations have been limited to organizing and staffing our company, business planning, raising capital, developing our product candidate, OPT-302, and licensing certain related technology, conducting research and development activities, including preclinical studies and clinical trials, and providing general and administrative support for these operations. Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect and/or an acceptable safety profile, gain regulatory approval and become commercially viable. We have not generated any revenue from product sales to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. We are not profitable and have incurred net losses since our inception. Our total comprehensive losses were $20.7 million and $16.5 million for the years ended June 30, 2019 and 2020. As of June 30, 2020, we had an accumulated loss of $102.6 million. We have spent, and expect to continue to spend, significant resources to fund research and development of, and seek regulatory approvals for, OPT-302 and any future product candidates. We expect to incur substantial and increasing operating losses over the next several years as our research, development, manufacturing and clinical trial activities increase. Additionally, if OPT-302 is approved for commercial sale, our commercialization expenses will increase significantly as we establish sales, marketing, distribution, manufacturing, supply chain and other commercial infrastructure. As a result, our accumulated losses will also increase significantly. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may negatively affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have a negative impact on our total (deficit) equity and working capital. The net losses we incur may fluctuate significantly from quarter-to-quarter such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. Even if we eventually generate product revenue, we may never be profitable and, if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

We currently have no source of product revenue and may never become profitable.

OPT-302 has not been approved for commercial sale, and we expect it to be several years before OPT-302 is approved, if ever, and we are able to commence sales of OPT-302. To date, we have not generated any revenue from the licensing or commercialization of OPT-302 and do not expect to receive revenue from it for a number of years, if ever. We will not be able to generate product revenue unless and until OPT-302 or any future product candidate, alone or with future partners, successfully completes clinical trials, receives regulatory approval and is successfully commercialized. Although we may seek to obtain revenue from collaboration or licensing agreements with third parties, we currently have no such agreements that could provide us with material, ongoing future revenue and we may never enter into any such agreements. Our ability to generate future product revenue

from OPT-302 or any future product candidates also depends on a number of additional factors, including our or our future partners' ability to:

- successfully complete research and clinical development of OPT-302 and any future product candidates and obtain regulatory approvals for commercialization;
- maintain supply and manufacturing relationships with third parties, and ensure adequate and legally compliant manufacturing of bulk drug substances and drug products to maintain that supply, including any scale up of manufacturing processes for OPT-302 to support our planned Phase 3 clinical program of OPT-302 in combination with anti-vascular endothelial growth factor-A, or anti-VEGF-A, therapy for the treatment of wet age-related macular degeneration, or AMD;
- launch and commercialize future product candidates for which we obtain marketing approval, if any, and, if launched independently, successfully establish a sales force, marketing and distribution infrastructure;
- demonstrate the necessary safety data post-approval to ensure continued regulatory approval;
- obtain coverage and adequate product reimbursement from third-party payors, including government payors;
- achieve market acceptance for our or our future partners' products, if any;
- establish, maintain, protect and enforce our intellectual property rights; and
- attract, hire and retain qualified personnel.

In addition, because of the numerous risks and uncertainties associated with biologic product development, including that OPT-302 may not advance through development, achieve the endpoints of applicable clinical trials or receive approval for use in combination with one or more approved therapies, we are unable to predict the timing or amount of increased expenses, or if or when we will achieve or maintain profitability. In addition, our expenses could increase beyond expectations if we decide, or are required by the U.S. Food and Drug Administration, or the FDA, or comparable non-U.S. regulatory authorities, including the European Medicines Agency, or the EMA, to perform studies or trials in addition to those that we currently anticipate. Even if we complete the development and regulatory processes described above, we anticipate incurring significant costs associated with launching and commercializing these products.

Even if we generate revenue from the sale of any of our product candidates that may be approved, we may not become profitable and may need to obtain additional funding to continue operations. If we fail to become profitable or do not sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce our operations.

We will require substantial additional capital to finance our operations, which may not be available to us on acceptable terms, or at all. As a result, we may not complete the development and commercialization of OPT-302 or develop new product candidates.

As a clinical-stage biopharmaceutical company, our operations have consumed significant amounts of cash since our inception. We expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we prepare to initiate our planned Phase 3 clinical trials of OPT-302 in combination with anti-VEGF-A therapy for the treatment of wet AMD and continue clinical development of OPT-302 in combination with aflibercept for the treatment of persistent diabetic macular edema, or DME, and other retinal diseases. Even if we are able to obtain regulatory approval for OPT-302 and any future product candidates that we may develop, we will require substantial additional capital to commercialize such product candidates.

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will fund our projected operating requirements until the third calendar quarter of 2023. Our forecast of the period

of time through which our financial resources will adequately support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed elsewhere in this "Risk Factors" section. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Our future funding requirements, both short and long-term, will depend on many factors, including:

- the initiation, progress, timing, costs and results of clinical trials for OPT-302 and any future product candidates we may develop, including whether the FDA or comparable non-U.S. regulatory authorities require additional clinical trials beyond our proposed Phase 3 clinical trials of OPT-302 in combination with anti-VEGF-A therapy for the treatment of wet AMD to support an approved label of OPT-302 in combination with multiple existing anti-VEGF-A therapies;
- the initiation, progress, timing, costs and results of additional clinical trials and studies to evaluate the potential for co-formulation of OPT-302 with approved and/or biosimilar forms of VEGF-A inhibitors to provide flexibility of treatment options for physicians and to reduce the frequency and number of injections for patients;
- the outcome, timing and cost of seeking and obtaining regulatory approvals from the FDA and comparable non-U.S. regulatory authorities;
- if approved, the costs of commercialization activities for OPT-302, or any other product candidate that receives regulatory approval;
- the cost to establish, maintain, expand, enforce and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, preparing, filing, prosecuting, defending and enforcing of any patents or other intellectual property rights;
- our headcount growth and associated costs as we expand our research and development capabilities and establish a commercial infrastructure;
- market acceptance of any approved product candidates, including product pricing and adequate reimbursement by third-party payors;
- the cost of acquiring, licensing or investing in additional businesses, products, product candidates and technologies;
- the cost of establishing sales, marketing and distribution capabilities for OPT-302 and any future product candidates for which we may receive regulatory approval and that we determine to commercialize ourselves or in collaboration with our future partners; and
- the costs of operating as a public company with securities listed in both Australia and the United States.

We will require additional capital to develop, obtain regulatory approval for and commercialize OPT-302 and any future product candidates. In particular, we will require additional capital to progress our ongoing and future planned clinical trials without delays, including payments in connection with the achievement of certain regulatory milestones. We do not have any committed external source of funds. We expect to finance future cash needs through public or private equity or debt offerings or collaborations. We also intend to continue to apply for tax incentives under the Research and Development Tax Incentive scheme provided by the Australian government. See "—Risks Related to Development and Commercialization of Our Product Candidates—We have received tax credits under the Research and Development Tax Incentive scheme in Australia that may become repayable if we did not or do not comply with the rules of the scheme, or we may become ineligible for tax credits in our current or future tax years, which could harm our business, financial condition and results of operations." Additional capital may not be available in sufficient amounts or on reasonable terms, if at all. If we are not able to raise additional capital, we may not be able to expand our operations or otherwise capitalize on our business opportunities, and our business and financial condition will be negatively impacted.

Raising additional capital may cause dilution to holders purchasing ADSs in this offering, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Holders purchasing ADSs in this offering could suffer dilution or be negatively affected by fixed payment obligations we may incur if we raise additional funds through the issuance of additional equity securities or debt. Further, these securities may have rights senior to those of our ordinary shares and could contain covenants or protective rights that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could negatively impact our ability to conduct our business. If we need to secure additional financing, such additional fundraising efforts may divert our management and research efforts from our day-to-day activities, which may negatively affect our ability to develop and commercialize OPT-302 and any future product candidates.

To the extent we obtain additional funding through product collaborations, these arrangements would generally require us to relinquish rights to some of our technologies, product candidates or products, and we may not be able to enter into such agreements, on acceptable terms, if at all. If we are unable to obtain additional funding on a timely basis, we may be required to curtail or terminate some or all of our development programs or product candidates.

Risks Related to Development and Commercialization of Our Product Candidates

Our business substantially depends on the success of OPT-302, our only product candidate under clinical development, which has not completed a pivotal Phase 3 clinical trial. If we are unable to obtain regulatory approval for and successfully commercialize OPT-302 or any future product candidates, or we experience significant delays in doing so, our business will be harmed.

To date, the primary focus of our product development has been OPT-302 in combination with anti-VEGF-A therapy for the treatment of patients with wet AMD and DME. Currently, OPT-302 is our only product candidate under clinical development. This may make an investment in our company riskier than similar companies that have multiple product candidates in active development and that therefore may be able to better sustain a failure of a lead candidate. Successful continued development and ultimate regulatory approval of OPT-302 combination therapy for the treatment of wet AMD, DME or other indications is critical to the future success of our business. We have invested, and will continue to invest, a significant portion of our time and financial resources in the clinical development of OPT-302. If we cannot successfully develop, obtain regulatory approval for and commercialize OPT-302, we may not be able to continue our operations. The future regulatory and commercial success of OPT-302 is subject to a number of risks, including the following:

- we may not have sufficient financial and other resources to complete the necessary clinical trials for OPT-302, including, but not limited to, the pivotal clinical trials needed to obtain drug approval;
- we may not be able to obtain adequate evidence from clinical trials of efficacy and safety for OPT-302 combination therapy for the treatment of wet AMD, DME or other indications;
- in our clinical trials for OPT-302, we may need to adjust our clinical trial procedures and may need additional clinical trial sites, which could delay our clinical trial progress;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable non-U.S. regulatory authorities for marketing approval;
- the standards implemented by clinical or regulatory agencies may change at any time and we cannot be certain what regulatory agencies may require in pivotal clinical trials for the approval of OPT-302;
- the results of later stage clinical trials may not be as favorable as the results we have observed to date in our preclinical studies and early clinical trials;
- we cannot be certain of the number and type of clinical trials and non-clinical studies that the FDA or comparable non-U.S. regulatory agencies will require in order to approve OPT-302 combination therapy

for the treatment of wet AMD, DME or any other indication, including an approved label for use of OPT-302 in combination with multiple anti-VEGF-A therapies for the treatment of wet AMD;

- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- obtaining and maintaining third-party coverage and adequate reimbursement;
- maintaining a continued acceptable safety profile of our products following approval, including when used in combination with existing therapies;
- effectively competing with other therapies; and
- enforcing and defending intellectual property rights and claims.

Many of these risks are beyond our control, including the risks related to clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any future collaborator. Of the large number of drugs in development in the pharmaceutical industry, only a small percentage result in the submission of a new drug application or a biologics license application, or BLA, to the FDA and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market OPT-302, any such approval may be subject to limitations on the indicated uses or patient populations for which we may market the products. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, we may be unable to successfully develop or commercialize OPT-302. If we or any of our future development collaborators are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize OPT-302, we may not be able to generate sufficient revenue to continue our business.

Clinical drug development involves a lengthy and expensive process with uncertain timelines and uncertain outcomes. Our clinical trials may fail to adequately demonstrate the safety and efficacy of OPT-302 or any future product candidates.

OPT-302 and any future product candidates will be subject to rigorous and extensive clinical trials and extensive regulatory approval processes implemented by the FDA and comparable non-U.S. regulatory authorities before obtaining marketing approval from these regulatory authorities. The drug development and approval process is lengthy and expensive, and approval is never certain. Investigational new drugs, such as OPT-302, may not prove to be safe and effective in clinical trials. We have no direct experience as a company in conducting pivotal stage clinical trials required to obtain regulatory approval. We may be unable to conduct clinical trials at preferred sites, enlist clinical investigators, enroll sufficient numbers of participants or begin or successfully complete clinical trials in a timely fashion, if at all. In addition, the design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced.

The protocols for our planned Phase 3 clinical trials for OPT-302 in combination with anti-VEGF-A therapy are subject to review by the FDA and comparable non-U.S. regulatory authorities. The FDA is not obligated to comment on our protocols within any specified time period or at all or to affirmatively clear or approve our Phase 3 clinical program. We have submitted summaries of the protocols for our Phase 3 clinical trials to the FDA and comparable non-U.S. regulatory authorities, including the EMA. The FDA or other regulatory authorities may request additional information, require us to conduct additional non-clinical trials or require us to modify our proposed Phase 3 clinical program, including its endpoints, patient enrollment criteria or selection of anti-VEGF-A therapies, to receive clearance to initiate such program or to continue such program once initiated. In addition, the FDA or other regulatory authorities may disagree with all or a portion of our proposed trial protocols, including whether our Phase 3 clinical trial protocol is sufficient for approval of OPT-302 in

combination with two or more approved anti-VEGF-A therapies for the treatment of wet AMD. Any such limitations could reduce the market acceptance of OPT-302 and harm our business, financial condition and results of operations.

If we experience delays in clinical testing, our commercial prospects will be harmed, our costs may increase and our business may be harmed.

Conducting clinical studies for any product candidates in the United States requires filing an investigational new drug application, or IND, and reaching agreement with the FDA on clinical protocols, finding appropriate clinical sites and clinical investigators, securing approvals for such studies from the institutional review board at each such site, manufacturing clinical quantities of product candidates and supplying drug product to clinical sites. Currently, we have an active IND with the FDA in the United States for OPT-302. If any such future IND is not approved by the FDA, our clinical development timeline may be negatively impacted and any future clinical programs may be delayed or terminated.

We cannot guarantee that we will be able to successfully accomplish required regulatory activities or all of the other activities necessary to initiate and complete clinical trials. As a result, our clinical trials may be extended, delayed or terminated, and we may be unable to obtain regulatory approvals or successfully commercialize our products. We do not know whether any other clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Our product development costs will increase if we experience delays in clinical testing. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize OPT-302 and any future product candidates or allow our competitors to bring products to market before we do, which would impair our ability to successfully commercialize OPT-302 or any future product candidates and may harm our business, results of operations and prospects. Events that may result in a delay or unsuccessful completion of clinical development include:

- the unavailability of financial resources to commence and completed planned trials;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites;
- revisions to labeling, including adding limitations on approved uses or the additions of additional warnings, contraindications or other safety information including boxed warnings;
- ongoing discussions with the FDA or comparable non-U.S. regulatory authorities regarding the scope or design of our clinical trials, including our planned pivotal Phase 3 clinical trials of OPT-302 in combination with anti-VEGF-A therapy for the treatment of wet AMD;
- deviations from the trial protocol by clinical trial sites and investigators, or failures to conduct the trial in accordance with regulatory requirements;
- the need to repeat clinical trials as a result of inconclusive or negative results or poorly executed testing or changes in required endpoints by the FDA or comparable non-U.S. authorities;
- unfavorable FDA inspection and review of a clinical trial site or records of any clinical or preclinical investigation;
- the placement of a clinical hold on a clinical trial by the FDA or comparable non-U.S. authorities;
- delays in obtaining, or the inability to obtain, required approvals from institutional review boards or other governing entities at clinical sites selected for participation in our clinical trials;
- failure of third parties, such as CROs, to satisfy their contractual duties to us or meet expected deadlines;
- delays in the testing, validation, manufacturing and delivery of the product candidates to the clinical sites;
- insufficient supply or deficient quality of product candidate materials or other materials necessary to conduct our clinical trials, including of drugs to be used in the proposed combination therapy with our product candidates;

- delays in enrolling participants into our clinical trials;
- delays in patients completing a trial or returning for post-treatment follow-up;
- delays caused by patients dropping out of a trial due to side effects, disease progression or otherwise;
- serious and unexpected drug-related adverse effects experienced by participants in our clinical trials;
- implementation of new, or changes to, guidance or interpretations from the FDA or comparable non-U.S. authorities with respect to approval pathways for any product candidates we are pursuing; and
- changes in government regulations or administrative actions or lack of adequate funding to continue the clinical trials.

Our or our future collaborators' inability to timely complete clinical trials could result in additional costs to us as well as impair our ability to generate product revenue, continue development, commercialize OPT-302 and any future product candidates and receive royalties on product sales. In addition, if we make changes to a product candidate, we may need to conduct additional nonclinical studies or clinical trials to bridge or demonstrate the comparability of our modified product candidate to earlier versions, which could delay our clinical development plan or marketing approval for our current product candidate and any future product candidates.

If we encounter difficulties in enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise negatively affected.

The timely completion of clinical trials largely depends on patient enrollment. We may encounter delays in enrolling, or be unable to enroll, a sufficient number of patients to complete any of our clinical trials, and even once enrolled, we may be unable to retain a sufficient number of patients to complete any of our trials. Many factors affect patient enrollment, including:

- the size and nature of the patient population, which may be limited due to eligibility requirements;
- the number and location of clinical sites;
- competition with other companies for clinical sites or patients;
- the availability and amount of any patient stipend;
- the eligibility and exclusion criteria for the trial;
- the design of the clinical trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- inability to obtain and maintain patient consents;
- significant adverse events or other side effects observed, if any;
- risk that enrolled participants will drop out before completion; and
- competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies.

In addition, other companies are conducting clinical trials for the same indications and seek to enroll patients in their trials that may otherwise be eligible for our clinical studies or trials, which could lead to slow recruitment and delays in our clinical programs. Further, since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which could further reduce the number of patients who are available for our clinical trials in these sites.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. If we are unable to enroll a sufficient number

of patients that will complete clinical testing, we will be unable to seek or gain marketing approval for OPT-302 and any future product candidates and our business will be harmed. Even if we are able to enroll a sufficient number of patients in our clinical studies or trials, delays in patient enrollment may result in increased costs or may affect the timing or outcome of our clinical trials, which could prevent completion of these trials and negatively affect our ability to advance the development of OPT-302 and any future product candidates.

OPT-302 and any future product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval or limit the commercial profile of an approved label.

Undesirable side effects caused by OPT-302 combination therapy or any future product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable non-U.S. regulatory authorities. Additional clinical studies may be required to evaluate the safety profile of OPT-302 combination therapy or any future product candidates. We have no clinical safety data on patient exposure to OPT-302 administered in combination with an anti-VEGF-A therapy for longer than 24 weeks.

Future results of our trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics, including, for example, immunogenicity. In such an event, we could suspend or terminate our trials or the FDA or comparable non-U.S. regulatory authorities could order us to cease clinical trials or deny approval of OPT-302 in combination with anti-VEGF-A therapy or any future product candidates for any or all targeted indications. Drug-related side effects could affect patient recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. Any of these occurrences could materially and negatively affect our business, financial condition, results of operations and prospects. While OPT-302 has been well tolerated in our completed clinical trials, dosed patients have experienced certain adverse events, including potentially treatment-related serious adverse events, or SAEs, of myocardial infarction, endophthalmitis and vitritis in our Phase 2b clinical trial of OPT-302 combination therapy for the treatment of wet AMD, and a potentially treatment-related SAE of stroke for one patient in our Phase 1b/2a clinical trial of OPT-302 combination therapy for the treatment of DME.

It may be difficult to discern whether certain events or symptoms observed during our clinical trials or by patients using our approved products are related to OPT-302 or any future product candidates or approved products, including anti-VEGF-A therapies used in combination with OPT-302, or some other factor. As a result, we and our development programs may be negatively affected even if such events or symptoms are ultimately determined to be unlikely related to OPT-302 or any future product candidates or approved products. We are developing OPT-302 to complement existing VEGF-A inhibitors, including ranibizumab and aflibercept. There are some potential side effects associated with intravitreal anti-VEGF-A therapies such as intraocular hemorrhage, intraocular pressure elevation, retinal detachment, inflammation, vasculitis, artery occlusion or infection inside the eye and over-inhibition of VEGF, as well as the potential for potential systemic side effects such as heart attack, stroke, wound healing problems and high blood pressure. Further, OPT-302 in combination with anti-VEGF-A therapies for the treatment of wet AMD is administered as sequential intravitreal injections over several weeks. There are risks inherent in the intravitreal injection procedure of drugs such as existing anti-VEGF-A therapies in combination with OPT-302 which can cause injury to the eye and other complications including conjunctival hemorrhage, punctate keratitis, eye pain, conjunctival hyperemia, which results in a discharge, intra-ocular inflammation and inflammation of the interior of the eye. For example, in our completed clinical trials, patients dosed with OPT-302 have experienced potentially treatment-related ocular adverse events such as eye pain, vitreous floaters, eye irritation and raised intraocular pressure.

We cannot assure you that additional or more severe adverse side effects than those observed to date related to OPT-302 combination therapy or any future product candidates will not be observed in our clinical trials or in the commercial setting. If observed, such adverse side effects could delay or preclude regulatory approval of OPT-302 combination therapy or any future product candidates, limit commercial use or result in the withdrawal

of previously granted marketing approvals. If we or others identify undesirable or unacceptable side effects caused by OPT-302 combination therapy or any future product candidates or products:

- we may be required to modify, suspend or terminate our clinical trials;
- we may be required to modify or include additional dosage and administration instructions, warnings and precautions, contraindications, boxed warnings, limitations, restrictions or other statements in the product label for our approved products, or issue field alerts to physicians and pharmacies;
- we, or any future collaborators, may be required to create a risk evaluation and mitigation strategy, or REMS, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers, and/or other elements to assure safe use;
- we may be required to conduct costly additional clinical trials;
- we may be subject to limitations on how we may promote our approved products;
- sales of our approved products may decrease significantly;
- regulatory authorities may require us to take our approved products off the market;
- we may be subject to regulatory investigations, government enforcement actions, litigation or product liability claims; and
- our products may become less competitive or our reputation may suffer.

Any of these results could decrease or prevent any sales of our approved product or substantially increase the costs and expenses of commercializing and marketing our product.

Even if we complete the necessary Phase 3 pivotal clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us or any future collaboration partners from obtaining approvals for the commercialization of OPT-302 for the treatment of wet AMD or any other indication as well as for any other product candidate we develop.

Any product candidate we may develop and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities in the United States and by comparable non-U.S. regulatory authorities. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate in a given jurisdiction. We have not received approval to market any product candidates from regulatory authorities in any jurisdiction and it is possible that none of the product candidates we may seek to develop in the future will ever obtain regulatory approval. While we expect to expand our internal regulatory function to support the marketing approval process for OPT-302, we have no prior experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely in part on third-party CROs or regulatory consultants to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the biologic product candidate's safety, purity, efficacy and potency. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Any product candidates we develop may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and in other jurisdictions, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product

candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit, or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of any product candidates we may develop, the commercial prospects for those product candidates, including for OPT-302 in other indications, may be harmed, and our ability to generate revenues will be materially impaired.

Lack of efficacy, adverse events or undesirable side effects may emerge in clinical trials conducted by third parties with product candidates for wet AMD or DME, which could negatively affect our stock price, our ability to attract additional capital and our development program.

Lack of efficacy, adverse events or undesirable side effects may emerge in clinical trials conducted by third parties developing product candidates for wet AMD or DME. In addition, other companies have developed products for wet AMD and DME, including product candidates administered in combination with anti-VEGF-A therapies, and have suffered setbacks and clinical trial failures in the past, including failures of primary endpoints in Phase 3 pivotal clinical trials following positive data from Phase 1 and 2 trials. Lack of efficacy, adverse events or undesirable side effects experienced by subjects in third party clinical trials currently being conducted or previously conducted could negatively affect our stock price, our ability to attract additional capital and our development of OPT-302 or even the viability of OPT-302 as a product candidate. In addition, any such adverse events or undesirable side effects may lead to increased regulatory requirements for, or additional regulatory review of, OPT-302, which may result in delays in development and commercialization of OPT-302 and harm our business, financial condition and results of operations.

The results of completed clinical trials may not be predictive of future results. Data from our clinical trials to date may not be indicative of results obtained when these trials are completed or in later stage trials.

There is a high failure rate for drugs and biologic products proceeding through clinical trials. Failure can occur at any time during the clinical trial process. The results of completed clinical trials of OPT-302 or any future product candidate may not be predictive of the results of later-stage clinical trials, including our planned Phase 3 trials of OPT-302 in combination with anti-VEGF-A therapy for the treatment of wet AMD, and the results of trials in certain patients may not be predictive of those obtained in another. In fact, many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late stage clinical trials even after achieving promising results in earlier stage clinical trials. In addition, data obtained from clinical activities is subject to varying interpretations, which may delay, limit or prevent regulatory approval.

The results of our Phase 2b clinical trial of OPT-302 combination therapy may not be predictive of the results of our Phase 3 clinical program due, in part, to the fact that we have no clinical data on OPT-302 in combination with anti-VEGF-A therapy in any clinical trial longer than 24 weeks and that we plan to conduct our Phase 3 clinical trials at many clinical centers that were not included in our Phase 2b clinical trial. The number of patients exposed to product candidates and the average exposure time in prior clinical trials may be inadequate to detect rare adverse events or findings that may only be detected once a product candidate is administered to more patients and for greater periods of time. Any approved label for OPT-302 combination therapy may also be limited if our Phase 3 clinical trial results do not show long-term clinically significant efficacy results, including for over 12 months or in combination with either of the approved anti-VEGF-A therapies. In addition, if a combination of OPT-302 with an anti-VEGF-A therapy in our Phase 3 clinical program for the treatment of wet

AMD does not achieve clinically significant superiority over anti-VEGF-A monotherapy with statistical significance on the primary endpoints of our Phase 3 clinical trials, or the FDA or a comparable non-U.S. regulatory authority requires additional clinical trials beyond our Phase 3 clinical program to support an approved label of OPT-302 used in combination with multiple anti-VEGF-A therapies, our ability to successfully commercialize OPT-302 in combination with anti-VEGF-A therapy for the treatment of wet AMD would be harmed.

Interim, topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or topline data from our clinical trials, which are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available. From time to time, we may also disclose interim data from our clinical trials. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available.

In addition, adverse changes between interim data and final data could significantly harm our business and prospects. Additional disclosure of interim data by us or by our competitors in the future could also result in volatility in the price of the ADSs and our ordinary shares after this offering. Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the topline data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, OPT-302 or any future product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects.

We may face substantial competition, which may result in others discovering, developing or commercializing competing products before or more successfully than us.

The biopharmaceutical industry is intensely competitive and subject to rapid innovation and significant technological advancements. We believe the key competitive factors that will affect the development and commercial success of OPT-302 and any future product candidates are efficacy, safety and tolerability profile, reliability, convenience of dosing, price, the level of generic competition and reimbursement. Our competitors include multinational pharmaceutical companies, specialized biotechnology companies, universities and other research institutions. A number of biotechnology and pharmaceutical companies are pursuing the development or marketing of pharmaceuticals that target the same diseases that we are targeting. Smaller or earlier-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies.

There are a number of large pharmaceutical and biotechnology companies that are currently pursuing the development of products for the treatment of wet AMD and DME, or have commercially approved products for the treatment of wet AMD or DME, including Roche, Regeneron and Novartis. The current standard of care for wet AMD is monotherapy administration of anti-VEGF-A therapies, including ranibizumab and aflibercept, as well as off-label use of bevacizumab. These drugs are well established therapies and are widely accepted by physicians, patients and third-party payors, which may make it difficult to convince these parties to switch to OPT-302 combination therapy. In addition to competition from other companies directly targeting wet AMD or DME, any products we may develop may also face competition from other types of therapies or patient and physician preferences. In addition, many companies are developing new therapeutics, and we cannot predict what the standard of care will be as OPT-302 or any future product candidates progress through clinical development.

If our competitors market products that are more effective, safer or cheaper than our products, that are more durable or have reduced injection burden compared to our products (including OPT-302), or that reach the market sooner than our products, we may not achieve commercial success. In addition, the biopharmaceutical industry is characterized by rapid technological change. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Technological advances or products developed by our competitors may render our technologies, products or product candidates obsolete, less competitive or not economical.

Many of our competitors have substantially greater financial, technical, human and other resources than we do and may be better equipped to develop, manufacture and market technologically superior products. In addition, many of these competitors have significantly longer operating histories and greater experience than we have in undertaking nonclinical studies and human clinical trials of new pharmaceutical products and in obtaining regulatory approvals of human therapeutic products. Clinical trials for the treatment of wet AMD and DME may be relatively costly and time consuming. The requirements for approval by the FDA and comparable non-U.S. regulatory authorities may change over time and this may require changes to ongoing or future clinical trial designs that could impact timelines and cost. Further, many of our competitors have established distribution channels for the commercialization of their products, whereas we have no such channel or capabilities. In addition, many competitors have greater name recognition and more extensive collaborative relationships.

As a result, our competitors may obtain regulatory approval of their products more rapidly than we do or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidate or any future product candidates. Our competitors may also develop and succeed in obtaining approval for drugs that are more effective, more convenient, more widely used and less costly or have a better safety profile than our products and these competitors may also be more successful than we are in manufacturing and marketing their products. If we are unable to compete effectively against these companies, then we may not be able to commercialize our product candidate or any future product candidates or achieve a competitive position in the market. This would negatively affect our ability to generate revenue. Our competitors also compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and enrolling patients for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our inability to compete effectively in any of these aspects of our business could harm our business, financial condition, results of operations and prospects.

We may encounter difficulties in managing our growth, which could negatively impact our operations.

As we advance our clinical development programs for product candidates, seek regulatory approval in the United States and elsewhere and increase the number of ongoing product development programs, we anticipate that we will need to increase our product development, scientific and administrative headcount. In particular, as we progress our Phase 3 clinical trials for OPT-302 in combination with anti-VEGF-A therapy for the treatment of wet AMD, we will require additional key staff for clinical development operations as well as additional key financial and administrative personnel. We will also need to establish commercial capabilities in order to commercialize any product candidates that may be approved. Such an evolution may impact our strategic focus and our deployment and allocation of resources.

Our ability to manage our operations and growth effectively depends upon the continual improvement of our procedures, reporting systems and operational, financial and management controls. We may not be able to implement administrative and operational improvements in an efficient or timely manner and may discover deficiencies in existing systems and controls. If we do not meet these challenges, we may be unable to execute our business strategies and may be forced to expend more resources than anticipated addressing these issues.

We may acquire additional technology and complementary businesses in the future. Acquisitions involve many risks, any of which could materially harm our business, including the diversion of management's attention from core business concerns, failure to effectively exploit acquired technologies, failure to successfully integrate the acquired business or realize expected synergies or the loss of key employees from either our business or the acquired businesses.

In addition, in order to continue to meet our obligations as a public listed company in both Australia and the United States and to support our anticipated long-term growth, we will need to increase our general and administrative capabilities. Our management, personnel and systems may not be adequate to support this future growth.

If we are unable to successfully manage our growth and the increased complexity of our operations, our business, financial position, results of operations and prospects may be harmed.

A fast track designation by the FDA, even if granted for OPT-302 or any other future product candidates, may not lead to a faster development or regulatory review or approval process and does not increase the likelihood that our product candidates will receive marketing approval.

If a drug or biologic is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address unmet medical needs for this condition, the sponsor may apply for FDA fast track designation for a particular indication. We may seek fast track designation for certain of our current or future product candidates, including OPT-302, but there is no assurance that the FDA will grant this status to any of our proposed product candidates. If granted, fast track designation makes a product eligible for more frequent interactions with FDA to discuss the development plan and clinical trial design, as well as rolling review of the application, which means that the company can submit completed sections of its marketing application for review prior to completion of the entire submission. Marketing applications of products candidates with fast track designation may qualify for priority review under the policies and procedures offered by the FDA, but the fast track designation does not assure any such qualification or ultimate marketing approval by the FDA. The FDA has broad discretion whether or not to grant fast track designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a fast track designation does not provide any assurance of ultimate FDA approval. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. In addition, the FDA may withdraw any fast track designation at any time.

OPT-302 and any future product candidates may not achieve adequate market acceptance among physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

Even if our product candidates receive regulatory approval, they may not gain adequate market acceptance among physicians, patients, healthcare payors and others in the medical community. Given the number of drugs in development or currently approved for the treatment of wet AMD and DME, if we are unsuccessful in achieving a differentiated profile with OPT-302, including in combination with existing therapies, based on efficacy, safety and tolerability, dosing and administration, market acceptance will be limited. For example, current treatments for wet AMD, including ranibizumab, aflibercept and low cost, off-label use of bevacizumab,

are well established in the medical community and perceived as demonstrating meaningful clinical response in many cases. As a result, doctors may continue to rely on these treatments without OPT-302 or may continue to use such existing treatments as first-line therapies. The medical community may also resist adopting a combination therapy over monotherapy for any of our targeted indications. In particular, recent clinical development has focused on maintaining vision gains with a VEGF-A inhibitor while reducing the number of injections. While we plan to evaluate the potential for co-formulation of OPT-302 with approved and/or biosimilar forms of VEGF-A inhibitors to provide flexibility of treatment options for physicians and to reduce the frequency and number of injections for patients, there can be no assurance that we will be successful or that any co-formulated product will have a favorable safety profile. If we are unable to reduce the injection burden of OPT-302 combination therapy or demonstrate sufficient efficacy improvements with a comparatively higher frequency and number of injections over standard of care anti-VEGF-A therapies, develop a co-formulation of OPT-302 for patients or otherwise increase the duration of efficacy of OPT-302 doses, or if physicians determine that a more frequent regimen is necessary, the market acceptance of OPT-302 may be limited which would harm our business, financial condition and results of operations.

In addition, the potential market opportunity for OPT-302 is difficult to estimate precisely. If OPT-302 receives marketing approval for the treatment of wet AMD, it will be approved solely for use in combination with one or more anti-VEGF-A therapies, and may be limited to use with only one anti-VEGF-A therapy for the treatment of wet AMD depending on the protocol for our planned Phase 3 clinical trials or whether the results from each of our Phase 3 clinical trials support an approved label for use of OPT-302 in combination with more than one anti-VEGF-A therapy. The market opportunity for OPT-302 will be dependent upon the continued use of anti-VEGF-A therapies in the treatment of wet AMD and the market share of such anti-VEGF-A therapies for which OPT-302 is approved as a combination therapy. The degree of market acceptance of any of our approved product candidates will depend on a number of factors, including:

- the efficacy, safety and dosing profile of the product candidate as demonstrated in clinical trials;
- the timing of market introduction of the product candidate as well as competitive products;
- the clinical indications for which the product candidate is approved;
- the imposition of a REMS which may include distribution or use restrictions;
- any restrictions on the use of our products to a subgroup of patients;
- acceptance of the product candidate as a safe and effective treatment by physicians and patients;
- the potential and perceived advantages of the product candidate over alternative treatments, including any similar generic treatments;
- the cost of treatment in relation to alternative treatments;
- the availability of coverage and adequate reimbursement and pricing by third parties and government authorities;
- patients' willingness to pay out-of-pocket in the absence of coverage and/or adequate reimbursement from third-party payors;
- the relative convenience and ease of administration;
- the frequency and severity of adverse events;
- the effectiveness of sales and marketing efforts; and
- unfavorable publicity relating to the product candidate.

Sales of medical products also depend on the willingness of physicians to prescribe the treatment, which is likely to be based on a determination by these physicians that the products are safe, therapeutically effective and cost effective. In addition, the inclusion or exclusion of products from treatment guidelines established by various physician groups and the viewpoints of influential physicians can affect the willingness of other

physicians to prescribe the treatment. We cannot predict whether physicians, physicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that our products are safe, therapeutically effective and cost effective as compared with competing treatments.

Efforts to educate the medical community and third-party payors on the benefits of OPT-302 combination therapy may require significant resources and may not be successful. Demonstrating the safety and efficacy of our product candidates and obtaining regulatory approvals will not guarantee future revenue. Our commercial success also depends on coverage and adequate reimbursement of our product candidates by third-party payors, including government payors, which may be difficult or time-consuming to obtain, may be limited in scope and may not be obtained in all jurisdictions in which we may seek to market our products.

If the market opportunities for any product that we or our strategic collaborators develop are smaller than we believe they are, our revenue may be negatively affected and our business may suffer.

We intend to focus our product candidate development on therapies for the treatment of wet AMD and additional retinal disease indications such as DME or retinal vein occlusion, or RVO. Our projections of addressable patient populations that have the potential to benefit from treatment with our product candidate are based on estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for our product candidates may not ultimately be amenable to treatment with our product candidates. Our market opportunity may also be limited by future competitor treatments that enter the market. If any of our estimates are inaccurate, the market opportunities for any of our product candidates could be significantly diminished and have an adverse impact on our business.

If OPT-302 is approved by the FDA as a combination therapy for the treatment of wet AMD, the approval will be limited to this specific indication and, unless we seek regulatory approval for additional indications, we will be prohibited from marketing OPT-302 for other indications. We may be subject to fines, penalties or injunctions if we are determined to have promoted or be promoting the use of OPT-302 for unapproved or "off-label" uses, resulting in damage to our reputation and business.

If OPT-302 receives marketing approval for the treatment of wet AMD, it will be approved solely for use in combination with one or more anti-VEGF-A therapies, and may be limited to only one anti-VEGF-A therapy for the treatment of wet AMD depending on the protocols for our planned pivotal Phase 3 clinical trials. Although we are also developing OPT-302 for other retinal diseases, any regulatory approval of OPT-302 for wet AMD would not be cover the treatment of any other indication. As a result, we would be prohibited from promoting OPT-302 for the treatment of DME unless we are granted FDA approval for such indication.

The FDA strictly regulates the promotional claims that may be made about prescription products. While physicians may choose to prescribe products for uses that are not described in the product's labeling and for uses that differ from those tested in clinical trials and approved by the regulatory authorities, we are prohibited from marketing and promoting the products for indications that are not specifically approved by the FDA or comparable non-U.S. regulatory authorities. These "off-label" uses are common across medical specialties and may constitute an appropriate treatment for some patients in varied circumstances. Regulatory authorities in the United States generally do not restrict or regulate the behavior of physicians in their choice of treatment within the practice of medicine. Regulatory authorities do, however, restrict communications by biotechnology or pharmaceutical companies on off-label use. If the FDA determines that our promotional activities constitute promotion of an off-label use, it could request that we modify our promotional materials and subject us to FDA regulatory or enforcement actions as well as actions by other agencies, including issuance of warning letters or untitled letters, suspension or withdrawal of an approved product from the market, mandatory or voluntary recalls, civil fines, disgorgement of money, operating restrictions, additional reporting requirements and/or

oversight if we become subject to a corporate integrity agreement or similar agreement, injunctions or criminal prosecution, any of which could significantly harm our business.

OPT-302 is being developed to be used as a combination therapy for use with anti-VEGF-A therapies, which exposes us to additional risks.

We are developing OPT-302 to be used in combination with currently approved VEGF-A inhibitors. Even if OPT-302 were to receive marketing approval or be commercialized, we would continue to be subject to the risks that the FDA or similar regulatory authorities could revoke approval of some or all approved anti-VEGF-A therapies for safety, efficacy, manufacturing or supply issues. This could result in OPT-302 being restricted from commercialization or being less commercially successful.

We may also evaluate OPT-302 or any other future product candidates in combination with one or more other product candidates that have not yet been approved for marketing by the FDA or similar foreign regulatory authorities. We will not be able to market and sell OPT-302 or any product candidate we develop in combination with any such unapproved therapies that do not ultimately obtain marketing approval.

If the FDA or similar foreign regulatory authorities do not approve these other product candidates or revoke their approval of, or if safety, efficacy, manufacturing, or supply issues arise with, the drugs we choose to evaluate in combination with OPT-302 or any product candidate we develop, we may be unable to obtain approval of or market OPT-302 or any product candidate we develop.

If we fail to develop and commercialize additional product candidates, we may be unable to grow our business.

Although the development and commercialization of OPT-302 is currently our primary focus, as part of our longer-term growth strategy, we plan to evaluate the development and commercialization of other therapies related to retinal diseases. The success of this strategy depends primarily upon our ability to identify and validate new therapeutic candidates, and to identify, develop and commercialize new drugs and biologics. Our research efforts may initially show promise in discovering potential new drugs and biologics, yet fail to yield product candidates for clinical development for a number of reasons, including:

- we may need to rely on third parties to generate molecules for some of our product candidate programs;
- we may encounter product manufacturing difficulties that limit yield or produce undesirable characteristics that increase the cost of manufacturing our product candidates, cause delays or make our product candidates unmarketable;
- product candidates may cause adverse effects in patients or subjects, even after successful initial toxicology studies, which may make the product candidates unmarketable;
- product candidates may not demonstrate a meaningful benefit to patients or subjects; and
- our future collaboration partners may change their development profiles or plans for potential product candidates or abandon a therapeutic area or the development of a partnered product.

If any of these events occur, we may be forced to abandon our development efforts for one or more programs, which could harm our business, operating results and prospects and could potentially cause us to cease operations. Future research programs to identify new product candidates may require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

Product candidates may require additional, time-consuming development efforts prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA and/or comparable non-U.S. regulatory

authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, be successfully commercialized, be widely accepted in the marketplace or be more effective than other commercially available alternatives.

We may expend our limited resources to pursue one or more particular indications and fail to capitalize on indications that may be more profitable or for which there is a greater likelihood of success.

We have limited financial and management resources. As a result, we may forego or delay pursuit of opportunities with other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future development programs for specific indications may not yield any commercially viable products. Any such failures would negatively affect our business and results of operations.

We must attract and retain highly skilled employees in order to succeed. If we are not able to retain our current senior management team and our scientific advisors or continue to attract and retain qualified scientific, technical and business personnel, our business will suffer.

We may not be able to attract or retain qualified personnel and consultants due to the intense competition for such individuals among in the biotechnology and pharmaceutical industries. If we are not able to attract and retain necessary personnel and consultants to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development and commercial objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of the members of our executive team, as well as other key employees and consultants. If we lose one or more of our executive officers or other key employees or consultants, our ability to implement our business strategy successfully could be seriously harmed. Any of our executive officers or other key employees or consultants may terminate their employment at any time with three months' notice, subject to certain exceptions, and replacing such individuals may be difficult and time-consuming because of the limited number of individuals in our industry with the necessary breadth of skills and experience. Competition to hire and retain employees and consultants from this limited pool is intense, and we may be unable to hire, train, retain or motivate such individuals. Additionally, we do not currently maintain "key person" life insurance on the lives of our executives or any of our employees. This lack of insurance means that we may not receive adequate compensation for the loss of the services of these individuals. If we are unable to continue to attract and retain high-quality personnel, the rate and success with which we can discover and develop product candidates and our business will be limited.

As we evolve from a company that is primarily involved in clinical development to a company that is also involved in preparing for commercialization, we may encounter difficulties in expanding our operations successfully.

As we advance our product candidates through clinical trials, we will need to expand our development, regulatory, manufacturing and marketing and sales capabilities and may need to further contract with third parties to provide these capabilities, such as collaborators, distributors, marketers and additional suppliers. We currently have no experience as a company in or infrastructure for sales, marketing and distribution, and our operations are currently limited to clinical development activities and as our operations expand, we likely will need to manage additional relationships with such third parties.

If OPT-302 or any future product candidate is approved, we intend either to establish a sales and organization with technical expertise and supporting distribution capabilities to commercialize OPT-302 or any

future product candidate or to outsource such functions to one or more third parties. Either of these options would be expensive and time-consuming. Some or all of these costs may be incurred in advance of any approval of OPT-302 or any future product candidate. In addition, we may not be able to hire a sales force that is sufficient in size or has adequate expertise in the medical markets that we intend to target.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or attain adequate numbers of physicians to prescribe any drugs;
- the inability to obtain sufficient access and reimbursement for our product candidate, if approved; and
- unforeseen costs and expenses associated with creating a sales and marketing organization.

Any failure or delay in the development of our internal sales, marketing and distribution capabilities would negatively affect the commercialization of OPT-302 and other future product candidates.

Maintaining third-party relationships for these purposes will impose significant added responsibilities on members of our management and other personnel. We must be able to effectively manage our development efforts, recruit and train sales and marketing personnel, effectively manage our participation in the clinical trials in which our product candidates are involved and improve our managerial, development, operational and finance systems, all of which may impose a strain on our administrative and operational infrastructure.

If we enter into arrangements with third parties to perform sales, marketing or distribution services, any product revenues that we receive, or the profitability of these product revenues to us, are likely to be lower than if we were to market and sell any products that we develop without the involvement of these third parties. In addition, we may not be successful in entering into arrangements with third parties to sell and market our products and can provide no assurance that the terms of any such arrangements will remain favorable for us over time. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our products.

Our business could be negatively affected by the effects of health epidemics, including the evolving effects of the COVID-19 pandemic, in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of clinical trial sites or other business operations.

Health epidemics in regions where we have concentrations of clinical trial sites or other business operations could negatively affect our business, including by causing significant disruption in the operations of third-party manufacturers and CROs upon whom we rely. For example, the novel coronavirus disease 2019, or COVID-19, pandemic has presented a substantial public health and economic challenge around the world and is affecting employees, patients, communities and business operations, as well as the U.S. economy and financial markets. Based on guidance issued by Australian federal and state governments, we transitioned to a remote work environment for all of our employees. In connection with these measures, we may be subject to claims based upon, arising out of, or related to COVID-19 and our actions and responses thereto, including any determinations that we may make to continue to operate or to re-open our facilities. Further, the effects of the shelter-in-place orders in Australia and across the world and our work-from-home policies may negatively impact productivity, disrupt our business and delay our clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course. These and similar, and perhaps more severe, disruptions in our operations could negatively impact our business, financial condition, results of operations and growth prospects.

As the pandemic continues, we may experience a negative impact on our ability to initiate clinical trial sites, maintain patient enrollment and enroll new patients which may impact timelines in the future. Our ability to attract additional clinical trial sites and principal investigators to conduct our clinical trials and to conduct the necessary clinical trial site initiation procedures may be impacted by quarantines, shelter-in-place and similar restrictions imposed by federal, state and local governments. These restrictions may also prohibit patients from enrolling in, or continuing to participate in, our clinical trials. Principal investigators and clinical trial site staff, as healthcare providers, may have heightened exposure to COVID-19 and if their health is impacted by COVID-19 it could negatively impact the conduct of our clinical trials at their sites. Similarly, potential participants in our clinical trials, many of whom are medically vulnerable, may be unwilling to enroll in, and enrolled patients may be unwilling to continue to participate in, our clinical trials due to an unwillingness to travel to sites for required screening and clinical trial visits and procedures. Enrolled patients may be unable to comply with clinical trial protocols if quarantines, shelter-in-place and similar restrictions continue to impede patient movement or interrupt healthcare services. In addition, we may be required to develop and implement additional clinical study policies and procedures designed to help protect patients from the COVID-19 disease, which may include using telemedicine visits, remote monitoring of patients and clinical trial sites, and measures designed to ensure that data from clinical trials that may be disrupted as result of the pandemic are collected pursuant to the study protocol and consistent with cGCPs, with any significant protocol deviation reviewed and approved by the clinical trial site institutional review board, or IRB, all or any of which could materially and negatively affect our clinical development timelines and our ability to obtain regulatory approvals of our product candidates, and could significantly increase our costs. We could also see an impact on our ability to report clinical trial results, or interact with regulators, ethics committees or other important agencies due to limitations in regulatory authority employee resources or otherwise. In addition, the FDA or comparable non-U.S. regulatory authorities may refuse to accept data from clinical trials conducted in geographies experiencing heightened impact from COVID-19.

Moreover, we rely on third-party CROs and other third parties to assist us with clinical development activities, and we cannot guarantee that they will continue to perform their contractual duties in a timely and satisfactory manner as a result of the COVID-19 pandemic. In addition, quarantines, shelter-in-place and similar government orders could impact personnel at third-party manufacturing facilities in the United States and other countries, or the availability or cost of materials, which would disrupt our supply chain. In particular, some of our suppliers of certain materials used in the production of our drug products are located in Europe. In any event, if the COVID-19 pandemic continues and persists for an extended period of time or more acutely impacts geographies with particular impact on our business, we could experience significant disruptions to our clinical development timelines, which would harm our business, financial condition, results of operations and growth prospects.

In addition, while the potential economic impact brought by, and the duration of, the COVID-19 pandemic may be difficult to assess or predict, the pandemic could result in significant and prolonged disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could harm our business and the value of our ordinary shares and ADSs offered hereby following this offering.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, otherwise prevent new products from being developed, approved or commercialized in a timely manner or at all, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, statutory, regulatory and policy changes, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a

result. In addition, government funding of other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, in recent years, including in 2018 and 2019, the U.S. government shut down several times and certain regulatory agencies, such as the FDA, had to furlough critical employees and stop critical activities. Separately, in response to the COVID-19 pandemic, in March 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities and products through April 2020. Also in March 2020, the FDA announced its intention to temporarily postpone routine surveillance inspections of domestic manufacturing facilities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic or issue guidance materially affecting the conduct of clinical trials. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews or other regulatory activities, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, upon completion of this offering and in our operations as a public company, future government shutdowns or delays could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Even if we commercialize OPT-302 or any future product candidate, we may face challenges to achieving profitability such as our products becoming subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which could harm our business.

In the United States and in other countries, patients who are prescribed treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. The availability of coverage and adequacy of reimbursement for our products by third-party payors, including government health care programs (e.g., Medicare, Medicaid, TRICARE), managed care providers, private health insurers, health maintenance organizations and other organizations is essential for most patients to be able to afford medical services and pharmaceutical products such as OPT-302 or any our product candidates. Third-party payors decide which medications they will pay for and establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and other third-party payors is essential for most patients to be able to afford treatments such as OPT-302.

In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, or HHS. CMS decides whether and to what extent our products will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. Factors payors consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Our ability to commercialize any products successfully will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors, including government health care programs and private health insurers. Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. If coverage

and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

In the United States, no uniform policy for coverage and reimbursement for products exists among third-party payors. Therefore, coverage and reimbursement for our products can differ significantly from payor to payor. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. One payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product. Third-party payors may also limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication.

Government authorities and other third-party payors in the United States and abroad have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications and for newly approved products, and as a result, they may not cover or provide adequate reimbursement for OPT-302 and future product candidates. Increasingly, certain third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that coverage and reimbursement will be available for any product that we or our future collaborators commercialize and, if reimbursement is available, what the level of reimbursement will be. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we or our future collaborators obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we and our future collaborators may not be able to successfully commercialize any product candidate for which marketing approval is obtained. A decision by a third-party payor not to cover or not to separately reimburse for our medical products or therapies using our products could reduce physician utilization of our products once approved. Assuming there is coverage for our product candidates, or therapies using our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States will be available for OPT-302 and any future product candidates and any reimbursement that may become available may not be adequate or may be decreased or eliminated in the future.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or comparable non-U.S. regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may only be temporary. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable reimbursement rates from both government-funded and private payors for any approved products that we develop could harm our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

The regulations that govern marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some non-U.S. markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price

regulations that delay or limit our commercial launch of the product, possibly for lengthy time periods, which could negatively impact the revenue we generate from the sale of the product in that particular country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

To become and remain profitable, we or any potential future collaborator must develop and eventually commercialize OPT-302 or any future product candidates with significant market potential at an adequate profit margin after cost of goods sold and other expenses. Commercialization of OPT-302 or any future product candidates may entail a substantial cost of goods sold and there can be no assurance that we will be able to achieve a suitable gross margin with respect to sales of OPT-302 or any future product candidates.

Changes in U.S. healthcare law and implementing regulations, as well as changes in healthcare policy, may impact our business in ways that we cannot currently predict and may harm our business and results of operations.

There have been, and likely will continue to be, several executive, legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. Among policy makers and payors in the United States there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access and the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively referred to as the Affordable Care Act, substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. The Affordable Care Act, among other things: (1) introduced a new average manufacturer price definition for drugs and biologics that are inhaled, infused, instilled, implanted or injected and not generally dispensed through retail community pharmacies; (2) increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and expanded rebate liability from fee-for-service Medicaid utilization to include the utilization of Medicaid managed care organizations as well; (3) established a branded prescription drug fee that pharmaceutical manufacturers of branded prescription drugs must pay to the federal government; (4) expanded the list of covered entities eligible to participate in the 340B drug pricing program by adding new entities eligible for the program; (5) established a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, or BBA, effective as of January 2019) point-of-sale discounts off negotiated prices of applicable branded drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; (6) extended manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations; (7) expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals, including individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability; (8) created a licensure framework for follow-on biologic products; and (9) established a Center for Medicare and Medicaid Innovation at the CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

There remain judicial and Congressional challenges to certain aspects of the Affordable Care Act, as well as efforts by the Trump administration to repeal or replace certain aspects of the Affordable Care Act. For example, the Tax Cuts and Jobs Act of 2017, or the TCJA, was enacted, which included a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas ruled that the individual mandate is a critical and inseverable feature of the Affordable Care Act, and

therefore, because it was repealed as part of the TCJA, the remaining provisions of the Affordable Care Act are invalid as well. On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit ruled that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. On March 2, 2020, the U.S. Supreme Court granted the petitions for writs of certiorari to review the case, although it is unclear when a decision will be made or how the Supreme Court will rule. In addition, there may be other efforts to challenge, repeal or replace the Affordable Care Act. We are continuing to monitor any changes to the Affordable Care Act that, in turn, may potentially impact our business in the future.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011 and subsequent laws, which began in 2013 and will remain in effect through 2030, unless additional Congressional action is taken. These Medicare sequester reductions will be suspended from May 1, 2020 through December 31, 2020 due to the COVID-19 pandemic. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. New laws may result in additional reductions in Medicare and other healthcare funding, which may materially negatively affect customer demand and affordability for our products and, accordingly, the results of our financial operations. Also, there has been heightened governmental scrutiny recently over the manner in which pharmaceutical companies set prices for their marketed products, which have resulted in several Congressional inquiries and proposed federal legislation, as well as state efforts, designed to, among other things, bring more transparency to product pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, at the federal level, the Trump administration's budget proposal for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the Trump administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. Further, the Trump administration previously released a "Blueprint," or plan, to lower drug prices and reduce out of pocket costs of drugs that contained proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. HHS has solicited feedback on some of these measures and has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. While some of these and other measures may require additional authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, individual states in the United States are increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions on coverage or access could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates that we successfully commercialize or put pressure on our product pricing.

We expect that these and other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, and put additional downward pressure on the price that we receive for any approved product. It is possible that additional governmental action is taken in response to the COVID-19 pandemic. For example, on August 6, 2020, the Trump administration issued another executive order that instructs the federal government to develop a list of "essential" medicines and then buy them and other medical supplies from U.S. manufacturers instead of from companies around the world, including China. The order is meant to reduce regulatory barriers to domestic pharmaceutical manufacturing and catalyze manufacturing technologies needed to keep drug prices low and the production of drug products in the United States. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drugs, once marketing approval is obtained. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability

As a company primarily based outside of the United States, our business is subject to economic, political, regulatory and other risks associated with international operations.

As a company with substantial operations in Australia and an international clinical trial program, our business is subject to risks associated with conducting business outside the United States. Many of our suppliers and clinical trial relationships are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- differing and changing regulatory requirements for product approvals;
- differing jurisdictions could present different issues for securing, maintaining or obtaining freedom to operate in such jurisdictions;
- potentially reduced protection for intellectual property rights;
- difficulties in compliance with different, complex and changing laws, regulations and court systems of multiple jurisdictions and compliance with a wide variety of foreign laws, treaties and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in non-U.S. currency exchange rates, Australian dollar, U.S. dollar, euro and currency controls;
- changes in a specific country's or region's political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by governments;
- differing reimbursement regimes and price controls in certain non-U.S. markets;
- negative consequences from changes in tax laws;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- litigation or administrative actions resulting from claims against us by current or former employees or consultants individually or as part of class actions, including claims of wrongful terminations, discrimination, misclassification or other violations of labor law or other alleged conduct;
- difficulties associated with staffing and managing international operations, including differing labor relations;

- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism, health epidemics, or natural disasters including earthquakes, typhoons, floods and fires.

If we fail to comply with non-U.S. regulatory requirements governing human clinical trials and marketing approval for drugs, we could be prevented from selling our product candidates in non-U.S. markets, which may negatively affect our operating results and financial condition.

The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement for marketing our product candidates outside the United States vary greatly from country to country and may require additional testing. We expect that our future clinical development of our product candidates will involve a number of clinical trials in non-U.S. jurisdictions. We have no direct experience as a company in obtaining non-U.S. regulatory approvals. The time required to obtain approvals outside the United States may differ from that required to obtain FDA approval. We may not obtain non-U.S. regulatory approvals on a timely basis, if at all. Approval by the FDA does not guarantee approval by comparable non-U.S. regulatory authorities, and approval by one non-U.S. regulatory authority does not ensure approval by regulatory authorities in other countries or by the FDA. Failure to comply with these regulatory requirements or obtain required approvals could impair our ability to develop non-U.S. markets for our product candidates and may harm our results of operations and financial condition.

Price controls may be imposed in non-U.S. markets, which may negatively affect our future profitability.

In some countries, particularly EU member states, Japan, Australia and Canada, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we or our collaborators may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, revenues or profitability could be harmed.

We have received tax incentives under the Research and Development Tax Incentive scheme in Australia that may become repayable if we did not or do not comply with the rules of the scheme, or we may become ineligible for tax incentives in our current or future tax years, which could harm our business, financial condition and results of operations.

We have received cash incentives in the past under the Research and Development Tax Incentive scheme, or the R&D Scheme, to offset the costs of our clinical trials and other qualifying expenses incurred both in Australia and other jurisdictions. Certain research and development costs that we incur in the future may be ineligible for cash incentives under the R&D Scheme. For example, costs incurred outside Australia in connection with our future clinical trials are generally not eligible for cash incentives under the R&D Scheme. In addition, the federal government of Australia and the Australian Taxation Office, or ATO, could change the rules of the regulatory regime or amend past tax returns and, as a result, amounts paid to us may become repayable to the ATO including the amount of tax incentives in respect of our fiscal year ended June 30, 2020 included as current receivables in our consolidated financial statements. We have received an aggregate of A$35.1 million in cash tax incentives during the five fiscal years ended June 30, 2020 under the R&D Scheme. As at June 30, 2020, our

current tax receivable under the R&D Scheme was A$14.6 million. This receivable amount as at June 30, 2020 is based on Australian legislation as enacted as at June 30, 2020. Any proposed changes to the legislation, such as the currently proposed rate change from 43.5% to 41%, may have a retrospective impact on our current tax receivable under the R&D Scheme. Any rule changes made to reduce the amount we are able to claim under the R&D Scheme currently or in the future and any retrospective changes made to the R&D Scheme that reduce the incentives that we have claimed in past tax years could harm our business, financial condition and results of operations.

Legal, political and economic uncertainty surrounding the planned exit of the U.K. from the EU are a source of instability and uncertainty.

On June 23, 2016, the U.K. held a referendum in which a majority of the eligible members of the electorate voted for the U.K. to leave the EU. The U.K's withdrawal from the EU is commonly referred to as "Brexit." The U.K. and the EU have agreed to a withdrawal agreement, or the Withdrawal Agreement, which was approved by the U.K. Parliament on January 24, 2020. Under the Withdrawal Agreement, the U.K. is subject to a transition period until December 31, 2020, or the Transition Period, during which EU rules will continue to apply. Negotiations between the U.K. and the EU are expected to continue in relation to the customs and trading relationship between the U.K. and the EU following the expiration of the Transition Period.

The uncertainty concerning the U.K's legal, political and economic relationship with the EU after the Transition Period may be a source of instability in the international markets, create significant currency fluctuations, and/or otherwise negatively affect trading agreements or similar cross-border cooperation arrangements (whether economic, tax, fiscal, legal, regulatory or otherwise). These developments, or the perception that any of them could occur, have had, and may continue to have, a significant negative impact on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and limit the ability of key market participants to operate in certain financial markets. In particular, it could also lead to a period of considerable uncertainty in relation to the regulatory process in Europe.

Brexit has created political and economic uncertainty, particularly in the U.K. and the EU, and this uncertainty may persist for years. A withdrawal could, among other outcomes, disrupt the free movement of goods, services and people between the U.K. and the EU, and result in increased legal and regulatory complexities, as well as potentially higher costs of conducting business in Europe. The U.K.'s vote to exit the EU could also result in similar referendums or votes in other European countries in which we do business. Given the lack of comparable precedent, it is unclear what financial, trade and legal implications the withdrawal of the U.K. from the EU would have and how such withdrawal would affect us.

Any new regulations could add time and expense to the conduct of our business, as well as the process by which our product candidate receives regulatory approval in the U.K., the EU and elsewhere. In addition, the announcement of Brexit and the withdrawal of the U.K. from the EU have had and may continue to negatively affect global economic conditions and the stability of global financial markets, and may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Any of these effects of Brexit, among others, could harm our business, our results of operations, liquidity and financial condition.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercialize any resulting products. Product liability claims may be brought against us by subjects enrolled in our clinical trials, patients, or others using our products. If we cannot successfully defend ourselves against claims that our product candidates or products that

we may develop caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- product recalls or a change in the indications for which products may be used;
- termination of clinical trial sites or entire trial programs;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial subjects or patients;
- loss of revenue;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize any products that we may develop.

Our clinical trial liability insurance coverage may not adequately cover all liabilities that we may incur. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. Our inability to obtain product liability insurance at an acceptable cost or to otherwise protect against potential product liability claims could prevent or delay the commercialization of any products or product candidates that we develop. We intend to expand our insurance coverage for products to include the sale of commercial products if we obtain marketing approval for our product candidates in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. If we are sued for any injury caused by our products, product candidates or processes, our liability could exceed our product liability insurance coverage and our total assets. Claims against us, regardless of their merit or potential outcome, may also generate negative publicity or harm our ability to obtain physician endorsement of our products or expand our business.

Our employees, contractors, vendors, principal investigators, consultants and future partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, contractors, vendors, principal investigators, consultants or future partners. Misconduct by these parties could include failures to comply with FDA or comparable non-U.S. authority regulations, to provide accurate information to the FDA or comparable non-U.S. regulators, to comply with U.S. federal and state and non-U.S. healthcare fraud and abuse laws and regulations, to report financial information or data timely, completely or accurately, or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Third-party misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. Although we have adopted a Code of Conduct, it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us resulting from this misconduct and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions. If we or our future partners market products in a manner that violates fraud and abuse and other healthcare laws, or if we or our future partners

violate government price reporting laws, we or our future partners may be subject to administrative civil and/or criminal penalties, among other sanctions.

Most states also have statutes or regulations similar to these federal laws, which may apply to items such as pharmaceutical products and services reimbursed by private insurers. We and/or our future partners may be subject to administrative, civil and criminal sanctions for violations of any of these federal and state laws. Pharmaceutical and other healthcare companies have been prosecuted under these laws for a variety of promotional and marketing activities, such as: providing free trips, free goods, sham consulting fees and grants and other monetary benefits to prescribers; reporting to pricing services inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in off-label promotion; and submitting inflated best price information to the Medicaid Rebate Program to reduce liability for Medicaid rebates. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations.

Our business operations and relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers are subject to broadly applicable healthcare laws and regulations, which could expose us civil to penalties, criminal sanctions, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidate for which we obtain regulatory approval. Our current and future arrangements may expose us to broadly applicable fraud and abuse and other healthcare laws that may constrain the business or financial arrangements and relationships through which we would market, sell and distribute our products. In particular, the research of our product candidates, as well as the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business or financial arrangements.

Such laws include, but are not limited to, the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid. The term "remuneration" has been broadly interpreted to include anything of value. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation. The Anti-Kickback Statute has been interpreted to apply to arrangements between biopharmaceutical manufacturers, on the one hand, and prescribers, purchasers and formulary managers, among others, on the other. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the federal criminal and civil false claims laws, including the False Claims Act, which imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that

are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or knowingly making or causing to be made, a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. Manufacturers can be held liable under the False Claims Act even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. When an entity is determined to have violated the False Claims Act, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false or fraudulent statements relating to healthcare matters; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, which also impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information on health plans, health care clearing houses, and certain healthcare providers and their business associates, defined as independent contractors or agents of covered entities that create, receive or obtain protected health information in connection with providing a service for or on behalf of a covered entity, as well as their subcontractors. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personally identifiable information, or personal information or personal data, in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;
- the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the government information related to payments or other "transfers of value" made to physicians, as defined by law, and teaching hospitals, and requires applicable manufacturers and group purchasing organizations to report annually to the ownership and investment interests held by such physicians and their immediate family members and payments or other "transfers of value" to such physician owners (covered manufacturers are required to submit reports to CMS by the 90th day of each calendar year). Effective January 1, 2022, these reporting obligations will extend to include transfers of value made in the previous year to certain non-physician providers such as physician assistants and nurse practitioners; and
- analogous state and non-U.S. laws and regulations, such as state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; and state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, and state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures or drug pricing; and state and local laws that require the registration of pharmaceutical sales representatives; and state and non-U.S. laws governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Pharmaceutical and other healthcare companies have been prosecuted under these laws for a variety of promotional and marketing activities, such as: providing free trips, free or discounted goods, improper consulting fees and grants and other monetary benefits to prescribers; reporting to pricing services inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in off-label promotion; and submitting inflated best price information to the Medicaid Rebate Program to reduce liability for Medicaid rebates. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If any actions are instituted against us for violation of these laws or regulations, and we are not successful in defending ourselves, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative sanctions, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, imprisonment, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations, any of which could harm our ability to operate our business and our results of operations.

The global data protection landscape is rapidly evolving, and we may be affected by or subject to new, amended or existing laws and regulations in the future, including as our operations continue to expand or if we operate in non-U.S. jurisdictions. Several non-U.S. jurisdictions, including the European Union, or EU, its member states, the United Kingdom, Japan and Australia, among others, have adopted legislation and regulations that increase or change the requirements governing the collection, use, disclosure and transfer of the personal information of individuals in these jurisdictions. Additionally, certain countries have passed or are considering passing laws that require local data residency and/or restrict the international transfer of data and/or impose data localization requirements with respect to certain personal information. These laws have the potential to increase costs of compliance, risks of noncompliance and penalties for noncompliance.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, disgorgement, fines, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, additional oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, that person or entity may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

We depend on our information technology systems and those of our third-party collaborators, service providers, contractors or consultants. Our internal computer systems, or those of our third-party collaborators, service providers, contractors or consultants, may fail or suffer security breaches, disruptions, or incidents, which could result in a material disruption of our development programs or loss of data or compromise the privacy, security, integrity or confidentiality of sensitive information related to our business and could harm our reputation, business, financial condition or results of operations.

In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. Our internal technology systems and infrastructure, and those of our current or future third-party collaborators, service providers, contractors and consultants are vulnerable to damage from computer viruses, unauthorized access or use resulting from malware, natural disasters, terrorism, war and telecommunication and electrical failures, denial-of-service attacks, cyber-attacks or cyber-intrusions over the Internet, hacking, phishing and other social engineering attacks, persons inside our organizations (including employees or contractors), loss or theft, or persons with access to systems inside our organization. Attacks on information technology systems are

increasing in their frequency, levels of persistence, sophistication and intensity, and they are being conducted by increasingly sophisticated and organized non-U.S. governments, groups and individuals with a wide range of motives and expertise. For example, in June 2020, a coordinated cyber security attack targeted Australian government entities and companies. In addition to extracting or accessing sensitive information, such attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the security, confidentiality, integrity and availability of information. The prevalent use of mobile devices that access sensitive information also increases the risk of data security incidents which could lead to such sensitive information (which may include confidential information, other intellectual property or personal information) being subject to unauthorized access or otherwise compromised. While to our knowledge we have not experienced any material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations or the operations of third-party collaborators, service providers, contractors and consultants, it could result in a material disruption of our development programs and significant reputational, financial, legal, regulatory, business or operational harm. The costs to us to mitigate, investigate and respond to potential security incidents, breaches, disruptions, network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position.

For example, the loss of clinical trial data from completed, ongoing or planned clinical trials for our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any real or perceived security breach affects our systems (or those of our third-party collaborators, service providers, contractors or consultants), or results in the loss of or accidental, unlawful or unauthorized access to, use of, release of, or other processing of personal information or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed. Such a breach may require notification to governmental agencies, the media or individuals pursuant to various non-U.S. domestic (federal and state) privacy and security laws, if applicable, including HIPAA, as amended by HITECH, and its implementing rules and regulations, as well as regulations promulgated by the Federal Trade Commission and state breach notification laws. In addition, our liability insurance may not be sufficient in type or amount to cover us against all losses and claims related to security breaches, cyberattacks and other related incidents.

Any failure or perceived failure by us or any third-party collaborators, service providers, contractors or consultants to comply with our privacy, confidentiality, data security or similar obligations, or any data security incidents or other security breaches that result in the accidental, unlawful or unauthorized access to, use of, release of, processing of, or transfer of sensitive information, including personal information, may result in negative publicity, harm to our reputation, governmental investigations, enforcement actions, regulatory fines, litigation or public statements against us, could cause third parties to lose trust in us or could result in claims by third parties, including those that assert that we have breached our privacy, confidentiality, data security or similar obligations, any of which could harm our reputation, business, financial condition or results of operations.

To the extent we maintain individually identifiable health information, we could be subject to fines and penalties (including civil and criminal) under HIPAA for any failure by us or our business associates to comply with HIPAA's requirements. Moreover, data security incidents and other security breaches can be difficult to detect, and any delay in identifying them may lead to increased harm. While we have implemented data security measures intended to protect our information, data, information technology systems, applications and infrastructure, there can be no assurance that such measures will successfully prevent service interruptions or data security incidents.

European data collection is governed by restrictive regulations governing the collection, use, processing and cross-border transfer of personal information.

We may collect, process, use or transfer personal information from individuals located in the European Economic Area in connection with our business, including in connection with conducting clinical trials in the European Economic Area, or the EEA. Additionally, if any of our product candidates are approved, we may seek to commercialize those products in the European Economic Area. The collection and use of personal health data in the European Economic Area is governed by the provisions of the General Data Protection Regulation ((EU) 2016/679), or the GDPR, along with other European Union and country-specific laws and regulations. The United Kingdom and Switzerland have also adopted data protection laws and regulations. These legislative acts (together with regulations and guidelines) impose requirements relating to having legal bases for processing personal data relating to identifiable individuals and transferring such data outside of the European Economic Area, including to the United States, providing details to those individuals regarding the processing of their personal data, keeping personal data secure, having data processing agreements with third parties who process personal data, responding to individuals' requests to exercise their rights in respect of their personal data, reporting security breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers or corporate representatives, conducting data protection impact assessments and record-keeping. The GDPR imposes additional responsibilities and liabilities in relation to personal data that we process and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. Failure to comply with the requirements of the GDPR and related national data protection laws of the member states of the European Economic Area and other states in the European Economic Area may result in substantial penalties, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater, other administrative penalties and civil claims being brought against us, which could harm our business, financial condition and results of operations. European data protection authorities may interpret the GDPR and national laws differently and may impose additional requirements, which adds to the complexity of processing personal data in or from the EEA or United Kingdom. Guidance on implementation and compliance practices are often updated or otherwise revised.

Our insurance policies are expensive and only protect us from some business risks, leaving us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. We believe that we maintain insurance customary for businesses of our size and type, including clinical trial liability insurance. However, there are types of losses we may incur that cannot be insured against or that we believe are not economically reasonable to insure. Moreover, any loss incurred could exceed policy limits and policy payments made to us may not be made on a timely basis. Such losses could negatively affect our business prospects, results of operations, cash flows and financial condition. We do not know if our current levels of coverage are adequate or if we will be able to obtain insurance with adequate levels of coverage in the future, if at all. Any significant uninsured liability may require us to pay substantial amounts, which could negatively impact our financial position and results of operations.

Disputes under key agreements or conflicts of interest with our scientific advisors or clinical investigators could delay or prevent development or commercialization of our product candidates.

Any agreements we have or may enter into with third parties, such as collaboration, license, formulation supplier, manufacturing, clinical research organization or clinical trial agreements, may give rise to disputes regarding the rights and obligations of the parties. Disagreements could develop over contract interpretation, rights to ownership or use of intellectual property, the scope and direction of research and development, the approach for regulatory approvals or commercialization strategy. We intend to conduct research programs in a range of therapeutic areas, but our pursuit of these opportunities could result in conflicts with the other parties to these agreements that may be developing or selling pharmaceuticals or conducting other activities in these same therapeutic areas. Any disputes or commercial conflicts could lead to the termination of our agreements, delay

progress of our product development programs, compromise our ability to renew agreements or obtain future agreements, lead to the loss of intellectual property rights, result in increased financial obligations for us or result in costly litigation.

We work with outside scientific advisors and collaborators at academic and other institutions that assist us in our research and development efforts. Our scientific advisors are not our employees and may have other commitments that limit their availability to us. If a conflict of interest between their work for us and their work for another entity arises, we may lose their services.

Unstable market and economic conditions may have serious adverse consequences on our business and financial condition.

Global credit and financial markets have experienced extreme disruptions at various points over the last few decades, characterized by diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. If another such disruption in credit and financial markets and deterioration of confidence in economic conditions occurs, our business may be harmed. If the equity and credit markets were to deteriorate significantly in the future, it may make any necessary debt or equity financing more difficult to complete, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could harm our growth strategy, financial performance and share price and could require us to delay or abandon development or commercialization plans. In addition, there is a risk that one or more of our service providers, manufacturers or other partners would not survive or be able to meet their commitments to us under such circumstances, which could directly affect our ability to attain our operating goals on schedule and on budget.

If we fail to implement and maintain an effective system of internal controls to remediate our material weaknesses over financial reporting, we may be unable to accurately report our results of operations, meet our reporting obligations or prevent fraud, and investor confidence in our company and the market price of the ADSs may be negatively impacted.

Section 404(a) of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, requires that our management assess and report annually on the effectiveness of our internal controls over financial reporting and identify any material weaknesses in our internal controls over financial reporting. During the audit of our consolidated financial statements for the fiscal year ended June 30, 2019, material weaknesses were identified in our internal control over financial reporting. Under standards established by the PCAOB, a "material weakness" is a deficiency, or combination of deficiencies in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the annual or interim financial statements will not be prevented or detected on a timely basis. The material weaknesses that have been identified relate to our lack of (i) sufficient accounting and financial reporting personnel with requisite knowledge of and experience in application of SEC rules and regulations and (ii) adequate controls to address segregation of duties. We and our independent registered public accounting firm were not required to perform an evaluation of our internal control over financial reporting as of June 30, 2019 and 2020 in accordance with the provisions of the Sarbanes-Oxley Act. Accordingly, we cannot assure you that we have identified all, or that we will not in the future have additional, material weaknesses.

We are in the process of implementing a number of measures to address the material weaknesses that have been identified including: (i) hiring additional accounting and financial reporting personnel with SEC reporting experience, (ii) expanding the capabilities of existing accounting and financial reporting personnel through continuous training and education in the accounting and reporting requirements under International Financial Reporting Standards, or IFRS, and SEC rules and regulations, (iii) establishing effective monitoring and oversight controls for non-recurring and complex transactions to ensure the accuracy and completeness of our company's consolidated financial statements and related disclosures and (iv) implementing formal processes and controls to identify, monitor and mitigate segregation of duties conflicts.

The presence of material weaknesses could result in financial statement errors which, in turn, could lead to errors in our financial reports or delays in our financial reporting, which could require us to restate our operating results or result in our auditors issuing a qualified audit report. In order to establish and maintain effective disclosure controls and procedures and internal controls over financial reporting, we will need to expend significant resources and provide significant management oversight. Developing, implementing and testing changes to our internal controls may require specific compliance training of our directors and employees, entail substantial costs in order to modify our existing accounting systems, take a significant period of time to complete and divert management's attention from other business concerns. These changes may not, however, be effective in establishing and maintaining adequate internal controls.

If either we are unable to conclude that we have effective internal controls over financial reporting or our independent auditors are unwilling or unable to provide us with an unqualified report on the effectiveness of our internal controls over financial reporting as required by Section 404(b) of the Sarbanes-Oxley Act, investors may lose confidence in our operating results, the price of the ADSs could decline and we may be subject to litigation or regulatory enforcement actions. In addition, if we are unable to meet the requirements of Section 404 of the Sarbanes-Oxley Act, we may not be able to remain listed on The Nasdaq Global Select Market, or Nasdaq.

Risks Related to Regulatory Approvals

If we are not able to obtain required regulatory approvals, we will not be able to commercialize OPT-302 or any future product candidate, and our ability to generate product revenue will be impaired.

OPT-302 and any future product candidate that we may develop, as well as the activities associated with their development and commercialization, including their design, research, testing, manufacture, safety, efficacy, recordkeeping, labeling, packaging, storage, approval, advertising, promotion, sale and distribution are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by similar regulatory authorities outside the United States. Failure to obtain marketing approval for, and thus commercialize any product candidate, could negatively impact our ability to generate any revenue from product sales.

We have not received approval from regulatory authorities to market any product candidate in any jurisdiction, and it is possible that our product candidate will never obtain the appropriate regulatory approvals necessary for us to commence product sales. Neither we nor any collaborator is permitted to market our product candidate in the United States or any other jurisdiction until we receive regulatory approval of a BLA from the FDA or similar application from regulatory authorities outside of the United States.

The time required to obtain approval of a BLA by the FDA or similar application from regulatory authorities outside of the United States is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authority. Prior to submitting a BLA to the FDA or any comparable application to any other non-U.S. regulatory authorities for approval of any product candidate, we will need to complete pivotal Phase 3 clinical trials and demonstrate favorable results with respect to safety, tolerability and efficacy. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions.

Securing marketing approvals requires the submission of extensive nonclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the safety and efficacy of our product candidate for the specified indications. We expect to rely on third-party CROs, consultants and our collaborators to assist us in filing and supporting the applications necessary to gain marketing approvals. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, regulatory authorities. Errors in the submission of applications for marketing approval or issues, including those related to gathering the appropriate data and the inspection process, may ultimately delay or affect our ability to obtain regulatory approval, commercialize our product candidate and generate product revenue.

Our failure to obtain regulatory approval in international jurisdictions would prevent us from marketing our product candidates outside the United States.

If we succeed in developing any products, we intend to market them in non-U.S. jurisdictions in addition to the United States. In order to market and sell our products in other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. We may not obtain non-U.S. regulatory approvals on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions. Approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. If we fail to obtain approval of any of our product candidates by regulatory authorities in another country we will be unable to commercialize our product in that country, and the commercial prospects of that product candidate and our business prospects could decline. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, we must secure product reimbursement approvals before regulatory authorities will approve the product for sale in that country. Obtaining non-U.S. regulatory approvals and compliance with non-U.S. regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries and regulatory approval in one country does not ensure approval in any other country, while a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. Also, regulatory approval for any of our product candidates may be withdrawn if we fail to comply with regulatory requirements, if problems occur after the product candidate reaches the market or for other reasons. If we fail to comply with the regulatory requirements in international markets and fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business will be negatively affected.

Even if OPT-302 combination therapy or any future product candidate receives regulatory approval, it may still face future development and regulatory difficulties.

Even if we obtained regulatory approval for a product candidate, it would be subject to ongoing requirements by the FDA and comparable non-U.S. regulatory authorities governing the manufacture, quality control, further development, labeling, packaging, storage, distribution, safety surveillance, import, export, advertising, promotion, recordkeeping and reporting of safety and other post-market information. The FDA and comparable non-U.S. regulatory authorities will continue to closely monitor the safety profile of any product even after approval. If the FDA, or comparable non-U.S. regulatory authorities, become aware of new safety information after approval of any of our product candidates, it may require labeling changes or establishment of a risk evaluation and mitigation strategy or similar strategy, impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance.

In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current good manufacturing practices, or cGMP, regulations and standards. If we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. If we, our product candidates or the manufacturing facilities for our product candidates fail to comply with applicable regulatory requirements, or undesirable side effects caused by such products are identified, a regulatory agency may:

- issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings about such product;

- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;
- revise labeling, including adding limitations on approved uses or the additions of additional warnings, contraindications or other safety information including boxed warnings;
- impose a REMS which may include distribution on or use restrictions;
- require that we conduct post-marketing studies;
- require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend marketing of, withdraw regulatory approval of or recall such product;
- suspend any ongoing clinical studies;
- refuse to approve pending applications or supplements to applications filed by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of products or require us to initiate a product recall.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our products and generate product revenue.

Advertising and promotion of any product candidate that obtains approval in the United States will be heavily scrutinized by the FDA, the Department of Justice, the Department of Health and Human Services' Office of Inspector General, state attorneys general, members of Congress and the public. Violations, including promotion of our products for unapproved (or off-label) uses, are subject to enforcement letters, inquiries and investigations and significant civil and criminal sanctions by the government. In the United States, engaging in the impermissible promotion of our products for off-label uses can also subject us to false claims litigation under federal and state statutes, which can lead to significant civil and criminal penalties. Additionally, comparable non-U.S. regulatory authorities will heavily scrutinize advertising and promotion of any product candidate that obtains approval outside of the United States.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would negatively affect our business, prospects and ability to achieve or sustain profitability.

Risks Related to Our Reliance on Third Parties

We have relied on, and expect to continue to rely on, third-party manufacturers to produce OPT-302 or any future product candidates. Any failure by a third-party manufacturer to produce acceptable product candidates for us pursuant to our specifications and regulatory standards may delay or impair our ability to initiate or complete our clinical trials, obtain and maintain regulatory approvals or commercialize approved products.

The manufacturing of biologic drugs such as OPT-302 is complex and the process of identifying the qualifying suppliers takes a significant investment of time and money. We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates, and we lack the resources and the capabilities to do so. As a result, we currently rely, and expect to rely for the foreseeable future, on third-party manufacturers to supply us with OPT-302 and any future product candidates.

We currently have a sole source relationship with Patheon N.V., a division of Thermo Fisher Scientific Inc., pursuant to which they supply us with OPT-302 drug substance and drug product. If there should be any disruption in our supply arrangement with Patheon, including any adverse events affecting Patheon or Thermo Fisher Scientific, it could have a negative effect on the clinical development of OPT-302 and other operations while we work to identify and qualify an alternate supply source. In addition, we do not have a long-term supply arrangement to purchase anti-VEGF-A therapy for use in combination with OPT-302 in our clinical trials and acquire such drug product on a purchase order basis. Any complications with our existing suppliers of anti-VEGF-A therapies could considerably delay our clinical trials for OPT-302, including our Phase 3 pivotal clinical program of OPT-302 for the treatment of wet AMD, or the regulatory approvals of OPT-302.

Reliance on third-party suppliers and manufacturers entails risks to which we would not be subject if we manufacture product candidates or products ourselves. For example, if we do not maintain our key manufacturing relationships, including with Patheon, we may fail to find replacement manufacturers or develop our own manufacturing capabilities in a timely manner or at all, which could delay or impair our ability to obtain regulatory approval for our products and substantially increase our costs or deplete profit margins, if any. If we do find replacement manufacturers, we may not be able to enter into agreements with them on terms and conditions favorable to us in a timely manner, if at all, and there could be a substantial delay before new facilities could be qualified and registered with or licensed by the FDA and other comparable non-U.S. regulatory authorities.

Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- failure of the third party to manufacture product candidates according to our schedule, or at all, including if our third-party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- breach of the manufacturing agreement by the third party because of factors beyond our control (including a failure to manufacture product candidates in accordance with our product specifications);
- the failure of the third-party manufacturer to comply with applicable regulatory requirements and reliance on third-parties for manufacturing process development, regulatory compliance and quality assurance;
- mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;
- clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales;
- misappropriation of our proprietary information, including our trade secrets and know-how;
- termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and
- reliance on the third party for regulatory compliance, quality assurance and safety and pharmacovigilance reporting.

The FDA and other comparable non-U.S. regulatory authorities require manufacturers to register manufacturing facilities. The FDA and other comparable non-U.S. regulatory authorities also inspect these facilities to confirm compliance with cGMP. Contract manufacturers may face manufacturing or quality control problems causing drug substance production and shipment delays or a situation where the contractor may not be able to maintain compliance with the applicable cGMP requirements. We may have little to no control regarding the occurrence of third-party manufacturer incidents. Failure by our third-party manufacturers and suppliers to pass such inspections and otherwise satisfactorily complete the FDA approval regimen with respect to our product candidate may result in regulatory actions such as the issuance of FDA Form 483 notices of

observations, warning letters or injunctions or the loss of operating licenses. In addition, our third-party manufacturers and suppliers are subject to numerous environmental, health and safety laws and regulations, including those governing the handling, use, storage, treatment and disposal of waste products, and failure to comply with such laws and regulations could result in significant costs associated with civil or criminal fines and penalties for such third parties. Any failure to comply with cGMP requirements or other FDA or comparable non-U.S. regulatory requirements could negatively impact our clinical research activities and our ability to develop OPT-302 or any future product candidates and market our products following approval.

If OPT-302 or any future product candidates are approved by the FDA or other comparable non-U.S. regulatory authorities for commercial sale, we may need to manufacture such product candidate in larger quantities. We intend to use third-party manufacturers for commercial quantities of OPT-302 to the extent we advance this product candidate and other product candidates. Our manufacturers may not be able to successfully increase the manufacturing capacity for any of our product candidates in a timely or efficient manner, or at all. If we are unable to successfully increase the manufacturing capacity for a product candidate, the regulatory approval or commercial launch of that product candidate may be delayed or there may be a shortage in the supply of the product candidate.

In addition, the operations of our third-party manufacturers may be subject to earthquakes, power shortages, telecommunications failures, failures or breaches of information technology systems, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, such as the recent COVID-19 pandemic, and other natural or man-made disasters or business interruptions. Damage or extended periods of interruption to our facilities due to fire, natural disaster, power loss, communications failure, unauthorized entry or other events could cause us to cease or delay development of some or all of our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may negatively affect our future profit margins and our ability to develop our product candidates and commercialize any products that receive regulatory approval on a timely basis.

In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer, we may have difficulty transferring such skills or technology to another third party and a feasible alternative many not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines and the manufacturer may be required to obtain applicable licenses or approvals. The delays associated with the verification of a new manufacturer, if we are able to identify an alternative source, could negatively affect our ability to develop product candidates in a timely manner or within budget.

The manufacture of biologic products is complex and we are subject to many manufacturing risks, any of which could substantially increase our costs and limit supply of our products.

The manufacture of biologic products is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of biologic products often encounter difficulties in production, particularly in scaling up and validating initial production and ensuring the avoidance of contamination. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, operator error and shortages of qualified personnel, as well as compliance with strictly enforced federal, state and non-U.S. regulations. We cannot assure you that any stability or other issues relating to the manufacture of OPT-302 will not occur in the future.

The process of manufacturing OPT-302 is complex, highly regulated and subject to several risks, including:

- the process of manufacturing biologics is susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error and improper storage conditions. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered in our product candidates or in the manufacturing facilities in which our product candidates are made, the manufacturing facilities may need to be closed for an extended period of time to investigate and eliminate the contamination;
- the manufacturing facilities in which our products are made could be negatively affected by equipment failures, labor and raw material shortages, financial difficulties of our contract manufacturers, natural disasters, power failures, local political unrest and numerous other factors; and
- any adverse developments affecting manufacturing operations for our product candidates may result in shipment delays, inventory shortages, lot failures, and for any approved products, product withdrawals, or recalls or other interruptions in the supply of our products. We may also have to record inventory write-offs and incur other charges and expenses for products that fail to meet specifications, undertake costly remediation efforts or seek costlier manufacturing alternatives.

To date, OPT-302 has been manufactured by a single third-party manufacturer, Patheon, solely for preclinical studies and Phase 1 and 2 trials. This manufacturer may not be able to scale production to the larger quantities required for large clinical trials, including our planned Phase 3 clinical trials of OPT-302 in combination with anti-VEGF-A therapy for the treatment of wet AMD, and to commercialize OPT-302, on a timely basis or at all. Any such failure will require us to seek alternative manufacturing sources, which may result in considerable additional expense and delays in our planned clinical trials. We have limited process development capabilities and have access only to external manufacturing capabilities. We do not have and we do not currently plan to acquire or develop the facilities or capabilities to manufacture bulk drug substance or filled drug product for use in human clinical trials or commercialization. Any delay or interruption in the supply of clinical trial materials, including as a result of breach by us or Patheon of our agreement with Patheon, or our inability to agree to the terms of supply or related services in any statement of work, could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely.

Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates proceed through nonclinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause OPT-302 or any future product candidate to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. Such changes may also require additional testing, FDA notification or FDA approval. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of OPT-302 or any future product candidate or jeopardize our ability to commence sales and generate revenue.

We rely on third parties to conduct our clinical trials and some aspects of our research and development activities, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing.

We currently rely on, and expect to continue to rely on, third parties, such as CROs, clinical data management organizations, medical institutions, consultants and clinical investigators, to conduct our clinical

trials and certain aspects of our research and development activities. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities and such alternative arrangements may not be available on terms acceptable to us.

Our reliance on these third parties for research and development activities will reduce our control over these activities, but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and clinical trial protocols. Moreover, the FDA requires us to comply with standards, commonly referred to as current Good Clinical Practices, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We are also required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements, standard operating procedures or clinical trial protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for OPT-302 or any future product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development, marketing approval and/or commercialization of OPT-302 or any future product candidates, producing additional losses and depriving us of potential revenue.

We may seek to establish commercial collaborations for our product candidates, and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. We may decide to collaborate with other pharmaceutical and biotechnology companies for the development and potential commercialization of our product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or comparable non-U.S. regulatory authorities, the potential market for the product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products and the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborators may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate.

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to

collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

Risks Relating to Intellectual Property

Our success depends upon our ability to obtain and maintain intellectual property protection for our products and technologies.

Our success will depend in significant part on our current or future licensors', licensees' or collaborators' ability to establish and maintain adequate protection of our owned and licensed intellectual property covering the product candidates we plan to develop, and the ability to develop these product candidates and commercialize the products resulting therefrom, without infringing the intellectual property rights of others. In addition to taking other steps to protect our intellectual property, we hold issued patents, we have applied for patents, and we intend to continue to apply for, patents with claims covering our technologies, processes and product candidates when and where we deem it appropriate to do so. We have filed patent applications both in the United States and in certain non-U.S. jurisdictions to obtain patent rights to inventions we have developed, with claims directed to compositions of matter, methods of use and other technologies relating to our programs. There can be no assurance that any of these patent applications will issue as patents or, for those applications that do mature into patents, that the claims of the patents will exclude others from making, using or selling our product candidates or products that compete with or are similar to our product candidates. In countries where we have not sought and do not seek patent protection, third parties may be able to manufacture and sell our product candidates without our permission, and we may not be able to stop them from doing so.

With respect to patent rights, we do not know whether any of the pending patent applications for any of our product candidates will result in the issuance of patents that effectively protect our technologies, processes and product candidates, or if any of our issued patents or our current or future licensors', licensees' or collaborators' issued patents will effectively prevent others from commercializing competitive technologies, processes and products. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or in some cases not at all, until they are issued as a patent. Therefore, we cannot be certain that we or our current or future licensors, licensees or collaborators were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our current or future licensors, licensees or collaborators were the first to file for patent protection of such inventions. For a description of our patent portfolio, see "Business—Intellectual Property."

Any changes we make to OPT-302 or any future product candidates to cause them to have what we view as more advantageous properties may not be covered by our existing patents and patent applications, and we may be required to file new applications and/or seek other forms of protection for any such altered product candidates. The patent landscape surrounding the technology underlying our product candidates is potentially crowded, and there can be no assurance that we would be able to secure patent protection that would adequately cover an alternative to OPT-302 or any future product candidates.

The patent prosecution process is expensive and time-consuming, and we and our current or future licensors, licensees or collaborators may not be able to prepare, file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our current or future licensors, licensees or collaborators will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection for them. Moreover,

in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain or enforce the patents, covering technology that we license from or license to third parties and may be reliant on our current or future licensors, licensees or collaborators to perform these activities, which means that these patent applications may not be prosecuted, and these patents enforced, in a manner consistent with the best interests of our business. If our current or future licensors, licensees or collaborators fail to establish, maintain, protect or enforce such patents and other intellectual property rights, such rights may be reduced or eliminated. If our current or future licensors, licensees or collaborators are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised.

Similar to the patent rights of other biotechnology companies, the scope, validity and enforceability of our owned and licensed patent rights generally are highly uncertain and involve complex legal and factual questions. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. In recent years, these areas have been the subject of much litigation in the industry. As a result, the issuance, scope, validity, enforceability and commercial value of our and our current or future licensors', licensees' or collaborators' patent rights are highly uncertain. Our and our current or future licensors', licensees' or collaborators' pending and future patent applications may not result in patents being issued that protect our technology or product candidates, or products resulting therefrom, in whole or in part, or that effectively prevent others from commercializing competitive technologies and products. The patent examination process may require us or our current or future licensors, licensees or collaborators to narrow the scope of the claims of pending and future patent applications, which would limit the scope of patent protection that is obtained, if any. Our and our current or future licensors', licensees' or collaborators' patent applications cannot be enforced against third parties practicing the technology that is currently claimed in such applications unless and until a patent issues from such applications, and then only to the extent the claims that issue are broad enough to cover the technology being practiced by those third parties.

Furthermore, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after the resulting products are commercialized. As a result, our owned and in-licensed patents may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. We expect to seek extensions of patent terms for our issued patents, where available. This includes in the United States under the Hatch-Waxman Act, which permits a patent term extension of up to five years beyond the original expiration date of the patent as compensation for regulatory delays. However, such a patent term extension cannot lengthen the remaining term of a patent beyond a total of 14 years from the product's approval date. Only one patent applicable to each regulatory review period may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended, with extended rights limited to the approved product, its approved uses and/or its manufacture. During the period of patent term extension, the claims of a patent are not enforceable for their full scope, but are instead limited to the scope of the approved product. In addition, the applicable authorities, including the FDA in the United States, and any comparable non-U.S. regulatory authorities, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. In addition, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to the expiration of relevant patents or otherwise failing to satisfy applicable requirements. If this occurs, any period during which we have the right to exclusively market our product will be shorter than we would otherwise expect, and our competitors may obtain approval of and launch products earlier than might otherwise be the case.

We may not be able to protect our intellectual property rights throughout the world.

The legal protection afforded to inventors and owners of intellectual property in countries outside of the United States may not be as protective or effective as that in the United States and we may, therefore, be unable to acquire and enforce intellectual property rights outside the United States to the same extent as in the United

States. Whether filed in the United States or abroad, our patent applications may be challenged or may fail to result in issued patents.

In addition, our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from practicing our technologies or from developing or commercializing competing products. Furthermore, others may independently develop or commercialize similar or alternative technologies or drugs, or design around our patents. Our patents may be challenged, invalidated, circumvented or narrowed, or fail to provide us with any competitive advantages. In many non-U.S. countries, patent applications and/or issued patents, or parts thereof, must be translated into the native language. If our patent applications or issued patents are translated incorrectly, they may not adequately cover our technologies; in some countries, it may not be possible to rectify an incorrect translation, which may result in patent protection that does not adequately cover our technologies in those countries.

Filing, prosecuting, enforcing and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States may be less extensive than those in the United States. In addition, the laws of some non-U.S. countries do not protect intellectual property rights to the same extent as federal and certain state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with OPT-302 or any future product candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in non-U.S. jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals. This could make it difficult for us to stop the infringement of our patents or the marketing of competing products in violation of our proprietary rights, generally. Proceedings to enforce our patent rights in non-U.S. jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could place our patent applications at risk of not issuing and could provoke third parties to assert claims against us or our collaborator. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful.

The requirements for patentability differ and certain countries have heightened requirements for patentability, requiring more disclosure in the patent application. In addition, certain countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we may have limited remedies if patents are infringed or if we are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. Accordingly, our efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect OPT-302 and any future product candidates.

As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property rights, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves technological and legal complexity, and obtaining and enforcing biopharmaceutical patents is

costly, time-consuming and inherently uncertain. The U.S. Supreme Court in recent years has issued rulings either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations or ruling that certain subject matter is not eligible for patent protection. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by Congress, the federal courts, the USPTO and equivalent bodies in non-U.S. jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce existing patents and patents we may obtain in the future.

Patent reform laws, such as the Leahy-Smith America Invents Act, or the Leahy-Smith Act, as well as changes in how patent laws are interpreted, could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. The Leahy-Smith Act made a number of significant changes to U.S. patent law. These include provisions that affect the filing and prosecution strategies associated with patent applications, including a change from a "first-to-invent" to a "first-inventor-to-file" patent system, and a change allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO-administered post-grant proceedings, including post-grant review, *inter partes* review and derivation proceedings. The USPTO has developed regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act and, in particular, the "first-inventor-to-file" provisions, became effective in 2013. The Leahy-Smith Act and its implementation may increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have harm our business, financial condition and results of operations.

We may be unable to obtain intellectual property rights or technology necessary to develop and commercialize OPT-302 and any future product candidates.

The patent landscape around our programs is complex, and there may be one or more third-party patents and patent applications containing subject matter that might be relevant to OPT-302. Depending on what claims may ultimately issue from these patent applications, and how courts construe the issued patent claims, as well as depending on the ultimate formulation and method of use of OPT-302 or any future product candidates, we may need to obtain a license to practice the technology claimed in such patents. There can be no assurance that such licenses will be available on commercially reasonable terms, or at all. If a third party does not offer us a necessary license or offers a license only on terms that are unattractive or unacceptable to us, we might be unable to develop and commercialize one or more of our product candidates, which would harm our business, financial condition and results of operations. Moreover, even if we obtain licenses to such intellectual property, but subsequently fail to meet our obligations under the relevant license agreements, or such license agreements are terminated for any other reasons, we may lose our rights to the technologies licensed under those agreements.

The licensing or acquisition of third-party intellectual property rights is an area in which many companies operate that have interests that are in conflict with ours, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment, or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could harm our business, financial condition, results of operations and prospects.

We may become involved in lawsuits or other proceedings to protect or enforce our intellectual property, which could be expensive, time-consuming and unsuccessful and have a negative effect on the success of our business.

Third parties may infringe our patents or misappropriate or otherwise violate our intellectual property rights. In the future, we may initiate legal proceedings to enforce or defend our intellectual property rights, to protect our trade secrets or to determine the validity or scope of intellectual property rights we own or control. Also, third parties may initiate legal proceedings against us to challenge the validity or scope of intellectual property rights we own, control or to which we have rights. For example, generic or biosimilar drug manufacturers or other competitors or third parties may challenge the scope, validity or enforceability of our patents, requiring us to engage in complex, lengthy and costly litigation or other proceedings. These proceedings can be expensive and time-consuming and many of our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating intellectual property rights we own, control or have rights to, particularly in countries where the laws may not protect those rights as fully as in the United States. Litigation could result in substantial costs and diversion of management resources, which could harm our business and financial results. In addition, if we initiated legal proceedings against a third party to enforce a patent covering a product candidate, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the United States, defendants usually assert counterclaims alleging invalidity or unenforceability. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. In an infringement or declaratory judgment proceeding, a court may decide that a patent owned by or licensed to us is invalid or unenforceable, or may refuse to stop the other party from using the subject matter alleged to be infringing on the grounds that our patents do not cover that subject matter. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, narrowed, held unenforceable or interpreted in such a manner that would not preclude third parties from entering the market with competing products.

Third-party pre-issuance submission of prior art to the USPTO, or opposition, derivation, revocation, reexamination, *inter partes* review or interference proceedings, or other pre-issuance or post-grant proceedings or other patent office proceedings or litigation in the United States or other jurisdictions provoked by third parties or brought by us, may be necessary to determine the inventorship, priority, patentability or validity of inventions with respect to our patents or patent applications. An unfavorable outcome could leave our technology or product candidates without patent protection, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or could require us to obtain license rights from the prevailing party in order to be able to manufacture or commercialize our product candidates without infringing third-party patent rights. Our business could be harmed if the prevailing party in such a case does not offer us a license on commercially reasonable terms, or at all. Even if we obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Even if we successfully defend such litigation or proceeding, we may incur substantial costs and our defense may distract our management and other employees.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, many non-U.S. jurisdictions have rules of discovery that are different than those in the United States and that may make defending or enforcing our patents extremely difficult. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could negatively affect the price of the ADSs and our ordinary shares.

Third parties may initiate legal proceedings against us alleging that we infringe their intellectual property rights or we may initiate legal proceedings against third parties to challenge the validity or scope of intellectual property rights controlled by third parties, the outcome of which would be uncertain and could harm our business.

Our commercial success depends upon our ability to develop, manufacture, market and sell OPT-302 and any future product candidates that we may develop and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and proprietary rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Third parties may initiate legal proceedings against us alleging that we infringe their intellectual property rights or we may initiate legal proceedings against third parties to challenge the validity or scope of intellectual property rights controlled by third parties, including in oppositions, interferences, revocations, reexaminations, *inter partes* review or derivation proceedings before the USPTO or its counterparts in other jurisdictions. These proceedings can be expensive and time-consuming and many of our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can.

We could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent of a third party. A finding of infringement could prevent us from commercializing OPT-302 or any future product candidates or force us to cease some of our business operations, which could materially harm our business.

We may not be aware of all third-party intellectual property rights potentially relating to OPT-302 or any future product candidates and technologies. We are not aware of any facts that would lead us to conclude that the valid and enforceable claims of any third-party patents would reasonably be interpreted to cover our product candidates. As to pending third-party applications, we cannot predict with any certainty which claims will issue, if any, or the scope of such issued claims. Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, enforceability or priority. A court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could materially and negatively affect our ability to commercialize any product candidates we may develop and any other product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If any such third-party patents (including those that may issue from such applications) were successfully asserted against us or other commercialization partners and we were unable to successfully challenge the validity or enforceability of any such asserted patents, then we and other commercialization partners may be prevented from commercializing our product candidates, or may be required to pay significant damages, including treble damages and attorneys' fees if we are found to willfully infringe the asserted patents, or obtain a license to such patents, which may not be available on commercially reasonable terms, or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. Any of the foregoing would harm our business, financial condition and operating results.

Although we have reviewed certain third-party patents and patent filings that we believe may be relevant to our therapeutic candidates or products, we have not conducted a freedom-to-operate search or analysis for any of our therapeutic candidates or products, and we may not be aware of patents or pending or future patent applications that, if issued, would block us from commercializing our therapeutic candidates or products. Thus, we cannot guarantee that our therapeutic candidates or products, or our commercialization thereof, do not and will not infringe any third party's intellectual property.

We may be subject to claims by third parties asserting misappropriation of intellectual property, or claiming ownership of what we regard as our own intellectual property.

Although we seek to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed confidential information or intellectual property, including trade secrets or other proprietary information, of any such employee's former employer, or that third parties have an interest in our patents as an inventor or co-inventor. Litigation may be necessary to defend against these claims. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or the services of personnel or sustain other damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms, or at all. Even if we successfully prosecute or defend against such claims, litigation could result in substantial costs and distract management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could harm our business, financial condition, results of operations and prospects.

Our inability to protect our confidential information and trade secrets would harm our business and competitive position.

In addition to seeking patents for some of our technology and product candidates, we also rely substantially on trade secrets, including unpatented know-how, technology and other proprietary materials and information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. However, these steps may be inadequate, we may fail to enter into agreements with all such parties or any of these parties may breach the agreements and disclose our trade secrets and there may be no adequate remedy available for such breach of an agreement. We cannot assure you that our trade secrets will not be disclosed or that we can meaningfully protect our trade secrets. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time consuming, and the outcome is unpredictable. In addition, some courts both within and outside the United States may be less willing, or unwilling, to protect trade secrets. If a competitor lawfully obtained or independently developed any technology or information that we protect as trade secret, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make products that are similar to OPT-302 and any future product candidates we may develop or utilize similar technology but that are not covered by the claims of the patents that we exclusively license or may own in the future;

- we, our licensors or our future collaborators, might not have been the first to make the inventions covered by the issued patents and pending patent applications that we exclusively license or may own in the future;
- we, our licensors or our future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or exclusively licensed intellectual property rights;
- it is possible that our pending patent applications or those that we may file in the future, including those that we have licensed, will not result in issued patents;
- issued patents to which we hold rights may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in major commercial markets in which we do not have sufficient patent rights to stop such sales;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may be asserted against our product candidates and technologies in a manner that harms our business; and
- we may choose not to file a patent application in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such trade secrets or know-how.

Should any of these events occur, they could harm our business, financial condition, results of operations and prospects.

If our trademarks and trade names are not maintained and adequately protected, we may not be able to build name recognition in our markets of interest, and our business may be negatively affected.

Failure to obtain trademark registrations in the future, could limit our ability to protect and enforce our trademarks and impede our marketing efforts in the countries in which we operate. We may not be able to protect our rights to trademarks and trade names which we may need to build name recognition with potential partners or customers in our markets of interest. As a means to enforce any future trademark rights and prevent infringement, we may be required to file trademark claims against third parties or initiate trademark opposition proceedings. This can be expensive and time consuming and can strain the financial resources of a company of our size, and we may not be successful in enforcing our trademark rights. In addition, our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented, declared generic or determined to be infringing on other marks.

Future trademark applications in the United States and in other non-U.S. jurisdictions where we may file may not be allowed or may subsequently be opposed. Even if these applications result in registration of trademarks, third parties may challenge our use or registration of these trademarks in the future. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be negatively affected.

Our product candidates may face competition sooner than anticipated from biosimilar products.

Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, our product candidates may face competition from biosimilar products. In the United States, our product candidates are regulated by the FDA. The Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated pathway for the approval of biosimilar and interchangeable biologic products. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar

biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our product candidates.

There is a risk that any exclusivity we may be afforded if any of our product candidates are approved as a biologic product under a BLA could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic or biosimilar competition sooner than anticipated. Moreover, the extent to which a biosimilar product, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biologic products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. In addition, a competitor could decide to forego the biosimilar approval path and submit a full BLA after completing its own preclinical studies and clinical trials. In such cases, any exclusivity to which we may be eligible under the BPCIA would not prevent the competitor from marketing its product as soon as it is approved.

In Europe, the European Commission has granted marketing authorizations for several biosimilar products pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In Europe, a competitor may reference data supporting approval of an innovative biological product, but will not be able to market it until 10 years after the time of approval of the innovative product. This 10-year marketing exclusivity period may be extended to 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. In addition, companies may be developing biosimilar products in other countries that could compete with our products, if approved.

If competitors are able to obtain marketing approval for biosimilars referencing our product candidates, if approved, such products may become subject to competition from such biosimilars, with the attendant competitive pressure and potential adverse consequences. Such competitive products may be able to immediately compete with us in each indication for which our product candidates may have received approval.

Risks Related to Ownership of the ADSs and this Offering

There has been no prior market for the ADSs and an active and liquid market for our securities may fail to develop, which could harm the market price of the ADSs.

While our ordinary shares have been listed on the Australian Securities Exchange, or ASX, since 1985, and certain ADSs have been traded on the over-the-counter market in the United States since June 2011 through our existing sponsored Level I ADR facility with The Bank of New York Mellon, as depositary, prior to this offering, there has been no public market on a U.S. national securities exchange for our ordinary shares or ADSs. Although the ADSs have been approved for listing on Nasdaq, an active trading market for the ADSs may never develop or be sustained following this offering. The initial offering price of the ADSs will be determined through negotiations between us and the underwriters and will be based, in part, on prevailing market prices of our ordinary shares on the ASX, after taking into account market conditions and other factors. This offering price may not be indicative of the market price of the ADSs after this offering. In the absence of an active trading market for the ADSs, investors may not be able to sell their ADSs at or above the offering price or at the time that they would like to sell.

The trading price and volume of the ADSs may be volatile, and purchasers of the ADSs or pre-funded warrants could incur substantial losses.

The price and trading volumes of our ordinary shares and ADSs may be significantly affected by events such as announcements regarding scientific and clinical results concerning product candidates currently being developed by us, our collaboration partners or our main competitors, changes in market conditions related to our sector of activity, announcements of new contracts, technological innovations and collaborations by us or our main competitors, developments concerning intellectual property rights, as well as the development, regulatory approval and commercialization of new products by us or our main competitors and changes in our financial results.

In addition, equity markets may be subject to considerable price and trading volume fluctuations, and often, these movements do not reflect the operational and financial performance of the listed companies concerned. In particular, biotechnology companies' share prices have been highly volatile in the past and may continue to be highly volatile in the future. As we operate in a single industry, we are especially vulnerable to these factors to the extent that they affect our industry. Fluctuations in the stock market as well as the macroeconomic environment could significantly affect the price of the ADSs. As a result of this volatility, investors may not be able to sell their ADSs at or above the price originally paid for the security. The market price and trading volume for the ADSs may be influenced by many factors, including:

- actual or anticipated fluctuations in our financial condition and operating results;
- actual or anticipated changes in our growth rate relative to our competitors;
- competition from existing products or new products that may emerge;
- announcements by us or our competitors of significant acquisitions, divestitures, spin-offs, strategic partnerships, joint ventures, collaborations, capital commitments or changes in business strategy;
- adverse results of delays in our or any of our competitors' preclinical studies or clinical trials;
- adverse regulatory decisions, including failure to receive regulatory approval for any of our product candidates;
- the termination of a strategic alliance or the inability to establish additional strategic alliances;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- issuance of new or updated research or reports by securities analysts;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- ADS price and volume fluctuations attributable to inconsistent trading volume levels of the ADSs;
- price and volume fluctuations in trading of our ordinary shares on the ASX;
- short selling or other market manipulation activities;
- fluctuations of exchange rates between the U.S. dollar and the Australian dollar;
- additions or departures of key management or scientific personnel;
- disruptions in our supply or manufacturing arrangements;
- disputes or other developments related to proprietary rights, including patents, litigation matters and our ability to obtain patent and other intellectual property protection for our technologies;
- changes to coverage policies or reimbursement levels by commercial third-party payors and government payors and any announcements relating to coverage policies or reimbursement levels;
- litigation involving our company;

- announcement or expectation of additional debt or equity financing efforts;
- natural disasters or other calamities or disease outbreaks, such as the COVID-19 pandemic;
- sales of the ADSs by us, our affiliates or our other shareholders; and
- general economic and market conditions.

These and other market and industry factors may cause the market price and demand for the ADSs to fluctuate, regardless of our actual operating performance, which may limit or prevent investors from readily selling their ADSs and may otherwise negatively affect the liquidity of the trading market for the ADSs.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, the price of the ADSs and their trading volume could decline.

The trading market for the ADSs depends in part on the research and reports that securities or industry analysts publish about us or our business. As a public listed company in Australia since 1985, our equity securities are currently subject to coverage by a number of analysts. If fewer securities or industry analysts cover our company, the trading price for the ADSs could be negatively impacted. If one or more of the analysts who covers us downgrades our equity securities or publishes incorrect or unfavorable research about our business, the price of the ADSs would likely decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, or downgrades our securities, demand for the ADSs could decrease, which could cause the price of the ADSs or their trading volume to decline.

We do not currently intend to pay dividends on our securities and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of the ADSs.

We have not declared or paid any cash dividends on our ordinary shares since February 2005 and do not currently intend to do so for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our operations and growth. Therefore, you are not likely to receive any dividends on your ADSs for the foreseeable future and the success of an investment in the ADSs will depend upon any future appreciation in its value. Consequently, investors may need to sell all or part of their holdings of the ADSs after price appreciation, which may never occur, as the only way to realize any future gains on their investment. There is no guarantee that the ADSs will appreciate in value or even maintain the price at which our shareholders have purchased them. Investors seeking cash dividends should consider not purchasing the ADSs.

While we do not anticipate paying any cash dividends on our ordinary shares in the foreseeable future, if such a dividend is declared, the depositary for the ADSs has agreed to pay to you the cash dividends or other distributions it or the custodian receives on our ordinary shares or other deposited securities after deducting its fees and expenses. You will receive these distributions in proportion to the number of our ordinary shares your ADSs represent. However, in accordance with the limitations set forth in the deposit agreement, it may be unlawful or impractical to make a distribution available to holders of ADSs. We have no obligation to take any other action to permit the distribution of the ADSs, ordinary shares, rights or anything else to holders of the ADSs. This means that you may not receive the distributions we make on our ordinary shares or any value from them if it is unlawful or impractical to make them available to you. These restrictions may negatively impact the value of your ADSs. In addition, exchange rate fluctuations may affect the amount of Australian dollars that we are able to distribute, and the amount in U.S. dollars that our shareholders receive upon the payment of cash dividends or other distributions we declare and pay in Australian dollars, if any. These factors could harm the value of the ADSs, and, in turn, the U.S. dollar proceeds that holders receive from the sale of the ADSs.

You will experience immediate and substantial dilution in the net tangible book value of the ADSs you purchase in this offering.

The initial public offering price of the ADSs is substantially higher than the net tangible book value per ADS or per ordinary share immediately after this offering. If you purchase ADSs or pre-funded warrants in this offering, you will suffer

immediate dilution of US$9.69 per ADS (or US$1.21 per ordinary share), or US$9.40 per ADS (or US$1.18 per ordinary share) if the underwriters exercise their option to purchase additional shares in full, representing the difference between our as adjusted net tangible book value per ADS or per ordinary share after giving effect to the sale of ADSs and pre-funded warrants in this offering and the initial public offering price of US$13.50 per ADS and US$13.49999 per pre-funded warrant. See "Dilution." If outstanding options or pre-funded warrants offered and sold in this offering are exercised in the future, you will experience additional dilution.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

We will have broad discretion in the application of the net proceeds that we receive from this offering as well as of our existing cash and cash equivalents and non-current financial assets, and we may spend or invest these funds in a way with which our shareholders or holders of the ADSs disagree. Our failure to apply these funds effectively could harm our business and financial condition. Pending their use, we may invest the net proceeds from the offering in a manner that does not produce income or that loses value. These investments may not yield a favorable return to our investors.

Future sales of ordinary shares or ADSs by existing holders could depress the market price of the ordinary shares or ADSs.

Based on 269,157,769 ordinary shares outstanding as of June 30, 2020, upon the closing of this offering, we will have outstanding a total of 337,664,169 ordinary shares (including ordinary shares represented by ADSs), assuming no exercise of the underwriters' option to purchase additional ADSs and no exercise of outstanding options or pre-funded warrants offered and sold in this offering. Each member of our senior management and board of directors and their affiliates are subject to lock-up agreements with the underwriters that restrict their ability to transfer ordinary shares, options and other securities convertible into, exchangeable for, or exercisable for ordinary shares during the period ending on, and including, the 90th day after the date of this prospectus, subject to specified exceptions. Citigroup Global Markets Inc. and SVB Leerink LLC may, in their discretion, permit our shareholders who are subject to these lock-up agreements to sell securities prior to the expiration of the lock-up agreements. As of the date of this prospectus, the exercise of all outstanding options exercisable for ordinary shares would enable the subscription of new ordinary shares representing approximately 7.6% of the diluted share capital.

After the lock-up agreements pertaining to this offering expire, 2,408,861 additional ordinary shares will be eligible for sale in the public market, all of which ordinary shares are held by members of our senior management and board of directors and will be subject to volume limitations under Rule 144 under the Securities Act of 1933, as amended, or the Securities Act. In addition, the ordinary shares subject to subscription under outstanding options exercisable for ordinary shares will become eligible for sale in the public market in the future, subject to certain legal and contractual limitations. Sales of a large number of the ordinary shares in the public market could depress the market price of the ADSs. See "Shares and American Depository Shares Eligible for Future Sale" for a more detailed description of sales that may occur in the future. If these additional ordinary shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of the ordinary shares and ADSs could decline substantially, which could impair our ability to raise additional capital through the issuance of ordinary shares, ADSs or other securities in the future.

The dual listing of our ordinary shares and the ADSs following this offering may negatively impact the liquidity and value of the ADSs.

Following this offering and after the ADSs are listed on Nasdaq, our ordinary shares will continue to be listed on the ASX. We cannot predict the effect of this dual listing on the value of our ordinary shares and ADSs. However, the dual listing of our ordinary shares and ADSs may dilute the liquidity of these securities in one or both markets and may negatively impact the development of an active trading market for the ADSs in the United States. The price of the ADSs could also be negatively impacted by trading in our ordinary shares on the ASX.

We are subject to risks associated with currency fluctuations, and changes in foreign currency exchange rates could impact our results of operations.

Our ordinary shares are quoted in Australian dollars on the ASX and the ADSs will be quoted in U.S. dollars. In the past year, the Australian dollar has generally weakened against the U.S. dollar; however, this trend may not continue and may be reversed. As such, any significant change in the value of the Australian dollar may have a negative effect on the value of the ADSs in U.S. dollars. In addition, if the Australian dollar weakens against the U.S. dollar, then, if we decide to convert our Australian dollars into U.S. dollars for any business purpose, appreciation of the U.S. dollar against the Australian dollar would have a negative effect on the U.S. dollar amount available to us. While we engage in limited hedging transactions to manage our foreign exchange risk, these activities may not be effective in limiting or eliminating foreign exchange losses. To the extent that we need to convert U.S. dollars we receive from this offering into Australian dollars for our operations, appreciation of the Australian dollar against the U.S. dollar would have a negative effect on the Australian dollar amount we would receive from the conversion. Consequently, appreciation or depreciation in the value of the Australian dollar relative to the U.S. dollar would affect our financial results reported in U.S. dollar terms without giving effect to any underlying change in our business or results of operations. As a result of such foreign currency fluctuations, it could be more difficult to detect underlying trends in our business and results of operations.

We will incur significant increased costs as a result of operating as a company with ADSs that are publicly traded in the United States, and our management will be required to devote substantial time to new compliance initiatives.

As a company whose ADSs will be publicly traded in the United States, we will incur significant legal, accounting, insurance and other expenses that we did not previously incur. In addition, the Sarbanes-Oxley Act, Dodd-Frank Wall Street Reform and Consumer Protection Act and related rules implemented by the SEC and Nasdaq have imposed various requirements on public companies listed in the United States including requiring establishment and maintenance of effective disclosure and financial controls. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives, and we will need to add additional personnel and build our internal compliance infrastructure. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. These laws and regulations could also make it more difficult and expensive for us to attract and retain qualified persons to serve on our board of directors, our board committees or as our senior management. Furthermore, if we are unable to satisfy our obligations as a public company listed in the United States, we could be subject to delisting of the ADSs, fines, sanctions and other regulatory action and potentially civil litigation.

U.S. investors may have difficulty enforcing civil liabilities against our company, our directors or members of senior management and the experts named in this prospectus.

Certain members of our senior management and board of directors named in this prospectus are non-residents of the United States, and a substantial portion of the assets of such persons are located outside the United States. As a result, it may be impracticable to serve process on such persons in the United States or to enforce judgments obtained in U.S. courts against them based on civil liability provisions of the securities laws of the United States. Even if you are successful in bringing such an action, there is doubt as to whether Australian courts would enforce certain civil liabilities under U.S. securities laws in original actions or judgments of U.S. courts based upon these civil liability provisions. In addition, awards of punitive damages in actions brought in the United States or elsewhere may be unenforceable in Australia or elsewhere outside the United States. An award for monetary damages under U.S. securities laws would be considered punitive if it does not seek to compensate the claimant for loss or damage suffered and is intended to punish the defendant. The enforceability of any judgment in Australia will depend on the particular facts of the case as well as the laws and treaties in effect at the time. The United States and Australia do not currently have a treaty or statute providing for recognition and enforcement of the judgments of the other country (other than arbitration awards) in civil and commercial matters.

As a result, our public shareholders may have more difficulty in protecting their interests through actions against us, our management or our directors than would shareholders of a corporation incorporated in a jurisdiction in the United States. In addition, as a company incorporated in Australia, the provisions of the Corporations Act 2001 (Cth), or the Corporations Act, regulate the circumstances in which shareholder derivative actions may be commenced which may be different, and in many ways less permissive, than for companies incorporated in the United States.

Australian takeover laws may discourage takeover offers being made for us or may discourage the acquisition of a significant position in our ordinary shares or ADSs.

We are incorporated in Australia and are subject to the takeover laws of Australia. Among other things, we are subject to the Corporations Act. Subject to a range of exceptions, the Corporations Act prohibits the acquisition of a direct or indirect interest in our issued voting shares if the acquisition of that interest will lead to a person's voting power in us increasing to more than 20%, or increasing from a starting point that is above 20% and below 90%. Australian takeover laws may discourage takeover offers being made for us or may discourage the acquisition of a significant position in our ordinary shares. This may have the ancillary effect of entrenching our board of directors and may deprive or limit our shareholders' opportunity to sell their ordinary shares and may further restrict the ability of our shareholders to obtain a premium from such transactions. See "Description of Share Capital—Change of Control."

Our Constitution and Australian laws and regulations applicable to us may adversely affect our ability to take actions that could be beneficial to our shareholders.

As an Australian company we are subject to different corporate requirements than a corporation organized under the laws of the United States. Our Constitution, as well as the Corporations Act, sets forth various rights and obligations that apply to us as an Australian company and which may not apply to a U.S. corporation. These requirements may operate differently than those of many U.S. companies. You should carefully review the summary of these matters set forth under "Description of Share Capital" as well as our Constitution, which is included as an exhibit to the registration statement of which this prospectus forms a part, prior to investing in our securities.

Purchasers of ADSs in this offering will not be directly holding our ordinary shares.

A holder of ADSs will not be treated as one of our shareholders and will not have direct shareholder rights. Our Constitution and Australian law govern our shareholder rights. The depositary, through the custodian or the custodian's nominee, will be the holder of the ordinary shares underlying ADSs held by purchasers of ADSs in this offering. Purchasers of ADSs in this offering will have ADS holder rights. The deposit agreement among us, the depositary and purchasers of ADSs in this offering, as an ADS holder, and all other persons directly and indirectly holding ADSs, sets out ADS holder rights, as well as the rights and obligations of us and the depositary.

Your right as a holder of ADSs to participate in any future preferential subscription rights offering or to elect to receive dividends in ordinary shares may be limited, which may cause dilution to your holdings.

The deposit agreement provides that the depositary will not make rights available to you unless the distribution to ADS holders of both the rights and any related securities are either registered under the Securities Act or exempted from registration under the Securities Act. If we offer holders of our ordinary shares the option to receive dividends in either cash or shares, under the deposit agreement the depositary may require satisfactory assurances from us that extending the offer to holders of ADSs does not require registration of any securities under the Securities Act before making the option available to holders of ADSs. We are under no obligation to file a registration statement with respect to any such rights or securities or to endeavor to cause such a registration statement to be declared effective. Moreover, we may not be able to establish an exemption from registration under the Securities Act. Accordingly, ADS holders may be unable to participate in our rights

offerings or to elect to receive dividends in shares and may experience dilution in their holdings. In addition, if the depositary is unable to sell rights that are not exercised or not distributed or if the sale is not lawful or reasonably practicable, it will allow the rights to lapse, in which case you will receive no value for these rights.

You may not be able to exercise your right to vote the ordinary shares underlying your ADSs.

Holders of ADSs may exercise voting rights with respect to the ordinary shares represented by the ADSs only in accordance with the provisions of the deposit agreement. The deposit agreement provides that, upon receipt of notice of any meeting of holders of our ordinary shares, the depositary will fix a record date for the determination of ADS holders who shall be entitled to give instructions for the exercise of voting rights. Upon timely receipt of notice from us, if we so request, the depositary shall distribute to the holders as of the record date (i) the notice of the meeting or solicitation of consent or proxy sent by us and (ii) a statement as to the manner in which instructions may be given by the holders.

You may instruct the depositary to vote the ordinary shares underlying your ADSs. Otherwise, you will not be able to exercise your right to vote, unless you withdraw the ordinary shares underlying the ADSs you hold. However, you may not know about the meeting far enough in advance to withdraw those ordinary shares. If we ask for your instructions, the depositary, upon timely notice from us, will notify you of the upcoming vote and arrange to deliver our voting materials to you and will try to vote ordinary shares as you instruct. We cannot guarantee you that you will receive the voting materials in time to ensure that you can instruct the depositary to vote your ordinary shares or to withdraw your ordinary shares so that you can vote them yourself. If we do not ask for your instructions, you can still send voting instructions to the depository and the depository may try to carry out those instructions, but it is not required to do so.

Under our Constitution, any resolution to be considered at a meeting of the shareholders shall be decided on a show of hands unless a poll is demanded in accordance with the terms of our Constitution. A poll may be demanded before a vote is taken, or, in the case of a vote taken on a show of hands, immediately before or immediately after, the declaration of the result of the show of hands. Under voting by a show of hands, multiple "yes" votes by ADS holders will only count as one "yes" vote and will be negated by a single "no" vote, unless a poll is demanded.

You may be subject to limitations on the transfer of your ADSs and the withdrawal of the underlying ordinary shares.

Your ADSs are transferable on the books of the depositary. However, the depositary may close its books at any time or from time to time when it deems expedient in connection with the performance of its duties. The depositary may refuse to deliver, transfer or register transfers of your ADSs generally when our books or the books of the depositary are closed, or at any time if we or the depositary think it is advisable to do so because of any requirement of law, government or governmental body, or under any provision of the deposit agreement, or for any other reason subject to your right to surrender your ADSs and receive the underlying ordinary shares. Temporary delays in the surrendering of your ADSs and receipt of the underlying ordinary shares may arise because the depositary has closed its transfer books or we have closed our transfer books, the transfer of ordinary shares is blocked to permit voting at a shareholders' meeting or we are paying a dividend on our ordinary shares. In addition, you may not be able to surrender your ADSs and receive the underlying ordinary shares when you owe money for fees, taxes and similar charges and when it is necessary to prohibit withdrawals in order to comply with any laws or governmental regulations that apply to ADSs or to the withdrawal of ordinary shares or other deposited securities. See "Description of American Depositary Shares."

Holders of ADSs are not treated as holders of our ordinary shares.

By participating in this offering you will become a holder of ADSs with underlying ordinary shares in an Australian public listed company. Holders of ADSs are not treated as holders of our ordinary shares, unless they surrender the ADSs to receive the ordinary shares underlying their ADSs in accordance with the deposit

agreement and applicable laws and regulations. The depositary is the holder of the ordinary shares underlying the ADSs. Holders of ADSs therefore do not have any rights as holders of our ordinary shares, other than the rights that they have pursuant to the deposit agreement. See "Description of American Depositary Shares."

ADS holders may not be entitled to a jury trial with respect to claims arising under the deposit agreement, which could result in less favorable outcomes to the plaintiff(s) in any such action.

The deposit agreement governing the ADSs provides that holders and beneficial owners of ADSs, including those holders and owners who acquired ADSs in secondary transactions, irrevocably waive the right to a trial by jury in any legal proceeding arising out of or relating to the deposit agreement or the ADSs, including in respect of claims under federal securities laws, against us or the depositary to the fullest extent permitted by applicable law. If this jury trial waiver provision is prohibited by applicable law, an action could nevertheless proceed under the terms of the deposit agreement with a jury trial. To our knowledge, the enforceability of a jury trial waiver under the federal securities laws has not been finally adjudicated by a federal court. However, we believe that a jury trial waiver provision is generally enforceable under the laws of the State of New York, which govern the deposit agreement, by a court of the State of New York or a federal court, which have non-exclusive jurisdiction over matters arising under the deposit agreement, applying such law. In determining whether to enforce a jury trial waiver provision, New York courts and federal courts will consider whether the visibility of the jury trial waiver provision within the agreement is sufficiently prominent such that a party has knowingly waived any right to trial by jury. We believe that this is the case with respect to the deposit agreement and the ADSs. In addition, New York courts will not enforce a jury trial waiver provision in order to bar a viable setoff or counterclaim sounding in fraud or one which is based upon a creditor's negligence in failing to liquidate collateral upon a guarantor's demand, or in the case of an intentional tort claim (as opposed to a contract dispute), none of which we believe are applicable in the case of the deposit agreement or the ADSs.

No condition, stipulation or provision of the deposit agreement or ADSs serves as a waiver by any holder or beneficial owner of ADSs or by us or the depositary of compliance with any provision of the federal securities laws. If you or any other holder or beneficial owner of ADSs brings a claim against us or the depositary in connection with such matters, you or such other holder or beneficial owner may not be entitled to a jury trial with respect to such claims, which may have the effect of limiting and discouraging lawsuits against us and/or the depositary. If a lawsuit is brought against us and/or the depositary under the deposit agreement, it may be heard only by a judge or justice of the applicable trial court, which would be conducted according to different civil procedures and may result in different outcomes than a trial by jury would have had, including results that could be less favorable to the plaintiff(s) in any such action, depending on, among other things, the nature of the claims, the judge or justice hearing such claims, and the venue of the hearing.

As the jury trial waiver relates to claims arising out of or relating to the ADSs or the deposit agreement, we believe that the waiver would likely continue to apply to ADS holders or beneficial owners who withdraw the ordinary shares from the ADS facility with respect to claims arising before the cancellation of the ADSs and the withdrawal of the ordinary shares, and the waiver would likely not apply to ADS holders or beneficial owners who subsequently withdraw the ordinary shares represented by ADSs from the ADS facility with respect to claims arising after the withdrawal. However, to our knowledge, there has been no case law on the applicability of the jury trial waiver to ADS holders or beneficial owners who withdraw the ordinary shares represented by the ADSs from the ADS facility.

We currently report our financial results under IFRS, which differs in certain significant respect from U.S. generally accepted accounting principles, or U.S. GAAP.

Currently we report our financial statements under IFRS. There have been and there may in the future be certain significant differences between IFRS and U.S. GAAP, including differences related to revenue recognition, intangible assets, share-based compensation expense, income tax and earnings per share. As a result, our financial information and reported earnings for historical or future periods could be significantly different if they were prepared in accordance with U.S. GAAP. In addition, we do not intend to provide a reconciliation

between IFRS and U.S. GAAP unless it is required under applicable law. As a result, you may not be able to meaningfully compare our financial statements under IFRS with those companies that prepare financial statements under U.S. GAAP.

As a foreign private issuer, we are exempt from a number of rules under the U.S. securities laws and are permitted to file less information with the SEC than a U.S. company.

We are a foreign private issuer, as defined in the SEC's rules and regulations and, consequently, we are not subject to all of the disclosure requirements applicable to public companies organized within the United States. For example, we are exempt from certain rules under the Exchange Act that regulate disclosure obligations and procedural requirements related to the solicitation of proxies, consents or authorizations applicable to a security registered under the Exchange Act, including the U.S. proxy rules under Section 14 of the Exchange Act. In addition, our senior management and directors are exempt from the reporting and "short-swing" profit recovery provisions of Section 16 of the Exchange Act and related rules with respect to their purchases and sales of our securities. Moreover, while we currently make annual and semi-annual filings with respect to our listing on the ASX and expect to file financial reports on an annual and semi-annual basis, we will not be required to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. public companies and will not be required to file quarterly reports on Form 10-Q or current reports on Form 8-K under the Exchange Act. In addition, foreign private issuers are not required to file their annual report on Form 20-F until four months after the end of each fiscal year. Accordingly, there may be less publicly available information concerning our company than there would be if we were not a foreign private issuer.

As a foreign private issuer, we are permitted to adopt certain home country practices in relation to corporate governance matters that differ significantly from Nasdaq corporate governance listing standards and these practices may afford less protection to shareholders than they would enjoy if we complied fully with Nasdaq corporate governance listing standards.

As a foreign private issuer listed on Nasdaq, we will be subject to their corporate governance listing standards. However, Nasdaq rules permit foreign private issuers to follow the corporate governance practices of its home country. Some corporate governance practices in Australia may differ from Nasdaq corporate governance listing standards. For example, we could include non-independent directors as members of our Remuneration and Nomination committees, and our independent directors may not necessarily hold regularly scheduled meetings at which only independent members of the board of directors are present. Currently, we intend to follow home country practice to the maximum extent possible. Therefore, our shareholders may be afforded less protection than they otherwise would have under corporate governance listing standards applicable to U.S. domestic issuers. For an overview of our corporate governance practices, see "Management."

We may lose our foreign private issuer status in the future, which could result in significant additional cost and expense.

While we currently qualify as a foreign private issuer, the determination of foreign private issuer status is made annually on the last business day of an issuer's most recently completed second fiscal quarter and, accordingly, our next determination will be made on June 30, 2021. In the future, we would lose our foreign private issuer status if we to fail to meet the requirements necessary to maintain our foreign private issuer status as of the relevant determination date. For example, if 50% or more of our securities are held by U.S. residents and more than 50% of our senior management or directors are residents or citizens of the United States, we could lose our foreign private issuer status. Immediately following the closing of this offering, approximately 20.3% of our outstanding ordinary shares (including ordinary shares in the form of ADSs) will likely be held by U.S. residents (assuming that all purchasers of ADSs in this offering are residents of the United States).

The regulatory and compliance costs to us under U.S. securities laws as a U.S. domestic issuer may be significantly more than costs we incur as a foreign private issuer. If we are not a foreign private issuer, we will be required to file periodic reports and registration statements on U.S. domestic issuer forms with the SEC, which

are more detailed and extensive in certain respects than the forms available to a foreign private issuer. We would be required under current SEC rules to prepare our financial statements in accordance with U.S. GAAP rather than IFRS, and modify certain of our policies to comply with corporate governance practices required of U.S. domestic issuers. Such conversion of our financial statements to U.S. GAAP would involve significant time and cost. In addition, we may lose our ability to rely upon exemptions from certain corporate governance requirements on U.S. stock exchanges that are available to foreign private issuers such as the ones described above and exemptions from procedural requirements related to the solicitation of proxies.

We are an "emerging growth company" under the JOBS Act and will be able to avail ourselves of reduced disclosure requirements applicable to emerging growth companies, which could make our ordinary shares ADSs less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act, and we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies," including not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. In addition, Section 107 of the JOBS Act also provides that an emerging growth company can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act, for complying with new or revised accounting standards. We will not take advantage of the extended transition period provided under Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards.

We cannot predict if investors will find the ordinary shares or ADSs less attractive because we may rely on these exemptions. If some investors find the ordinary shares or ADSs less attractive as a result, there may be a less active trading market for the ordinary shares or ADSs and the price of the ordinary shares or ADSs may be more volatile. We may take advantage of these exemptions until such time that we are no longer an emerging growth company. We would cease to be an emerging growth company upon the earliest to occur of (i) the last day of the fiscal year in which we have more than $1.07 billion in annual revenue; (ii) the last day of the fiscal year in which we qualify as a "large accelerated filer"; (iii) the date on which we have, during the previous three-year period, issued more than $1.0 billion in non-convertible debt securities; and (iv) the last day of the fiscal year in which the fifth anniversary of this offering occurs.

There is no public market for the pre-funded warrants being offered in this offering.

There is no established public trading market for the pre-funded warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply to list the pre-funded warrants on any securities exchange or nationally recognized trading system, including the Nasdaq Global Select Market. Without an active market, the liquidity of the pre-funded warrants will be limited.

Holders of our pre-funded warrants will have no rights as a holder of ADSs or our ordinary shares until they acquire ADSs or our ordinary shares.

Until you acquire ADSs upon exercise of your pre-funded warrants, you will have no rights with respect to the ADSs (or underlying ordinary shares) issuable upon exercise of your pre-funded warrants. Upon exercise of your pre-funded warrants, you will be entitled to exercise the rights of an ADS holder only as to matters for which the record date occurs after the exercise date.

The pre-funded warrants are speculative in nature.

The pre-funded warrants offered hereby do not confer any rights of ADS or ordinary share ownership on their holders, such as voting rights or the right to receive dividends, but rather merely represent the right to acquire ADSs at a fixed price. Specifically, commencing on the date of issuance, holders of the pre-funded

warrants may acquire ADSs issuable upon exercise of such warrants at an exercise price of US$0.00001 per ADS. Moreover, following this offering, the market value of the pre-funded warrants is uncertain and there can be no assurance that the market value of the pre-funded warrants will equal or exceed their public offering price.

If we are a passive foreign investment company, there could be adverse U.S. federal income tax consequences to U.S. holders.

Based on the nature and composition of our income, assets, activities and market capitalization for our taxable year ended June 30, 2019, we believe that we were not classified as a passive foreign investment company, or PFIC, for the taxable year ended June 30, 2019. Based on the nature and composition of our income, assets, activities and market capitalization for our taxable year ended June 30, 2020, we believe that we would not be classified as a PFIC for the taxable year ended June 30, 2020. However, there can be no assurance that we will not be considered a PFIC in any past, current or future taxable year. A separate determination must be made after the close of each taxable year as to whether we are a PFIC for that year. As a result, our PFIC status may change from year to year. Our status as a PFIC will depend on the composition of our income (including whether we receive certain grants or subsidies and whether such amounts will constitute gross income for purposes of the PFIC income test) and the composition and value of our assets, which may be determined in large part by reference to the market value of the ADSs and our ordinary shares, which may be volatile, from time to time. Our status may also depend, in part, on how quickly we utilize the cash proceeds from this offering in our business. Our U.S. counsel expresses no opinion regarding our conclusions or our expectations regarding our PFIC status.

Under the Code, a non-U.S. company will be considered a PFIC for any taxable year in which (1) 75% or more of its gross income consists of passive income or (2) 50% or more of the average quarterly value of its assets consists of assets that produce, or are held for the production of, passive income. For purposes of these tests, passive income includes dividends, interest, gains from the sale or exchange of investment property and certain rents and royalties. In addition, for purposes of the above calculations, a non-U.S. corporation that directly or indirectly owns at least 25% by value of the shares of another corporation is treated as if it held its proportionate share of the assets and received directly its proportionate share of the income of such other corporation. If we are a PFIC for any taxable year during which a U.S. holder (as defined in the section titled "Material United States Federal Income Tax and Australian Tax Considerations—Material United States Federal Income Tax Considerations") holds our ordinary shares or ADSs, we will continue to be treated as a PFIC with respect to such U.S. holder in all succeeding years during which the U.S. holder owns the ordinary shares or ADSs, regardless of whether we continue to meet the PFIC test described above, unless the U.S. holder is eligible to make and makes a mark-to-market election or makes a specified election once we cease to be a PFIC. If we are classified as a PFIC for any taxable year during which a U.S. holder holds our ordinary shares or ADSs, the U.S. holder may be subject to adverse tax consequences regardless of whether we continue to qualify as a PFIC, including ineligibility for any preferred tax rates on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred, and additional reporting requirements. For further discussion of the PFIC rules and the adverse U.S. federal income tax consequences in the event we are classified as a PFIC, see "Material United States Federal Income Tax and Australian Tax Considerations—Material United States Federal Income Tax Considerations."

If a United States person is treated as owning at least 10% of our ordinary shares, such holder may be subject to adverse U.S. federal income tax consequences.

If a U.S. holder is treated as owning, directly, indirectly or constructively, at least 10% of the value or voting power of our ordinary shares or ADSs, such U.S. holder may be treated as a "United States shareholder" with respect to each "controlled foreign corporation" in our group, if any. While our group does not currently include any U.S. subsidiaries, if we form or acquire any U.S. subsidiaries in the future any of our current non-U.S. subsidiaries and any future newly formed or acquired non-U.S. subsidiaries will be treated as controlled foreign corporations, regardless of whether we are treated as a controlled foreign corporation. A United States shareholder of a controlled foreign corporation may be required to annually report and include in

its U.S. taxable income its pro rata share of "Subpart F income," "global intangible low-taxed income" and investments in U.S. property by controlled foreign corporations, regardless of whether we make any distributions. An individual that is a United States shareholder with respect to a controlled foreign corporation generally would not be allowed certain tax deductions or foreign tax credits that would be allowed to a United States shareholder that is a U.S. corporation. Failure to comply with controlled foreign corporation reporting obligations may subject a United States shareholder to significant monetary penalties. We cannot provide any assurances that we will furnish to any United States shareholder information that may be necessary to comply with the reporting and tax paying obligations applicable under the controlled foreign corporation rules of the Code. U.S. holders should consult their tax advisors regarding the potential application of these rules to their investment in our ordinary shares or ADSs.

Future changes to tax laws could materially adversely affect our company and reduce net returns to our shareholders.

Our tax treatment is subject to the enactment of, or changes in, tax laws, regulations and treaties, or the interpretation thereof, tax policy initiatives and reforms under consideration and the practices of tax authorities in jurisdictions in which we operate, including those related to the Organization for Economic Co-Operation and Development's Base Erosion and Profit Shifting Project, the European Commission's state aid investigations and other initiatives. Such changes may include (but are not limited to) the taxation of operating income, investment income, dividends received or (in the specific context of withholding tax) dividends paid. We are unable to predict what tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices, could affect our financial position and overall or effective tax rates in the future in countries where we have operations, reduce post-tax returns to our shareholders, and increase the complexity, burden and cost of tax compliance.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future results of operations, financial condition, business strategy and plans and objectives of management for future operations, are forward-looking statements. In some cases, you can identify forward-looking statements because they contain words such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," or "would," or the negative of these words or other similar terms or expressions.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of known and unknown risks, uncertainties, other factors and assumptions, including the risks described in "Risk Factors" and elsewhere in this prospectus, regarding, among other things:

- the success, cost and timing of our product development activities and clinical trials;
- our expectations about the timing or likelihood of achieving regulatory approval and the cost of our development programs;
- our reliance on the success of OPT-302 as our only product candidate;
- our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates;
- the commercialization of our product candidates, if approved;
- our plans to research, develop and commercialize our product candidates;
- our ability to maintain, expand, protect and enforce our intellectual property portfolio;
- our ability to operate our business without infringing, misappropriating or otherwise violating the intellectual property rights of third parties;
- our ability to attract collaborators with development, regulatory and commercialization expertise;
- business disruptions affecting the initiation, patient enrollment, development and operation of our clinical trials, including as a result of a public health emergency, such as the global outbreak of the COVID-19 pandemic;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidate;
- future agreements with third parties in connection with the commercialization of our product candidates;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates;
- regulatory developments in the United States, Australia and other jurisdictions;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;

- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act;
- our use of the proceeds from this offering;
- the future trading price of the ADSs and impact of securities analysts' reports on these prices; and
- other risks and uncertainties, including those listed under "Risk Factors."

These risks are not exhaustive. Other sections of this prospectus may include additional factors that could harm our business and financial performance. New risk factors may emerge from time to time and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements.

You should not rely on forward-looking statements as predictions of future events. We have based the forward-looking statements contained in this prospectus primarily on our current expectations and projections about future events and trends that we believe may affect our business, financial condition and operating results. We undertake no obligation to update any forward-looking statements made in this prospectus to reflect events or circumstances after the date of this prospectus or to reflect new information or the occurrence of unanticipated events, except as required by law. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based on information available to us as of the date of this prospectus. While we believe that information provides a reasonable basis for these statements, that information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all relevant information. These statements are inherently uncertain, and investors are cautioned not to unduly rely on these statements.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement of which this prospectus is a part with the understanding that our actual future results, levels of activity, performance and achievements may be different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

INDUSTRY AND MARKET DATA

This prospectus contains estimates and information concerning our industry and our business, including estimated market size and projected growth rates of the markets for our product candidates. Unless otherwise expressly stated, we obtained this industry, business, market, medical and other information from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources.

This information involves a number of assumptions and limitations. Although we are responsible for all of the disclosure contained in this prospectus and we believe the third-party market position, market opportunity and market size data included in this prospectus are reliable, we have not independently verified the accuracy or completeness of this third-party data. In addition, projections, assumptions and estimates of our future performance and the future performance of the industry in which we operate are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in "Risk Factors." These and other factors could cause results to differ materially from those expressed in these publications and reports.

USE OF PROCEEDS

We estimate that the net proceeds to us from the sale of 8,563,300 ADSs and pre-funded warrants to purchase 936,700 ADSs in this offering will be approximately US$116.4 million (or approximately US$134.3 million if the underwriters exercise their option to purchase 1,425,000 additional ADSs in full), based on the initial public offering price of US$13.50 per ADS and US$13.49999 per pre-funded warrant, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We expect to use the net proceeds from this offering, together with our existing cash and cash equivalents, as follows:

- approximately US$130 million to US$135 million to advance the clinical development of OPT-302 for the treatment of wet AMD, including the initiation of and reporting of topline data from two pivotal Phase 3 clinical trials;
- approximately US$5 million to US$7 million to advance the development of, and non-clinical studies for, a co-formulation of OPT-302 with an approved and/or biosimilar anti-VEGF-A therapy; and
- the remaining proceeds for other research and development activities for OPT-302 in potential additional indications, including DME, and for working capital and general corporate purposes.

However, due to the uncertainties inherent in the product development process, it is difficult to estimate with certainty the exact amounts of the net proceeds from this offering that may be used for the above purposes. Our management will have broad discretion over the use of the net proceeds from this offering. The amounts and timing of our expenditures will depend upon numerous factors including the results of our research and development efforts, the timing and success of preclinical studies and any ongoing clinical trials or clinical trials we may commence in the future, the timing of regulatory submissions and the amount of cash obtained through future collaborations, if any.

We believe opportunities may exist from time to time to expand our current business through acquisitions or in-licensing of complementary companies, medicines or technologies. While we have no current agreements, commitments or understandings for any specific acquisitions or in-licensing at this time, we may use a portion of the net proceeds for these purposes.

As of June 30, 2020, we had cash and cash equivalents of A$62 million (or US$42.6 million). We believe our cash and cash equivalents, together with the net proceeds of this offering, will be sufficient to fund our operations through the third calendar quarter of 2023. In particular, we estimate that such funds, together with such existing cash and cash equivalents, will be sufficient to enable us to (i) advance the clinical development of OPT-302 for the treatment of wet AMD through the reporting of topline data from two pivotal Phase 3 clinical trials in 2023 and (ii) advance the development of a co-formulation of OPT-302 with an approved and/or biosimilar anti-VEGF-A therapy through the completion of manufacturing activities and IND-enabling safety toxicology studies to support an IND filing in the second half of 2021. In the event the net proceeds are insufficient for each of the uses set forth above, we intend to prioritize the allocation of the use of proceeds to the clinical development of OPT-302 for the treatment of wet AMD. We have based these estimates on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Following this offering, we will require additional funding to complete clinical development and commercialize OPT-302 in any indication, including wet AMD.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments.

DIVIDEND POLICY

We have not declared or paid any dividends on our ordinary shares since February 2005. We intend to retain any earnings for use in our business and do not currently intend to pay cash dividends on our ordinary shares. Dividends, if any, on our outstanding ordinary shares will be declared by and subject to the discretion of our board of directors, and subject to Australian law.

Any dividend we declare will be paid to the holders of ADSs, subject to the terms of the deposit agreement, to the same extent as holders of our ordinary shares, to the extent permitted by applicable law and regulations, less the fees and expenses payable under the deposit agreement. Any dividend we declare will be distributed by the depositary bank to the holders of the ADSs, subject to the terms of the deposit agreement. See "Description of American Depositary Shares—Dividends and Distributions."

CAPITALIZATION

The following table sets forth our cash and our capitalization as of June 30, 2020, on:

- an actual basis; and
- an as adjusted basis to give effect to the issuance and sale of 8,563,300 ADSs and pre-funded warrants to purchase 936,700 ADSs in this offering at the initial public offering price of US$13.50 per ADS and US$13.49999 per pre-funded warrant, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, and assuming no exercise of any pre-funded warrants offered and sold in this offering.

You should read this information in conjunction with our consolidated financial statements and the related notes included elsewhere in this prospectus, the information set forth in "Management's Discussion and Analysis of Financial Condition and Results of Operations" and other financial information contained elsewhere in this prospectus.

	As of June 30, 2020			
	Actual[1]		As Adjusted[1][2]	
	(in thousands, except share data)			
Total cash and cash equivalents	A$ 62,020	US$ 42,565	A$ 226,501	US$158,937
Contributed equity: 269,157,769 ordinary shares, no par value, outstanding, actual; 337,664,169 ordinary shares, no par value, outstanding, as adjusted	A$ 162,102	US$111,251	A$ 308,710	US$214,978
Accumulated losses	(102,589)	(70,407)	(102,589)	(70,407)
Reserves	5,295	3,634	23,168	16,279
Total equity	64,808	44,478	229,289	160,850
Total capitalization	A$ 64,808	US$ 44,478	A$ 229,289	US$160,850

(1) Amounts have been translated from Australian dollars to U.S. dollars at an assumed exchange rate of A$1.4571 per US1.00, which was the official exchange rate published by the Reserve Bank of Australia on June 30, 2020.

(2) The gross proceeds from the offering and sale of the pre-funded warrants to purchase ADSs have been allocated to Reserves.

The outstanding ordinary share information in the table above is based on 269,157,769 ordinary shares outstanding as of June 30, 2020, and excludes:

- 18,044,000 ordinary shares issuable upon the exercise of outstanding options as of June 30, 2020 with a weighted-average exercise price of A$0.68 per ordinary share under our equity incentive plans;
- 4,000,000 ordinary shares issuable upon the exercise of outstanding options granted under our non-executive director share and option plan to certain of our non-employee directors subsequent to June 30, 2020, of which an option to purchase 2,000,000 ordinary shares has an exercise price of A$2.99 per ordinary share and an option to purchase 2,000,000 ordinary shares has an exercise price of A$4.49 per ordinary share;
- 3,000,000 ordinary shares issuable upon the exercise of an option to be granted to one of our non-employee directors upon approval by our shareholders at a future meeting of shareholders following the closing of this offering (see "Management—Remuneration of Non-Employee Directors"); and
- 12,446,777 ordinary shares reserved for future issuance under our Long Term Incentive Plan.

DILUTION

If you invest in the ADSs or pre-funded warrants in this offering, your ownership interest will be immediately diluted to the extent of the difference between the initial public offering price per ADS and the as adjusted net tangible book value per ordinary share or ADS immediately after this offering.

As of June 30, 2020, our historical net tangible book value was A$64.8 million (or US$44.5 million), or A$1.93 (or US$1.32) per ADS. Historical net tangible book value per ADS represents our total tangible assets less total liabilities, divided by the number of ordinary shares outstanding as of June 30, 2020, converted to ADSs at an ADS-to-ordinary share ratio of 1-to-8.

After giving effect to the receipt of the net proceeds from our sale of 8,563,300 ADSs and pre-funded warrants to purchase 936,700 ADSs in this offering at an initial public offering price of US$13.50 per ADS and US$13.49999 per pre-funded warrant, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2020 was A$229.3 million (or US$160.9 million), or A$5.43 (or US$3.81) per ADS, equivalent to A$0.68 (or US$0.48) per ordinary share, in each case based on an ADS-to-ordinary share ratio of 1-to-8. This represents an immediate increase in net tangible book value of A$3.51 (or US$2.49) per ADS, equivalent to A$0.44 or (US$0.31) per ordinary share, to our existing shareholders and immediate dilution of A$13.65 (or US$9.69) per ADS, equivalent to A$1.71 (or US$1.21) per ordinary share, to investors purchasing ADSs in this offering, in each case based on an ADS-to-ordinary share ratio of 1-to-8.

The following table illustrates this dilution on a per ADS basis, assuming all ordinary shares outstanding as of June 30, 2020 converted to ADSs at an ADS-to-ordinary share ratio of 1-to-8:

Assumed initial public offering price per ADS		US$13.50
Historical net tangible book value per ADS as of June 30, 2020	US$1.32	
Increase in net tangible book value per ADS attributed to investors purchasing ADSs in this offering	2.49	
As adjusted net tangible book value per ADS after this offering		3.81
Dilution in net tangible book value per ADS to investors in this offering		US$ 9.69

If the underwriters exercise their option to purchase 1,425,000 additional ADSs in full, the as adjusted net tangible book value after the offering would be US$4.10 per ADS, the increase in net tangible book value per ADS to existing shareholders would be US$2.77 per ADS and the dilution per ADS to new investors in this offering would be US$9.40 per ADS, at an initial public offering price of US$13.50 per ADS and US$13.49999 per pre-funded warrant.

The discussion and table above assume no exercise of any pre-funded warrants offered and sold in this offering.

The following table summarizes, as of June 30, 2020:

- the total number of ordinary shares purchased from us by existing shareholders and the equivalent number of ordinary shares underlying ADSs purchased by investors in this offering, assuming no exercise of any pre-funded warrants offered and sold in this offering;

- the total consideration paid to us by our existing shareholders and by investors purchasing ADSs in this offering, at an initial public offering price of US$13.50 per ADS, before deducting underwriting discounts and commissions and estimated offering expenses payable by us in connection with this offering, and assuming no exercise of any pre-funded warrants offered and sold in this offering; and
- the average price per ordinary share paid by existing shareholders and the average price per ADS or equivalent number of ordinary shares.

	Ordinary Shares (Directly or in the Form of ADSs)		Total Consideration		Average Price Per Share	Average Price per ADS
	Number	Percent	Amount (in millions)	Percent		
Existing shareholders	269,157,769	80%	US$130.5	53%	US$0.48	US$ 3.88
Purchasers of ADSs	68,506,400	20	115.6	47	US$1.69	US$13.50
Total	337,664,169	100%	US$246.1	100%		

If the underwriters exercise their option to purchase 1,425,000 additional ADSs in full, our existing shareholders would own 77% and investors in this offering would own 23% of the total number of ordinary shares outstanding (including shares underlying ADSs) upon the closing of this offering.

The outstanding ordinary share information in the tables above is based on 269,157,769 ordinary shares as of June 30, 2020, and excludes:

- 18,044,000 ordinary shares issuable upon the exercise of outstanding options as of June 30, 2020, with a weighted-average exercise price of A$0.68 per ordinary share under our equity incentive plans;
- 4,000,000 ordinary shares issuable upon the exercise of outstanding options granted under our non-executive director share and option plan to certain of our non-employee directors subsequent to June 30, 2020, of which an option to purchase 2,000,000 ordinary shares has an exercise price of A$2.99 per ordinary share and an option to purchase 2,000,000 ordinary shares has an exercise price of A$4.49 per ordinary share;
- 3,000,000 ordinary shares issuable upon the exercise of an option to be granted to one of our non-employee directors upon approval by our shareholders at a future meeting of shareholders following the closing of this offering (see “Management—Remuneration of Non-Employee Directors”); and
- 12,446,777 ordinary shares reserved for future issuance under our Long Term Incentive Plan.

To the extent any outstanding options or the pre-funded warrants offered and sold in this offering are exercised, there will be further dilution to investors purchasing in this offering.

SELECTED CONSOLIDATED FINANCIAL DATA

The following tables summarize our consolidated financial and other data. The summary consolidated statement of profit or loss and other comprehensive income data for the years ended June 30, 2019 and 2020 have been derived from our audited consolidated financial statements included elsewhere in this prospectus. Our audited consolidated financial statements have been prepared in accordance with IFRS, as issued by the IASB, as of and for the years ended June 30, 2019 and 2020.

You should read the consolidated financial and other data set forth below in conjunction with our consolidated financial statements and the accompanying notes and the information in "Management's Discussion and Analysis of Financial Condition and Results of Operations" contained elsewhere in this prospectus.

Consolidated Statement of Profit or Loss and Other Comprehensive Income Data

	Year Ended June 30,	
	2019	2020
	(in thousands, except per share data)	
Revenue	A$ 159	A$ 87
Other income[1]	837	784
Research and development expenses	(31,348)	(17,954)
Patent expenses	(161)	(429)
Intellectual property costs	(113)	(114)
Administrative expenses	(5,175)	(7,001)
Occupancy expenses	(109)	(34)
Net foreign exchange gain (loss)	363	(401)
Loss before income tax	(35,547)	(25,062)
Income tax benefit	14,637	8,533
Loss for the year	(20,910)	(16,529)
Other comprehensive income:		
Items that will not be reclassified subsequently to profit or loss:		
Fair value gains on investments in financial assets	260	59
Other comprehensive income for the period, net of tax	260	59
Total comprehensive loss for the year	A$(20,650)	A$(16,470)
Total comprehensive loss for the year is attributable to:		
Owners of the Company	(20,650)	(16,470)
	A$(20,650)	A$(16,470)
Loss per share attributable to Owners of the Company—basic and diluted (in cents)	A$ (8.98)	A$ (6.34)

(1) Other income primarily comprises finance income from interest on bank deposits, funding under a one-time Australian government grant from the Commonwealth Scientific and Industrial Research Organization during the year ended June 30, 2019, and funding under a one-time government grant from the ATO during the year ended June 30, 2020.

Consolidated Statement of Financial Position Data

	As of June 30,	
	2019	2020
	(in thousands)	
Cash and cash equivalents	A$ 21,535	A$ 62,020
Working capital[(1)]	30,376	64,398
Total assets	37,660	71,887
Total liabilities	6,541	7,079
Accumulated losses	(86,060)	(102,589)
Total equity	31,120	64,808

(1) Working capital is defined as current assets less current liabilities.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following "Management's Discussion and Analysis of Financial Condition and Results of Operations" should be read together the section titled "Selected Consolidated Financial Data" and our consolidated financial statements and the accompanying notes included elsewhere in this prospectus. This discussion includes both historical information and forward-looking information based upon current expectations that involve risk, uncertainties and assumptions. Our actual results may differ materially from management's expectations as a result of various factors, including, but not limited to, those discussed in "Risk Factors" and elsewhere in this prospectus.

Overview

We are a clinical stage biopharmaceutical company developing a novel therapy for the treatment of highly prevalent and progressive retinal diseases. We are developing our Phase 3-ready product candidate, OPT-302, a biologic designed to inhibit VEGF-C and VEGF-D, to complement VEGF-A inhibitors for the treatment of ophthalmic diseases. Anti-VEGF-A therapies represent the standard of care for wet age-related macular degeneration, or AMD, and other retinal diseases; however, there remains a significant unmet medical need as many patients do not adequately respond to these treatments. As the only biologic inhibitor of VEGF-C and VEGF-D in clinical development, OPT-302 differs from standard of care therapies and when administered in combination with a VEGF-A inhibitor, is designed to achieve broader inhibition of the vascular endothelial growth factor, or VEGF, family and target a mechanism of clinical resistance to improve visual acuity. Our lead indication for OPT-302 combination therapy is wet AMD, a chronic, progressive disease and the leading cause of vision loss for individuals over the age of 50. In a 366-patient Phase 2b clinical trial for the treatment of wet AMD, 2.0 mg OPT-302, in combination with a standard of care anti-VEGF-A therapy, ranibizumab (Lucentis), met the primary endpoint of a statistically significant superior mean gain in visual acuity over ranibizumab monotherapy at week 24. We intend to initiate two pivotal Phase 3 clinical trials in treatment-naive patients with wet AMD to evaluate the efficacy and safety of OPT-302 in combination with anti-VEGF-A therapies compared to anti-VEGF-A monotherapy in the first half of 2021. We expect to report topline data from these Phase 3 clinical trials in 2023. In addition to our clinical trials in wet AMD, we have observed evidence of improved clinical outcomes in a Phase 1b/2a clinical trial of OPT-302 in combination with another standard of care anti-VEGF-A therapy, aflibercept (Eylea), in patients with treatment-refractory diabetic macular edema, or DME. We retain worldwide rights to develop and commercialize OPT-302 for the treatment of wet AMD and DME and believe that the novel treatment mechanism of OPT-302 has the potential to provide therapeutic benefit for other progressive eye diseases.

We were founded in 1984 and completed our initial public offering and listing of ordinary shares on the Australian Securities Exchange in 1985. In April 2007, we acquired intellectual property relating to VEGF receptor 3 and subsequently developed the intellectual property for our lead product candidate, OPT-302. Our development focus on the treatment of retinal diseases began in 2013. Since then, we have devoted substantially all of our efforts to organizing and staffing our company, business planning, raising capital, developing and manufacturing our lead product candidate, OPT-302, conducting research and development activities, including preclinical studies and clinical trials, and providing general and administrative support for these operations. Our operations relating to the development of OPT-302 have been financed primarily through the issuance and sale of new ordinary shares totaling A$112.7 million through June 30, 2020. We have also received an aggregate of A$35.1 million in cash tax incentives for the five fiscal years ended June 30, 2020 under the Research and Development, or R&D, Tax Incentive Scheme for the funding of the development of and clinical trials for OPT-302.

We have incurred operating losses since 2013. Our ability to generate product revenue sufficient to achieve profitability will be dependent on the successful development and eventual commercialization of OPT-302 and any future product candidates. Our total comprehensive loss was A$20.7 million and A$16.5 million for the years

ended June 30, 2019 and 2020, respectively. As of June 30, 2020, we had an accumulated loss of A$102.6 million. We expect to continue to incur significant expenses for at least the next several years as we advance OPT-302 through late-stage clinical development, including our planned pivotal Phase 3 trials of OPT-302 in combination with anti-VEGF-A therapy for the treatment of wet AMD, and, if these results are favorable, seek regulatory approval for OPT-302. In addition, we may also pursue development of OPT-302 for the treatment of additional indications, including DME, retinal vein occlusion and other indications in which OPT-302 has the potential to provide therapeutic benefit. In addition, if we obtain marketing approval for OPT-302, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Upon the completion of this offering, we expect to incur additional costs associated with operating as a public company in the United States, including significant additional legal, accounting, investor relations, compliance and other expenses.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings, or other capital sources, which may include collaborations with other companies or other strategic transactions as well as Australian research and development tax incentives. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as and when needed, we may have to significantly delay, scale back or discontinue the development and commercialization of OPT-302.

Because of the numerous risks and uncertainties associated with the development of biopharmaceutical product candidates, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may never become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to scale back or discontinue our operations.

As of June 30, 2020, we had cash and cash equivalents of A$62.0 million. We believe that the anticipated net proceeds from this offering, together with our existing cash and cash equivalents as of June 30, 2020, will enable us to fund our operating and research and development expenses through the third calendar quarter of 2023. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See "—Liquidity and Capital Resources."

Impact of COVID-19

We are closely monitoring how the COVID-19 pandemic is affecting our employees, business, preclinical studies and clinical trials. In response to the COVID-19 pandemic, all of our employees have transitioned to working remotely and travel has been restricted. Although operations to date have not been materially affected by the COVID-19 pandemic, at this time, there is significant uncertainty relating to the trajectory of the pandemic. The impact of related responses and disruptions caused by the COVID-19 pandemic may result in difficulties or delays in initiating, enrolling, conducting or completing our planned clinical trials and the incurrence of unforeseen costs as a result of disruptions in clinical supply or clinical trial delays. The impact of COVID-19 on our future results will largely depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the pandemic, travel restrictions and social distancing in Australia, the United States and other countries, business closures or business disruptions, the ultimate impact on financial markets and the global economy and the effectiveness of actions taken in Australia, the United States and other countries to contain and treat the disease.

Components of Our Results of Operations

Revenue

Revenue consists of sales-based royalties in connection with the out-licensing of certain intellectual property assets that are unrelated to our core business and the development of OPT-302 and are not currently

under development. These licenses are primarily used by third-party licensees for research purposes, and we expect revenue from these out-licensing arrangements to be nominal in future periods. These are variable consideration amounts and are recognized when the sales by our license partners to third parties occur, as the performance obligation to transfer the intellectual property to the license partner is already satisfied.

To date, we have not generated any revenue from sales of approved products. Because of the numerous risks and uncertainties associated with product development and regulatory approval, we are unable to predict the amount, timing or whether we will be able to obtain revenue from sales of approved products, and we may never succeed in obtaining regulatory approval for OPT-302 or any other product candidate. If our development efforts for OPT-302 are successful and result in an approved and marketed product, or if we enter into additional collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from such collaboration or license agreements.

Other Income

Other income primarily comprises finance income from interest on bank deposits and funding under a one-time Australian government grant from the Commonwealth Scientific and Industrial Research Organization, or the CSIRO, and the Australian Tax Office.

Operating Expenses

Research and Development Expenses. Research and development expenses comprise the research project costs related to the development programs, including clinical trials, for OPT-302 for the treatment of wet AMD and DME. R&D expenses also include:

- expenses incurred in connection with the clinical development of our product candidates, including under agreements with third parties, such as consultants and contract research organizations, or CROs;
- the cost of manufacturing and purchasing drug products for use in our clinical trials, including under agreements with third parties, such as consultants and contract manufacturing organizations, or CMOs;
- facilities, depreciation and other expenses, which include direct or allocated expenses for rent, maintenance of facilities and insurance;
- costs related to compliance with regulatory requirements; and
- clinical trial insurance.

We expense R&D costs as incurred and have not capitalized any amounts of R&D costs as of June 30, 2020. For the years ended June 30, 2019 and 2020, we did not make any advance payments for goods or services to be received in future periods for use in R&D activities.

Our direct R&D expenses are tracked on a program-by-program basis for our product candidate and consist primarily of external costs, such as fees paid to CROs, CMOs, research laboratories and outside consultants in connection with our process development, manufacturing and clinical development activities. We do not allocate employee costs associated with our research efforts, laboratory supplies and facilities, including depreciation and other indirect costs, to specific programs because these costs are deployed across multiple development activities and indications for OPT-302 and, as such, are not separately classified. We use internal resources primarily to conduct our research activities as well as for managing our process development, manufacturing and clinical development activities. These employees work across multiple development programs and, therefore, we do not track these costs by program.

R&D expenses in fiscal years after June 30, 2020 are expected to comprise costs of a similar nature to that recorded to date. Product candidates in later stages of clinical development, such as OPT-302, generally have

higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our R&D expenses will increase in connection with our planned clinical development, manufacturing and regulatory approval activities in the near term and in the future, including as we initiate our planned pivotal Phase 3 clinical trials of OPT-302 in combination with anti-VEGF-A therapy for the treatment of wet AMD.

At this time, we cannot accurately estimate or know the nature, timing and costs of the efforts that will be necessary to complete the clinical development of OPT-302 and any future product candidates. We may never succeed in achieving regulatory approval for any of our product candidates. The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors, including:

- the scope, rate of progress and expense of our planned clinical trials as well as other R&D activities;
- clinical trial results;
- the terms and timing of regulatory approvals;
- the expense of filing, maintaining, prosecuting, defending and enforcing patent claims and other intellectual property rights;
- the ability to raise necessary additional funds;
- the ability to obtain and maintain third-party insurance coverage and adequate reimbursement;
- the ability to market, commercialize and achieve market acceptance for any products that receive regulatory approval;
- a continued acceptable safety profile of OPT-302 combination therapy following approval in any indication; and
- establishing and maintaining agreements with third-party suppliers and manufacturers for clinical supply and commercial manufacturing of OPT-302, or any other product candidate, if approved.

A change in the outcome of any of these factors with respect to the development of OPT-302 could significantly change the duration, costs and timing associated with clinical trials and development of OPT-302.

Patent Expenses. Patent expenses comprise the cost of outside patent attorneys to manage and prosecute our patent portfolio.

Intellectual Property Costs. Intellectual property costs relate to the license and patent assignment costs in respect of our in-license agreements for certain technologies not currently under development and unrelated to our out-licensing arrangements under which we receive sales-based royalties.

Administrative Expenses. Administrative expenses comprise employee benefit expenses, including share-based payment expenses; investor relations expenses; insurance costs; audit, accountancy and legal fees; other personnel-related expenses; and depreciation expense. We anticipate that our administrative expenses will increase in the future as we increase our headcount to support development of OPT-302 and our continued research activities. We also anticipate that we will incur increased accounting, audit, legal, regulatory, compliance and director and officer insurance costs as well as investor and public relations expenses associated with being a public company in the United States.

Occupancy Expenses. Occupancy expenses represent the costs relating to our headquarters in Melbourne, Australia, including lease maintenance and incidental costs.

Net Foreign Exchange Gain (Loss)

Net foreign exchange gain (loss) represents the impact of the variance in exchange rates between the Australian dollar and the U.S. dollar, Euro, British Pound and Canadian dollar on our cash and cash equivalents, financial assets, financial liabilities and foreign currency denominated transactions.

Income Tax Benefit

Income tax benefit represents the cash incentive amount receivable under the R&D Tax Incentive Scheme, an Australian Federal Government program under which eligible companies with annual aggregated revenue of less than A$20.0 million can receive cash amounts equal to 43.5% of eligible R&D expenditures from the Australian Taxation Office, or the ATO. The ATO may reduce this rate to 41% for the year ended June 30, 2020 if the Australian Federal Government enacts changes to the legislation that governs the scheme in October 2020. The ATO may also make other changes to the eligibility of R&D expenditures, including placing a cap on the amount of non-clinical trial R&D expenses claimed under the scheme. If the rate were to reduce to 41%, the current tax receivable recorded in our consolidated statement of financial position as at June 30, 2020 would be reduced by A$490 thousand, with no change as at June 30, 2019. In addition, if a cap on non-clinical trial R&D expenses were introduced, any effect on our amount claimed under the scheme in respect of the fiscal years ended June 30, 2019 and 2020 would be de minimis.

The R&D Tax Incentive Scheme incentive relates to eligible expenditures incurred in Australia and, under certain circumstances, in other countries in connection with the development of OPT-302. The R&D tax incentive is applied annually to eligible expenditures incurred during the fiscal year following an annual application and subsequent filing of our income tax return subsequent to fiscal year end. We estimate the amount of R&D tax incentive after the completion of a fiscal year based on eligible Australia and overseas expenditures incurred during that year. We expect to continue applying for the R&D tax incentive as we further develop OPT-302. In particular, we intend to apply for the costs expected to be incurred in Australia related to our planned pivotal Phase 3 clinical trials of OPT-302 in combination with anti-VEGF-A therapy for the treatment of wet AMD to be eligible for the R&D tax incentive for future fiscal years once incurred. However, there can be no assurance that the ATO will allow these costs to be eligible for the tax incentive.

Results of Operations for the Fiscal Years Ended June 30, 2019 and 2020

The following table sets forth a summary of our consolidated statement of profit or loss and other comprehensive income for the periods presented.

	Year Ended June 30,	
	2019[1]	2020[2]
	(in thousands)	
Revenue	A$ 159	A$ 87
Other income	837	784
Research and development expenses	(31,348)	(17,954)
Patent expenses	(161)	(429)
Intellectual property costs	(113)	(114)
Administrative expenses	(5,175)	(7,001)
Occupancy expenses	(109)	(34)
Net foreign exchange gain (loss)	363	(401)
Loss before income tax	(35,547)	(25,062)
Income tax benefit	14,637	8,533
Loss for the year	(20,910)	(16,529)
Other comprehensive income:		
Items that will not be reclassified subsequently to profit or loss:		
Fair value gains on investments in financial assets	260	59
Other comprehensive income for the period, net of tax	260	59
Total comprehensive loss for the year	A$(20,650)	A$(16,470)

(1) The consolidated statement of profit or loss and other comprehensive income for the year ended June 30, 2019 reflects the impact of the adoption of IFRS 15 “Revenue from Contracts with Customers” and IFRS 9

"Financial Instruments," which became applicable on January 1, 2018. The impact of the adoption of IFRS 15 and IFRS 9 was not material to the consolidated statement of profit or loss and other comprehensive income.

(2) The consolidated statement of profit or loss and other comprehensive income for the year ended June 30, 2020 reflects the impact of the adoption of IFRS 16 "Leases" which became applicable on January 1, 2019. The details on the impact of the transition are presented in note 5 to our consolidated financial statements appearing elsewhere in this prospectus.

Revenue

Revenue was A$159 thousand for the year ended June 30, 2019, compared to A$87 thousand for the year ended June 30, 2020. This decrease was due to lower sales-based royalties received under our out-licensing arrangements. Revenue for the years ended June 30, 2019 and 2020 consisted of sales-based royalties in connection with the out-licensing of certain intellectual property assets that are unrelated to our core business and the development of OPT-302 and are not currently under development.

Other Income

Other income was A$837 thousand for the year ended June 30, 2019, compared to A$784 thousand for the year ended June 30, 2020. This decrease was primarily due to lower finance income from interest on bank deposits and receipt of a A$78 thousand one-time Australian government grant from the CSIRO during the year ended June 30, 2019, partially offset by receipt of a A$63 thousand one-time ATO grant during the year ended June 20, 2020.

Research and Development Expenses

Research and development expenses were A$31.3 million for the year ended June 30, 2019, compared to A$18.0 million for the year ended June 30, 2020. This decrease was primarily due to costs related to our Phase 2b clinical trial of OPT-302 in wet AMD completed during the year ended June 30, 2019, partially offset by increased chemistry manufacturing and controls costs incurred during the year ended June 30, 2020 related to manufacturing activities in preparation for our planned Phase 3 clinical trials of OPT-302 in combination with anti-VEGF-A therapy for the treatment of wet AMD. Our research and development expenses are broken down as set forth in the table below:

	Year Ended June 30,	
	2019	2020
	(in thousands)	
Costs related to the Phase 2b clinical trial of OPT-302 in wet AMD	A$20,718	A$ 3,197
Costs related to the Phase 1b/2a clinical trial of OPT-302 in DME	9,646	8,022
Chemistry manufacturing and controls	675	5,890
Other direct non-clinical expenses	309	845
Total research and development expenses	A$31,348	A$17,954

Patent Expenses

Patent expenses were A$161 thousand for the year ended June 30, 2019, compared to A$429 thousand for the year ended June 30, 2020. This increase was primarily due to validation work carried out on our European patent application across multiple jurisdictions.

Intellectual Property Costs

Intellectual property costs were A$113 thousand for the year ended June 30, 2019, compared to A$114 thousand for the year ended June 30, 2020. This increase was due to fluctuations in exchange rates.

Intellectual property costs for the years ended June 30, 2019 and 2020 consisted of the license and patent assignment costs in respect of our in-license agreements for certain technologies not currently under development and unrelated to our out-licensing arrangements under which we receive sales-based royalties.

Administrative Expenses

Administrative expenses were A$5.2 million for the year ended June 30, 2019, compared to A$7.0 million for the year ended June 30, 2020. This increase was primarily due to a A$0.1 million increase in share-based payments, a A$1.3 million increase in professional fees and expenses and a A$0.2 million increase in personnel-related expenses, each resulting from expansion of supporting administrative functions to aid continued research and development and capital raising activities in the year ended June 30, 2020, as well as a A$0.1 million increase in depreciation expense and a A$0.1 million increase in insurance costs.

Occupancy Expenses

Occupancy expenses were A$109 thousand for the year ended June 30, 2019, compared to A$34 thousand for the year ended June 30, 2020. This decrease was primarily due to a reduction in lease rental costs under the lease for our headquarters in Melbourne, Australia of A$77 thousand resulting from the reclassification of lease rental expenses into depreciation of right-of-use assets. This reclassification followed our adoption of accounting treatments required by IFRS 16 “Leases” during the fiscal year ended June 30, 2020.

Net Foreign Exchange Gain (Loss)

Net foreign exchange differences were a gain of A$363 thousand for the year ended June 30, 2019, compared to a loss of A$401 thousand for the year ended June 30, 2020, primarily as a result of net variances of the exchange rate between the Australian dollar and U.S. dollar on U.S. dollar-denominated cash and cash equivalents, financial assets, financial liabilities and foreign currency denominated transactions.

Income Tax Benefit

Income tax benefit was A$14.6 million for the year ended June 30, 2019, compared to A$8.5 million for the years ended June 30, 2020. This decrease was due to lower R&D tax incentive receivable recognized during the year ended June 30, 2020.

Liquidity and Capital Resources

The liquidity and capital resources discussion that follows contains certain estimates as of the date of this prospectus of our estimated future sources and uses of liquidity (including estimated future capital resources and capital expenditures) and future financial and operating results. These estimates reflect numerous assumptions made by us with respect to industry performance, general business, economic, regulatory, market and financial conditions and other future events, and matters specific to our businesses, all of which are difficult or impossible to predict and many of which are beyond our control.

Sources and Uses of Liquidity

Our operations relating to the development of OPT-302 have been financed primarily through the issuance and sale of new ordinary shares totaling A$112.7 million through June 30, 2020. We have also received an aggregate of A$35.1 million in the five fiscal years ended June 30, 2020 under the R&D Tax Incentive Scheme for the funding of the development and clinical trials of OPT-302.

As of June 30, 2020, we had cash and cash equivalents of A$62.0 million to fund the manufacturing of sufficient clinical grade OPT-302 drug product and complete the regulatory and clinical preparation activities to initiate our planned pivotal Phase 3 clinical trials of OPT-302 in combination with anti-VEGF-A therapy for the treatment of wet AMD. As of June 30, 2020, we had an accumulated loss of A$102.6 million.

Funding Requirements

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating and research and development expenses through the third calendar quarter of 2023. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect.

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, continue or initiate clinical trials of, and seek marketing approval for, OPT-302 and any future product candidates. In addition, if we obtain marketing approval for OPT-302 or any future product candidates, we expect to incur significant commercialization expenses related to sales, marketing, manufacturing and distribution to the extent that such sales, marketing and distribution are not the responsibility of any future collaborators. Further, following the completion of this offering, we expect to incur additional costs associated with operating as a public company in the United States. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations.

Until we can generate a sufficient amount of revenue from the sale of approved products, if ever, we expect to finance our operating activities through our existing liquidity, the net proceeds from this offering and future financing activities, including a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a holder of ADSs. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, intellectual property, future revenue streams or product candidates. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our present and future funding requirements will depend on many factors, including, among other things:

- the initiation, progress, timing, costs and results of our clinical trials for OPT-302, including our planned pivotal Phase 3 clinical trials of OPT-302 in combination with anti-VEGF-A therapies for the treatment of wet AMD, and any future product candidates we may develop;
- costs associated with expanding our organization, including our management infrastructure;
- the costs involved in filing patent applications and maintaining and enforcing patents or defending against claims of infringement raised by third parties;
- the time and costs involved in obtaining regulatory approval for our product candidates and any delays we may encounter as a result of evolving regulatory requirements or adverse results with respect to any of these product candidates;
- selling and marketing activities undertaken in connection with the commercialization of OPT-302, together with the costs involved in the creation of a sales and marketing organization; and
- the costs of operating as a public listed company in both Australia and the United States.

Conducting clinical trials is a time-consuming, expensive and uncertain process that takes many years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, OPT-302 or any future product candidate, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of OPT-302 and any future product candidate that we do not expect to be commercially available for many years, if at all. Accordingly, we

will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. For more information as to the risks associated with our future funding needs, see "Risk Factors—Risks Related to Our Financial Position and Need for Capital."

Cash Flows

The following table summarizes our cash flows for the periods presented:

	Year Ended June 30,	
	2019	2020
	(in thousands)	
Net cash used in operating activities	A$(24,185)	A$ (8,782)
Net cash provided by investing activities	321	476
Net cash provided by financing activities	12,630	48,980
Net (decrease)/increase in cash and cash equivalents	A$(11,234)	A$40,674

Operating Activities

For the year ended June 30, 2019, net cash used in operating activities was A$24.2 million, attributable to a net loss of A$20.9 million adjusted for A$13.9 million in non-cash items as well as a net cash outflow from changes in operating assets and liabilities of A$1.4 million, partially offset by a R&D tax incentive of A$12.0 million. Non-cash adjustments of A$13.9 million consisted of A$14.6 million in income tax benefit recognized in profit or loss and A$259 thousand in net exchange differences, partially offset by A$967 thousand in share-based payments and A$33 thousand in depreciation expense.

For the year ended June 30, 2020, net cash used in operating activities was A$8.8 million, attributable to a net loss of A$16.5 million adjusted for A$6.9 million in non-cash items as well as a net cash flow from changes in operating assets and liabilities of A$18 thousand, partially offset by a R&D tax incentive of A$14.6 million. Non-cash adjustments of A$6.9 million consisted of A$8.5 million in income tax benefit recognized in profit or loss and A$401 thousand in net exchange differences, partially offset by A$1.1 million in share-based payments and A$144 thousand in depreciation expense.

Investing Activities

For the years ended June 30, 2019 and 2020, net cash provided by investing activities was A$321 thousand and A$476 thousand, respectively, attributable to A$339 thousand and A$482 thousand, respectively, in cash received on disposal of our financial asset of shares and options in Antisense Therapeutics Ltd., an ASX-listed company, offset by cash payments of A$18 thousand and A$7 thousand, respectively, for the purchase of computer equipment.

Financing Activities

For the year ended June 30, 2019, net cash provided by financing activities was A$12.6 million from the issuance of new ordinary shares on the exercise of options previously issued in connection with a capital raise.

For the year ended June 30, 2020, net cash provided by financing activities was A$49.0 million, attributable to A$420 thousand received on the exercise of options granted to employees and A$48.7 million from the issuance of new ordinary shares in a private placement to institutional investors in Australia and the United Kingdom. Net cash provided by financing activities also included A$100 thousand in respect of the payment of lease liabilities.

Contractual Obligations

The following table summarizes our contractual obligations as of June 30, 2020:

	Payments Due By Period				
	Total	Less than 1 Year	1-3 Years	3-5 Years	More than 5 Years
			(in thousands)		
June 30, 2020					
Operating lease commitments[1]	24	7	17	—	—
Purchase obligations[2]	8,625	8,285	340	—	—
License agreements[3]	218	22	87	—	109
Total	A$8,867	A$8,314	A$444	A$—	A$109

(1) Amounts represent payments due for low value leases of office equipment not included in our consolidated financial statements appearing elsewhere in this prospectus.

(2) Amounts consist of purchase obligations of OPT-302 drug product under our manufacturing services agreement with Patheon Biologics Company Australia Pty Ltd. and Patheon Biologics Company B.V.

(3) Amounts represent payments due under in-license agreements with the Schepens Eye Research Institute and the University of Siena for technologies not currently under development and unrelated to our out-licensing arrangements under which we receive sales-based royalties.

The commitment amounts in the table above are associated with contracts that are enforceable and legally binding and that specify all significant terms, including fixed or minimum services to be used, fixed, minimum or variable price provisions, and the approximate timing of the actions under the contracts. The table does not include obligations under agreements that we can cancel without a significant penalty.

We enter into agreements in the normal course of business with contract research organizations for clinical trials and with vendors for other services and products for operating purposes which are cancelable at any time by us. These payments are not included in this table of contractual obligations.

Commercial License Agreement with Selexis SA

In October 2013, we entered into a commercial license agreement, or the Selexis Agreement, with Selexis SA, or Selexis, under which Selexis granted us a non-exclusive, worldwide, sublicensable license under certain patents, know-how and other intellectual property controlled by Selexis to use certain cell lines, deliverables and materials provided by Selexis to manufacture OPT-302 and related products and to use, sell and otherwise exploit such products.

We paid Selexis a nominal upfront payment upon entering into the Selexis Agreement. We are also required to make certain payments under the Selexis Agreement totaling approximately US$1.3 million upon the achievement of certain development and commercial milestones. We are also obligated to pay a low single-digit running royalty on worldwide net sales of the licensed products. Our royalty obligations will continue, on a product-by-product and country-by-country basis, until the expiration of the relevant patents, but will not extend beyond October 2024 in any event. After the expiration of the royalty term, our license will continue and become full paid, perpetual and irrevocable.

The Selexis Agreement will expire on the date of expiration of the last-to-expire of the license patents. Either party may terminate the Selexis Agreement for the other party's uncured material breach or bankruptcy. We may also terminate the Selexis Agreement at any time upon prior notice to Selexis.

Off-Balance Sheet Arrangements

During the periods presented, we did not, and we do not currently, engage in off-balance sheet financing arrangements as defined under SEC rules, such as relationships with other entities or financial partnerships,

which are often referred to as structured finance or special purpose entities, established for the purpose of facilitating financing transactions that are not required to be reflected on our consolidated statement of financial position. In addition, we do not engage in trading activities involving non-exchange traded contracts.

Critical Accounting Policies and Estimates

We believe that the following accounting policies involve a high degree of judgment and complexity. Accordingly, these are the policies we believe are the most critical to aid in fully understanding and evaluating our consolidated financial condition and results of our operations. See note 3 to our consolidated financial statements appearing elsewhere in this prospectus for a description of our other significant accounting policies. The preparation of our consolidated financial statements in conformity with IFRS requires us to make estimates and judgments that affect the amounts reported in those financial statements and accompanying notes. Although we believe that the estimates we use are reasonable, due to the inherent uncertainty involved in making those estimates, actual results reported in future periods could differ from those estimates.

Research and Development Costs

The majority of our expenditures is incurred as a result of our clinical trials for OPT-302. During the years ended June 30, 2019 and 2020, we completed a Phase 2b clinical trial of OPT-302 combination therapy for the treatment of wet AMD. During the years ended June 30, 2019 and 2020, we progressed a Phase 1b/2a clinical trial of OPT-302 combination therapy for the treatment of DME. A key measure of our performance is the level of expenditures incurred on the research and development of OPT-302.

Judgement is required in relation to:

- the classification of expenses in the income statement between research and development costs and operating expenses; and
- whether costs relate to research or development, and consequently if they meet the capitalization criteria under International Accounting Standards, or IAS, 38 “Intangible Assets.”

We have determined that we are still in a research phase, and accordingly, no development costs have been capitalized as of June 30, 2019 or June 30, 2020.

Share-based Payment Transactions

We provide benefits to our directors and employees (including key management personnel) in the form of share-based payments, whereby employees render services in exchange for ordinary shares or rights over ordinary shares (equity-settled transactions). The cost of these equity-settled transactions with employees is measured by reference to the fair value at the date at which they are granted. Binomial models are used to value the options issued, with key assumptions being the listed price per ordinary share on the grant date, the option exercise price, expected volatility of the underlying ordinary shares based on the historical share price volatility and the risk-free interest rate.

The cost of the equity-settled transactions is recognized, together with a corresponding increase in equity, over the period in which the performance conditions are fulfilled (the vesting period), ending on the date on which the relevant employees become fully entitled to the award (the vesting date). The charge to profit or loss for the period is the cumulative amount less the amounts already charged in previous periods. There is a corresponding credit to equity.

Until an award has vested, any amounts recorded are contingent and will be adjusted if more or fewer awards vest than were originally anticipated to do so.

Income Tax—Research and Development Tax Incentive

The R&D Tax Incentive Scheme is an Australian Federal Government program under which eligible companies with annual aggregated revenue of less than A$20 million can receive cash amounts equal to 43.5% of eligible research and development expenditures from the ATO. The R&D Tax Incentive Scheme incentive relates to eligible expenditures incurred in Australia and, under certain circumstances, overseas on the development of our lead candidate OPT-302. The R&D tax incentive is applied annually to eligible expenditures incurred during our financial year following an annual application and subsequent filing of our income tax return after the financial year end.

We estimate the amount of R&D tax incentive after the completion of the financial year based on eligible Australia and overseas expenditures incurred during that year.

We have presented incentives in respect of the R&D Tax Incentive Scheme within income tax benefit in the Statement of Profit or Loss and Other Comprehensive Income by analogizing with IAS 12 "Income Taxes."

Judgment is required as to the eligibility for the R&D tax incentive in respect of:

- our ability to make claims and its continued compliance under the scheme;
- research and development and other supporting costs previously approved by Australian tax authorities;
- estimated amounts, timing and geographical location of future costs related to the projects for which applications have been approved to date; and
- assessment of whether expenditure on projects for which approval has been given by Australian tax authorities relate to Australian or overseas expenditure.

For the years ended June 30, 2019 and 2020, we have recognized an R&D tax incentive receivable of A$14.6 million and $8.5 million, respectively within our consolidated statement of financial position with a corresponding amount recognized within income tax benefit within the consolidated statement of profit or loss and other comprehensive income. The R&D tax incentive receivable as at June 30, 2020 is based on the legislation as currently enacted as at June 30, 2020. Any proposed changes to the legislation, such as rate changes to the eligibility requirements, may have a retrospective impact if the legislation is passed in its currently proposed form.

Investment tax credits such as the R&D tax incentive are outside of the scope of IAS 12 "Income Taxes" and IAS 20 "Accounting for Government Grants and Disclosure of Government Assistance." Based on the guidance in IAS 8 "Accounting Policies, Changes in Accounting Estimates and Errors," companies need to make an accounting policy choice on how to present these incentives, which in practice is done by either analogizing with IAS 12 or with IAS 20. We have determined that the R&D tax incentive should be presented by analogizing to IAS 12 because the nature of the incentive is considered to be more closely aligned to income taxes, based on the following considerations:

- The R&D tax incentive is considered an income tax offset which will be offset against our tax obligation if and when we return to a net tax payable position. In addition, while we are currently eligible to receive cash payments under the Scheme since our consolidated revenue is currently below A$20 million, if and when we generate revenue in excess of A$20 million, the R&D tax incentive will become non-refundable and can only be offset against any future income tax payable by us.
- The ATO, which is the tax authority in Australia, manages the annual claims process as the R&D tax incentive is included in our annual income tax return.
- The ATO is also responsible for making the R&D tax incentive cash payment if a company is eligible for a cash refund under the program, oversees compliance with the requirements of the R&D tax incentive scheme and performs pre-issuance reviews.

Recently Adopted Accounting Pronouncements

Amendments to Accounting Standards that are Mandatorily Effective for the Current Year

We have adopted all of the new and revised Standards and Interpretations issued by the IASB that are relevant to our operations and effective for the current year.

New and revised Standards and amendments thereof and Interpretations effective for the current year that are relevant to us include:

- IFRS 16 "Leases";
- Annual Improvements to IFRS Standards 2015–2017 Cycle Amendments to IFRS 3 "Business Combinations", IFRS 11 "Joint Arrangements", IAS 12 "Income Taxes" and IAS 23 "Borrowing Costs"; and
- IFRIC 23 "Uncertainty over Income Tax Treatments".

IFRS 16 Leases

In the current year, we applied IFRS 16 Leases, which is effective for annual periods that begin on or after January 1, 2019.

IFRS 16 introduces new or amended requirements with respect to lease accounting. It introduces significant changes to lessee accounting by removing the distinction between operating and finance leases and requiring the recognition of a right-of-use asset and a lease liability at commencement for all leases, except for short-term leases and leases of low value assets. Details of these new requirements are described in note 3 to our consolidated financial statements appearing elsewhere in this prospectus.

The date of initial application of IFRS 16 for us is July 1, 2019. We have applied IFRS 16 using the cumulative catch-up approach which:

- requires us to recognize the cumulative effect of initially applying IFRS 16 as an adjustment to the opening balance of retained earnings at the date of initial application; and
- does not permit restatement of comparatives, which continue to be presented under IAS 17 "Leases" and IFRIC 4 "Determining whether an Arrangement Contains a Lease."

We have made use of the practical expedient available on transition to IFRS 16 to not reassess whether a contract is or contains a lease. Accordingly, the definition of a lease in accordance with IAS 17 and IFRIC 4 will continue to be applied to those leases entered or changed before July 1, 2019.

The change in definition of a lease mainly relates to the concept of control. IFRS 16 determines whether a contract contains a lease on the basis of whether the customer has the right to control the use of an identified asset for a period of time in exchange for consideration. This is in contrast to the focus on "risks and rewards" in IAS 17 and IFRIC 4.

Impact on Lease Accounting

Former Operating Leases

IFRS 16 changes how we account for leases previously classified as operating leases under IAS 17, which operating lease payments were recognized as an expense in profit or loss on a straight-line basis over the lease term.

Applying IFRS 16, for all leases (except as noted below), we have:

- Recognize right-of-use assets and lease liabilities in the consolidated statement of financial position, initially measured at the present value of the future lease payments;
- Recognize depreciation of right-of-use assets and interest on lease liabilities in profit or loss; and
- Separate the total amount of cash paid into a principal portion (presented within financing activities) and interest (presented within operating activities) in the consolidated statement of cash flows.

Lease incentives (e.g. rent-free period) are recognized as part of the measurement of the right-of-use assets and lease liabilities whereas under IAS 17 they resulted in the recognition of a lease incentive, amortized as a reduction of rental expenses generally on a straight-line basis. Under IFRS 16, right-of-use assets are tested for impairment in accordance with IAS 36 "Impairment of Assets".

For short-term leases (lease term of 12 months or less) and leases of low-value assets (such as photo copiers and telephones), we have opted to recognize a lease expense on a straight-line basis as permitted by IFRS 16. This expense is presented within "administrative expenses" in profit or loss.

Financial Impact of the Initial Application of IFRS 16

The previous lease for our headquarters expired on July 14, 2019. The adoption of IFRS 16 did not have a material impact on our results on the date of transition. Following the renewal of the leased office premises on July 15, 2019, we recognized a right-of-use asset of A$365,264 and a corresponding lease liability of $365,264 in respect of this lease. The impact on profit or loss during the fiscal year ended June 30, 2020 was to decrease occupancy expenses by A$110,800; increase depreciation by A$121,754; and increase finance interest expense by A$7,680.

Under IAS 17, all lease payments on operating leases are presented as part of cash flows from operating activities. During the year ended June 30, 2020, the impact of the changes under IFRS 16 reduced the cash used in operating activities by A$100,189 and decreased net cash generated from financing activities by the same amount.

Other Pronouncements Adopted for the First Time in the Year Ended June 30, 2020

During the fiscal year ended June 30, 2020, we applied a number of amendments to IFRS and Interpretations issued by the IASB that are effective for an annual period that begins on or after January 1, 2019. Their adoption has not had any material impact on the disclosures or on the amounts reported in our consolidated financial statements.

New and Revised International Financial Reporting Standards and Interpretations on Issue But not Yet Effective

The new and revised International Financial Reporting Standards, Interpretations and amendments that have been issued but are not yet effective, are not expected to have a material impact on the amounts recognized or disclosures included in our consolidated financial statements.

Qualitative and Quantitative Disclosures about Market Risk

We are exposed to market risks in the ordinary course of our business. Market risk represents the risk of loss that may impact our financial position due to adverse changes in financial market prices and rates. Our market risk exposure is primarily the result of fluctuations in interest rates and foreign currency exchange rate risk.

Interest Rate Risk

As of June 30, 2020, we had cash and cash equivalents of A$62.0 million. We have limited exposure to interest rate risk. Our exposure to market interest rates relates primarily to the short-term deposits. The deposits

are held with two of Australia's largest banks. Our cash and cash equivalents are not locked into long-term deposits at fixed rates so as to mitigate the risk of earning interest below the current floating rate. We do not have any credit facilities bearing variable interest rates.

Foreign Currency Exchange Rate Risk

As a result of services provided by non-related entities in the United States, Canada, United Kingdom and Europe, part of our financial assets and liabilities and foreign currency denominated transactions are affected by movements in the applicable exchange rate. We do not enter into any hedging transactions. We enter into forward rate foreign exchange rate contracts in respect of the settlement of supplier invoices denominated in U.S. dollars to mitigate the risk of movements in the U.S. dollar and Australian dollar exchange rates. We are primarily exposed to foreign exchange risk inherent in U.S. dollar-denominated contracts related to our clinical development activities. As of June 30, 2019 and June 30, 2020, we had A$4.5 million and A$5.0 million, respectively, in net exposure to the U.S. dollar, primarily in payables. An increase or decrease of the Australian dollar to U.S. dollar exchange rate by 10% would increase our after tax loss by A$319 thousand (2019: A$285 thousand) or decrease our after tax loss by A$390 thousand (2019: A$349 thousand), respectively. As we continue our clinical development activities, we expect to face continued exposure to exchange rate risk from the U.S. dollar. There was minimal or insignificant exposure to the British Pound, Euro and Canadian dollar during the years ended June 30, 2019 and 2020.

Emerging Growth Company Status

As a company with less than $1.07 billion in revenue during our last fiscal year, we qualify as an "emerging growth company" as defined in the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- exemption from the auditor attestation requirement of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, in the assessment of our internal controls over financial reporting; and
- to the extent that we no longer qualify as a foreign private issuer, (i) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and (ii) exemptions from the requirements of holding a non-binding advisory vote on executive compensation, including golden parachute compensation.

We may take advantage of these exemptions until such time that we are no longer an emerging growth company. Accordingly, the information that we provide shareholders and holders of the ADSs may be different than you might obtain from other public companies. We will cease to be an emerging growth company upon the earliest to occur of (i) the last day of the fiscal year in which we have more than $1.07 billion in annual revenue; (ii) the last day of the fiscal year in which we qualify as a "large accelerated filer"; (iii) the date on which we have, during the previous three-year period, issued more than $1.0 billion in non-convertible debt securities; and (iv) the last day of the fiscal year in which the fifth anniversary of this offering occurs.

In addition, Section 107 of the JOBS Act provides that an emerging growth company can use the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Given that we currently report and expect to continue to report under IFRS, as issued by the IASB, we have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required by the IASB.

Foreign Private Issuer Status

We are also considered a "foreign private issuer" under U.S. securities laws. In our capacity as a foreign private issuer, we are exempt from certain rules under the Securities Exchange Act of 1934, as amended, that

impose certain disclosure obligations and procedural requirements for proxy solicitations under Section 14 of the Exchange Act. In addition, our senior management, the members of our board of directors and our principal shareholders are exempt from the reporting and "short-swing" profit recovery provisions of Section 16 of the Exchange Act and the rules under the Exchange Act with respect to their purchases and sales of our securities. Moreover, we are not required to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. companies whose securities are registered under the Exchange Act. In addition, we are not required to comply with Regulation FD, which restricts the selective disclosure of material information.

We may take advantage of these exemptions until such time as we are no longer a foreign private issuer. We will remain a foreign private issuer until such time that 50% or more of our outstanding voting securities are held by U.S. residents and any of the following three circumstances applies: (i) the majority of the members of board of directors or our senior management are U.S. citizens or residents; (ii) more than 50% of our assets are located in the United States; or (iii) our business is administered principally in the United States.

We have taken advantage of certain reduced reporting and other requirements in this prospectus. Accordingly, the information contained herein may be different from the information you receive from other public companies.

BUSINESS

Overview

We are a clinical stage biopharmaceutical company developing a novel therapy for the treatment of highly prevalent and progressive retinal diseases. We are developing our Phase 3-ready product candidate, OPT-302, a biologic designed to inhibit VEGF-C and VEGF-D, to complement VEGF-A inhibitors for the treatment of ophthalmic diseases. Anti-VEGF-A therapies represent the standard of care for wet age-related macular degeneration, or AMD, and other retinal diseases; however, there remains a significant unmet medical need as many patients do not adequately respond to these treatments. As the only biologic inhibitor of VEGF-C and VEGF-D in clinical development, OPT-302 differs from standard of care therapies and when administered in combination with a VEGF-A inhibitor, is designed to achieve broader inhibition of the vascular endothelial growth factor, or VEGF, family and target a mechanism of clinical resistance to improve visual acuity. Our lead indication for OPT-302 combination therapy is wet AMD, a chronic, progressive disease and the leading cause of vision loss for individuals over the age of 50. In a 366-patient Phase 2b clinical trial for the treatment of wet AMD, 2.0 mg OPT-302, in combination with a standard of care anti-VEGF-A therapy, ranibizumab (Lucentis), met the primary endpoint of a statistically significant superior mean gain in visual acuity over ranibizumab monotherapy at week 24. We intend to initiate two pivotal Phase 3 clinical trials in treatment-naive patients with wet AMD to evaluate the efficacy and safety of OPT-302 in combination with anti-VEGF-A therapies compared to anti-VEGF-A monotherapy in the first half of 2021. We expect to report topline data from these Phase 3 clinical trials in 2023. In addition to our clinical trials in wet AMD, we have observed evidence of improved clinical outcomes in a Phase 1b/2a clinical trial of OPT-302 in combination with another standard of care anti-VEGF-A therapy, aflibercept (Eylea), in patients with treatment-refractory diabetic macular edema, or DME. We retain worldwide rights to develop and commercialize OPT-302 for the treatment of wet AMD and DME and believe that the novel treatment mechanism of OPT-302 has the potential to provide therapeutic benefit for other progressive eye diseases.

Wet AMD is a rapidly progressing disease with loss of central vision developing over a period of weeks to months in which abnormal new blood vessels form in the back of the eye in a process called choroidal neovascularization, or CNV. These newly formed vessels are highly permeable, leaking exudate leading to fluid accumulation and retinal lesion formation. This, in turn, adversely affects sensory cells in the retina and if left untreated, results in rapid loss of visual acuity.

Wet AMD affects approximately one million people in the United States and 2.5 million people in Europe. The standard of care for wet AMD and other ocular neovascular diseases is the administration of monotherapies that primarily inhibit VEGF-A. These therapeutic agents, which include ranibizumab and aflibercept, prevent VEGF-A molecules from binding to, and activating, VEGF receptors and thereby inhibit the formation and permeability of blood vessels. As the risk of developing wet AMD increases with age, it is predicted that the overall aging of the population will result in a significant increase in the number of wet AMD cases, both in the United States and worldwide. Many wet AMD patients also experience suboptimal clinical responses despite receiving one or both of the leading standard of care treatments ranibizumab and aflibercept, which had combined annual worldwide sales of over US$11.9 billion in 2019. In addition, nearly half of wet AMD patients are treated with off-label bevacizumab as a lower cost alternative anti-VEGF-A therapy. As a result, we believe there is a significant and expanding market opportunity for novel therapies that can improve vision in patients with wet AMD, which has the potential to lead to sales greater than the combined annual sales of ranibizumab and aflibercept.

Despite the widespread use and commercial success of VEGF-A inhibitors, at least 45% of wet AMD patients treated with a VEGF-A inhibitor experience some degree of suboptimal clinical response, with a majority of patients failing to achieve 20/40 vision after 12 months of treatment, providing further opportunity for visual acuity improvement. Furthermore, many patients have persistent retinal fluid and insufficient gains in visual acuity to resume routine daily activities such as driving and reading following regular treatment with a

VEGF-A inhibitor. In addition, improvements in visual acuity following regular administration of VEGF-A monotherapy are often not sustained with long-term use.

OPT-302 is designed to address a deficiency in the treatment paradigm for wet AMD and other retinal diseases, such as DME, by targeting alternate members of the VEGF family, namely VEGF-C and VEGF-D, which are not targeted by current standard of care therapies. VEGF-C and VEGF-D function in parallel with VEGF-A to drive neovascularization and vascular leakage, which are key hallmarks of both wet AMD and DME. In addition, treatment with VEGF-A inhibitors leads to upregulation of VEGF-C and VEGF-D to compensate for VEGF-A inhibition, which may represent an important mechanism of clinical resistance to anti-VEGF-A monotherapy. We are developing OPT-302 to be used in combination with standard of care anti-VEGF-A monotherapies to achieve broader inhibition of the VEGF family, with the goal of improving overall efficacy and demonstrating superior vision gains over that which can be achieved by inhibiting VEGF-A alone.

In our completed Phase 2b wet AMD clinical trial, 2.0 mg OPT-302 in combination with ranibizumab demonstrated a statistically significant superior mean gain in visual acuity at week 24 compared to patients treated with ranibizumab with a sham injection, which we refer to as ranibizumab monotherapy. The trial was an international, multi-center, double-masked trial in 366 treatment-naive patients with wet AMD. Patients were randomized into three groups and received intravitreal injections every four weeks of either 0.5 mg or 2.0 mg OPT-302 in combination with 0.5 mg ranibizumab or 0.5 mg ranibizumab monotherapy. Treatments were administered by intravitreal injections once every four weeks for 20 weeks (six treatments in total). The primary endpoint was the mean change at week 24 in best corrected visual acuity, or BCVA, from baseline on the Early Treatment of Diabetic Retinopathy Study, or ETDRS, standardized eye chart, which we refer to as visual acuity. Patients treated with 2.0 mg OPT-302 combination therapy demonstrated a statistically significant improvement in visual acuity compared to patients treated with ranibizumab monotherapy. In the patients that received 2.0 mg OPT-302 combination therapy, visual acuity improved at week 24 from baseline by a mean of +14.2 letters compared to +10.8 letters for those treated with ranibizumab monotherapy, a statistically significant benefit of +3.4 letters. Patients that received 2.0 mg OPT-302 combination therapy also demonstrated improvements in retinal anatomy which were consistent with the visual acuity gains observed in the trial, including reductions in retinal fluid and lesion size by week 24. In a pre-specified subgroup analysis, greater activity of OPT-302 was observed in lesion types that are considered more difficult to treat with anti-VEGF-A therapy. Our clinical experience to date, which includes administration of over 1,800 doses of OPT-302 to 399 patients with retinal disease, indicates that OPT-302 intravitreal injections are well tolerated, with the incidence of treatment-emergent adverse events, or TEAEs, comparable to anti-VEGF-A monotherapy in our clinical trials.

We are planning to initiate two concurrent pivotal Phase 3 clinical trials for the treatment of wet AMD. These double-masked, sham-controlled Phase 3 clinical trials will enroll treatment-naive patients and assess the efficacy and safety of 2.0 mg of OPT-302 in combination with ranibizumab (Lucentis) (referred to as the ShORe trial) or aflibercept (Eylea) (referred to as the COAST trial), compared to ranibizumab or aflibercept monotherapy in each respective trial. In addition, to understand the durability of OPT-302 treatment effect with less frequent dosing, each trial will compare the clinical efficacy of OPT-302 administered in combination with the applicable VEGF-A inhibitor on an every four-week and every eight-week dosing regimen. For consistency, the ShORe and COAST Phase 3 trials build upon and maintain key features of our Phase 2b clinical trial of OPT-302 combination therapy for the treatment of wet AMD, while evaluating the administration of OPT-302 combination therapy over a longer treatment period and in a greater number of patients. The primary endpoint of both trials will be the mean change in visual acuity from baseline at week 52. Patients will continue to be dosed until week 96 to further assess long-term safety at week 100. We expect to initiate the trials in the first half of 2021 and to report topline data in 2023. If the results at the completion of the primary efficacy phase at week 52 of the Phase 3 clinical trials are favorable, we intend to file for marketing approval for OPT-302 for the treatment of wet AMD in the United States, European Union and other territories.

In addition to our planned pivotal Phase 3 clinical trials, we plan to develop a co-formulation of OPT-302 with an approved and/or biosimilar anti-VEGF-A therapy designed to achieve VEGF-A, VEGF-C and VEGF-D inhibition following the administration of a single intravitreal injection of the co-formulated product. OPT-302 is

currently administered as a combination therapy consisting of a sequential injection of OPT-302 following intravitreal administration of a VEGF-A inhibitor. We believe that a co-formulated OPT-302 and VEGF-A inhibitor product could provide flexibility of treatment options for physicians and reduce the frequency and number of injections for patients. We expect to file an investigative new drug application, or IND, for the co-formulated product in the second half of 2021 and subsequently investigate the co-formulated product in a Phase 1 clinical trial for the treatment of wet AMD.

We are also investigating the therapeutic potential of OPT-302 for DME. DME is a progressive eye disease and a complication of diabetic retinopathy, or DR, a condition caused by chronically elevated glucose levels in diabetics that damages the retina. DME can cause blurred vision, severe vision loss and blindness. Wet AMD and DME share a similar underlying pathophysiology, including retinal neovascularization and increased vascular permeability, and as a result, VEGF-A inhibitors are also considered the standard of care treatment for DME. Based on its mechanism of action and clinical results to date, we believe that OPT-302 also has the potential to deliver therapeutic benefit in DME patients. In our Phase 1b/2a clinical trial of OPT-302 in combination with aflibercept in patients with treatment-refractory DME, we observed evidence of improved clinical outcomes following OPT-302 combination therapy in this indication.

We also believe that our novel treatment mechanism has the potential to provide therapeutic benefit for other progressive retinal diseases beyond wet AMD and DME. We may further investigate the efficacy of OPT-302 to improve clinical outcomes in patients with polypoidal choroidal vasculopathy, or PCV, a form of wet AMD that is highly prevalent in Asian populations and less responsive to anti-VEGF-A therapy than other wet AMD subtypes. Beyond wet AMD and DME, we may explore applications of OPT-302 in other retinal diseases in which a VEGF-C or VEGF-D inhibitor could have therapeutic potential, such as retinal vein occlusion, or RVO.

Our Company

We are a public company listed on the Australian Securities Exchange. We have assembled a team of experts with deep scientific, clinical and business expertise in biotechnology and specifically in neovascular disease. Megan Baldwin, Ph.D., our Chief Executive Officer and Managing Director, has over 20 years of research and development and biopharmaceutical industry experience on neovascularization and therapeutic strategies in ophthalmic indications and cancer. Prior to joining our company, she was a postdoctoral research fellow and an associate market planning manager at Genentech, where she conducted angiogenesis research before joining the anti-angiogenic therapy commercial group. Mike Tonroe, our Chief Financial Officer and Company Secretary, was previously Chief Financial Officer of the Australian Synchrotron in Melbourne and has over 20 years of experience in financial management, including as Chief Financial Officer to other companies as well as board-level positions for private and listed companies in Australia, United Kingdom, the United States and Canada. We believe that the breadth of experience and successful track record of our senior management, combined with our established relationships with leaders in the industry and medical community, provide us with unique insights into biologic drug development for the treatment of neovascular disease.

Our Strategy

Our goal is to become a leader in developing and commercializing therapeutics for the treatment of retinal diseases. The key elements of our strategy are to:

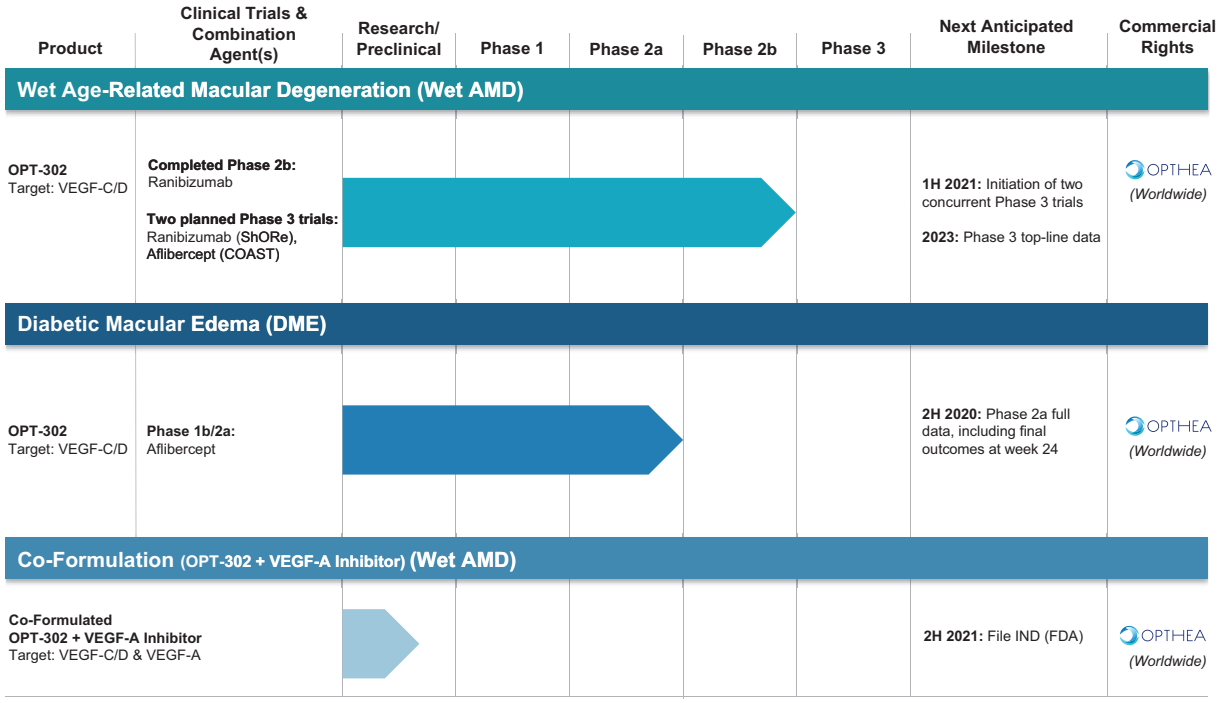
- **Advance OPT-302 through two concurrent Phase 3 trials for the treatment of wet AMD.** Based on the positive results of our Phase 2b trial in wet AMD, we plan to initiate two concurrent pivotal Phase 3 clinical trials in treatment-naive patients with wet AMD to evaluate the efficacy and safety of OPT-302 in combination with anti-VEGF-A therapy. We expect to initiate these trials in the first half of 2021 with top-line results in 2023. If these results are favorable, we plan to file for marketing approval for OPT-302 for the treatment of wet AMD in the United States, European Union and other territories.
- **Optimize OPT-302 administration and develop a co-formulation to reduce injection burden for patients and provide treatment flexibility.** Currently, OPT-302 is administered as an injection

following intravitreal administration of a VEGF-A inhibitor. We plan to investigate the efficacy and durability of less frequent administration of OPT-302 in clinical trials based on OPT-302's pharmacokinetic profile, structural similarity to aflibercept and potential for improved and prolonged clinical efficacy over time. In addition, we plan to develop a co-formulation of OPT-302 with an approved and/or biosimilar anti-VEGF-A therapy to provide flexibility of treatment options for physicians and to reduce the frequency and number of injections for patients.

- **Expand clinical development of OPT-302 in wet AMD, DME and other retinal diseases**. Due to similarities in the underlying pathophysiology, we anticipate that OPT-302 in combination with VEGF-A inhibitors may provide therapeutic benefit to patients with other neovascular ophthalmic diseases, such as DME. We reported positive data from a Phase 1b/2a trial of OPT-302 in combination with aflibercept for the treatment of DME, and we plan to continue further development in this indication. We also continue to explore the potential benefit of OPT-302 in PCV and other ocular diseases, such as RVO and DR, in which there is a strong scientific and clinical rationale.
- **Maximize the commercial potential of OPT-302.** We retain worldwide rights for the development and commercialization of OPT-302. If OPT-302 receives marketing approval in the United States and European Union for wet AMD or any other retinal indications we are pursuing, we intend to establish our own commercial organization in these key territories. We may also enter into collaborations where we believe there is an opportunity to accelerate the development and commercialization of OPT-302 in select territories.

Our Pipeline

The following table summarizes the stage of clinical development and status of our product candidate, OPT-302.

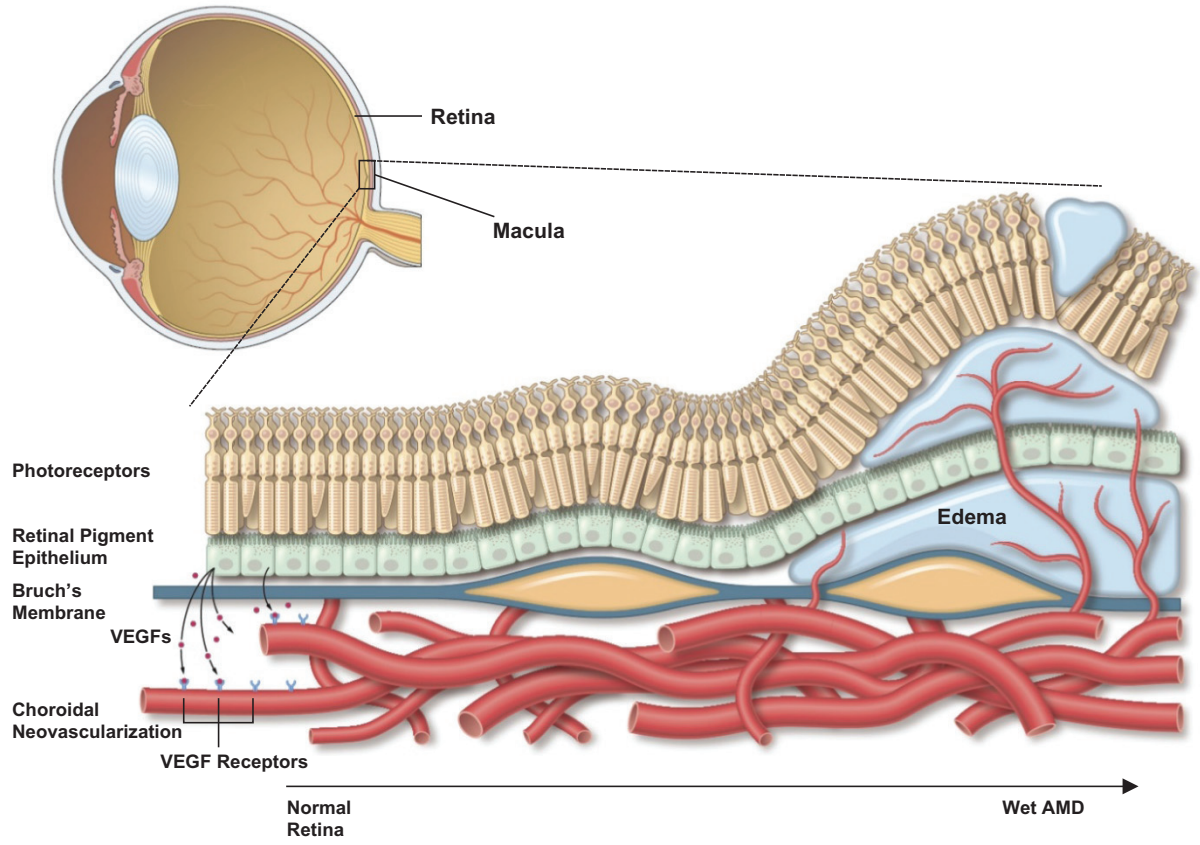


VEGFs in Ocular Diseases

Multiple ophthalmic diseases and conditions, including wet AMD and DME, involve aberrant blood vessel formation and growth, as well as vascular permeability and resulting leakage that contributes to disease

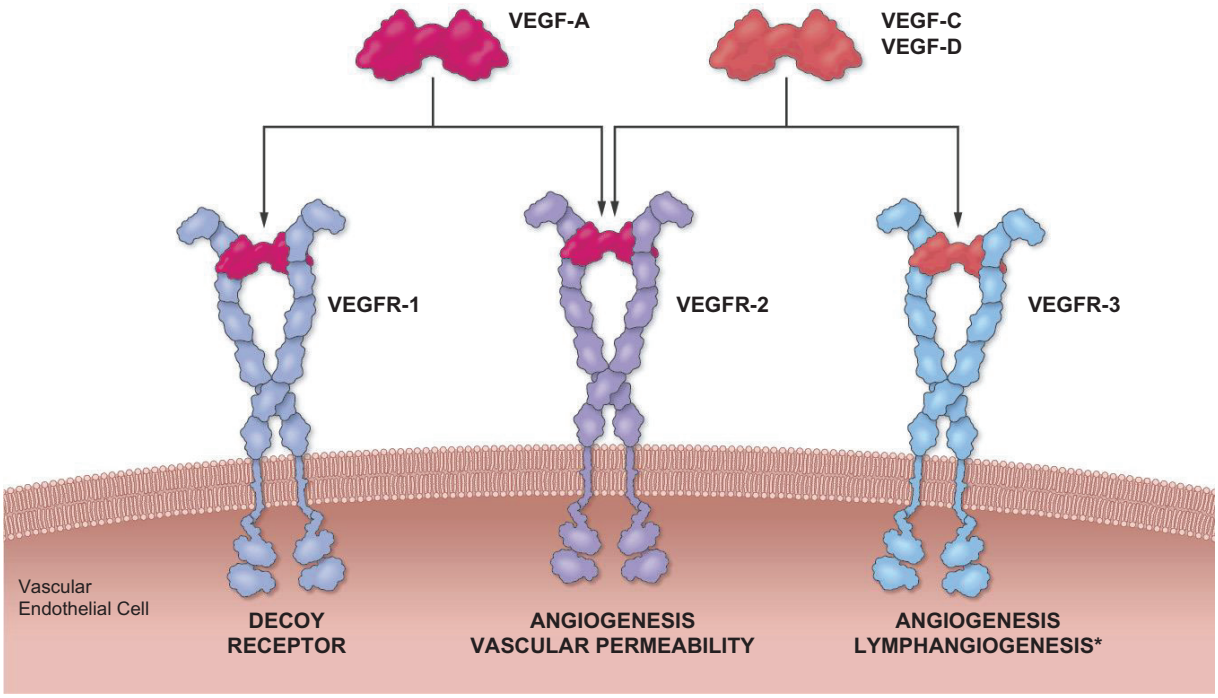
progression. In wet AMD, lesions consist of newly formed blood vessels that are typically fragile and leak, leading to the accumulation of fluid in the retinal tissue at the back of the eye. As shown in the figure below, if left untreated, this fluid can cause retinal swelling that disrupts the local architecture and function of sensory cells and neurons in the eye, resulting in vision loss. In patients with DME, high blood glucose levels drive physiological changes resulting in vascular permeability that also result in fluid accumulation, or edema, in the macula, the central region of the retina, and loss of visual acuity.

Neovascularization and Vascular Permeability are Key Hallmarks of a Number of Retinal Diseases, Leading to Lesion Formation, Edema and Distortion of the Retina Photoreceptor Layer Causing Loss of Vision



Neovascularization and vascular permeability associated with retinal disease progression are driven by a family of related growth factors known as VEGFs. Members of the VEGF family, including VEGF-A, VEGF-C and VEGF-D, exert their activity by binding and activating VEGF receptors referred to as VEGFR-1, VEGFR-2, and VEGFR-3. Receptor activation triggers signaling pathways that lead to the development of new blood vessels, a process known as angiogenesis, as well as vascular permeability.

Members of the VEGF Family of Growth Factors Have Overlapping but Distinct Specificities for VEGFRs



* Lymphangiogenesis refers to the proliferation of lymphatic vessels from pre-existing lymphatic vessels.

VEGF-A

VEGF-A is the most well-characterized member of the VEGF family of growth factors and was the first to be targeted for therapeutic intervention. VEGF-A is a potent growth factor and its relevance in ophthalmic neovascularization has been well-established. Overexpression of VEGF-A in animal models has shown VEGF-A to be a causal factor in the development of neovascularization and vascular permeability, which are key hallmarks in the progression of wet AMD. In wet AMD patients, VEGF-A levels are shown to be elevated in the aqueous humor fluid of the eye. VEGF-A binds to VEGFR-1, which acts to regulate VEGF-A activity, and VEGFR-2, which is a key driver of neovascularization and vascular permeability. Several inhibitors of VEGF-A have been approved to treat a number of neovascular ocular diseases. The two leading ocular VEGF-A inhibitors by revenue, ranibizumab and aflibercept, had combined annual worldwide sales of over US$11.9 billion in 2019.

VEGF-C and VEGF-D

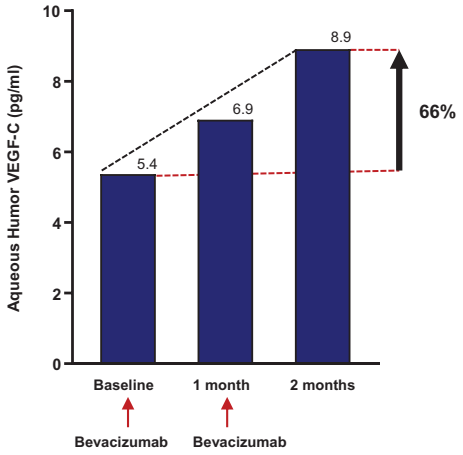
VEGF-C and VEGF-D contribute to the development and persistence of neovascular diseases, as evidenced by their elevated levels in multiple pathological conditions. Both VEGF-C and VEGF-D can stimulate neovascularization and VEGF-C can induce permeability by binding to VEGFR-2, independent of VEGF-A activity. Additionally, VEGF-C and VEGF-D bind to VEGFR-3, a receptor that is not activated by VEGF-A, which confers biological activities to both VEGF-C and VEGF-D that are distinct from those of VEGF-A. Activation of VEGFR-3 can stimulate vascular proliferation and modulate vascular permeability, vascular leakage and edema formation. The receptor binding profiles and the distinct biological activities of VEGF-C and VEGF-D suggest that inhibiting VEGF-C and VEGF-D may have therapeutic potential in ocular diseases by acting independently of, and in tandem with, the activity of VEGF-A inhibitors. There are currently no other therapies either approved or in clinical development that are designed to specifically target VEGF-C or VEGF-D.

Resistance to VEGF-A Therapies May be Driven by VEGF-C and VEGF-D

Standard of care treatments for wet AMD and DME inhibit VEGF-A activation of its receptors that are typically expressed on vascular endothelium. This can lead to inhibition of blood vessel growth and leakage which can stabilize disease and improve clinical outcomes, including visual acuity, in patients with retinal eye conditions. However, not all patients fully respond to VEGF-A inhibition. A substantial proportion of patients with wet AMD and DME have further opportunity for visual acuity gain and/or a need for resolution of persistent retinal fluid following anti-VEGF-A treatment. Furthermore, gains in visual acuity are often not sustained over the long term, even when anti-VEGF-A therapies are administered regularly. This resistance may occur as anti-VEGF-A monotherapies do not fully address the multifactorial pathogenesis of wet AMD and DME, including having no activity to block VEGF-C and VEGF-D.

VEGF-C and VEGF-D are implicated in the development of resistance to clinical use of anti-VEGF-A therapies. Levels of VEGF-C and/or VEGF-D have been observed to be upregulated in response to anti-VEGF-A therapies, most notably in patients with wet AMD. In a study conducted by third-party researchers in wet AMD patients, a 66% increase in the level of VEGF-C in the aqueous humor fluid in eyes was observed following two monthly doses of the VEGF-A inhibitor, bevacizumab (Avastin). This is illustrated in the figure below.

VEGF-C Levels are Increased in Aqueous Fluid of the Eye in Wet AMD Patients Treated with Monthly Intravitreal Bevacizumab



Study conducted by Cabral et al. (2018)

Upregulation of VEGF-C and VEGF-D can continue to drive signaling through VEGFR-2, even in the presence of a VEGF-A inhibitor, as well as signal through VEGFR-3, both of which may contribute to ongoing angiogenesis and vascular permeability associated with persistent wet AMD. VEGF-C and VEGF-D mediated activation of VEGFR-2 and VEGFR-3, as well as their compensatory elevation following VEGF-A inhibition, may contribute to sub-optimal clinical response to anti-VEGF-A monotherapy. We believe OPT-302 in combination with a VEGF-A inhibitor can address a key mechanism of clinical sub-responsiveness to standard of care treatments for serious retinal eye diseases by broad blockade of the VEGF family of growth factors which is not achieved by anti-VEGF-A monotherapies.

OPT-302

We are developing our Phase 3-ready product candidate, OPT-302, a biologic designed to inhibit VEGF-C and VEGF-D, to complement existing VEGF-A inhibitors, for the treatment of ophthalmic diseases, including wet AMD and DME. Anti-VEGF-A therapies represent the standard of care for wet AMD and other retinal

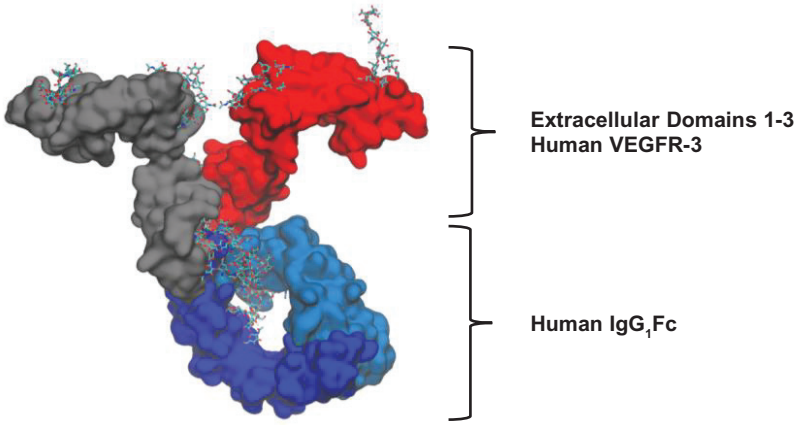
diseases. However, there remains a significant unmet need as many patients do not adequately respond to these treatments. As the only biologic inhibitor of VEGF-C and VEGF-D in clinical development, OPT-302 differs from standard of care VEGF-A inhibitors, and in combination with a VEGF-A inhibitor, is designed to address the sub-optimal clinical responses of anti-VEGF-A monotherapies by achieving broader inhibition of the VEGF family to improve visual acuity over standard of care anti-VEGF-A monotherapies.

In 2019, we completed a 366-patient Phase 2b clinical trial of OPT-302 in combination with ranibizumab for the treatment of wet AMD, which met the primary endpoint of a statistically significant superior mean gain in visual acuity over ranibizumab monotherapy at week 24. We intend to initiate two pivotal Phase 3 clinical trials in treatment-naive patients with wet AMD to evaluate the efficacy and safety of OPT-302 in combination with anti-VEGF-A therapy compared to a standard of care monotherapy. We intend to initiate two pivotal Phase 3 clinical trials in treatment-naive patients with wet AMD to evaluate the efficacy and safety of OPT-302 in combination with anti-VEGF-A therapy compared to anti-VEGF-A monotherapy in the first half of 2021. We expect to report topline data from these Phase 3 clinical trials in 2023. In addition, in our Phase 1b/2a clinical trial of OPT-302 in combination with aflibercept for the treatment of persistent DME, we observed evidence of clinical activity and improvements in visual acuity outcomes compared to aflibercept monotherapy. OPT-302 was observed to be well tolerated across Phase 1 and Phase 2 clinical studies in two disease indications following intravitreal administration of over 1,800 doses of OPT-302 to 399 patients either as monotherapy or in combination with standard of care VEGF-A inhibitors.

OPT-302 Mechanism of Action

We have designed OPT-302 to function as a ligand trap, capable of binding and sequestering VEGF-C and VEGF-D, thereby preventing these growth factors from activating VEGFR-2 and VEGFR-3. OPT-302 is comprised of the first three extracellular domains of human VEGFR-3, fused to the Fc domain, or the constant fragment of human immunoglobulin G_1, or IgG_1, as illustrated in the figure below. VEGF-C and VEGF-D function independent of, but in parallel with, VEGF-A to drive neovascularization and vascular leakage, key hallmarks of both wet AMD and DME. In addition, treatment with VEGF-A inhibitors leads to upregulation of VEGF-C and VEGF-D to compensate for VEGF-A inhibition, which may represent an important mechanism of clinical resistance to VEGF-A monotherapy.

Structure of OPT-302



Ligand trap therapeutics that include the receptor-binding domains for other ligands have been approved for a number of indications. One such agent is aflibercept, marketed as Eylea, a ligand trap consisting of extracellular domains of VEGFR-1 and VEGFR-2, which primarily mediates its activity by binding and inhibiting VEGF-A. Aflibercept has marketing approval for the treatment of wet AMD, DME, macular edema

secondary to RVO and DR. In rabbits, OPT-302 has been shown to have a comparable ocular biodistribution and intravitreal pharmacokinetic profile as aflibercept, with low systemic exposure.

Wet AMD

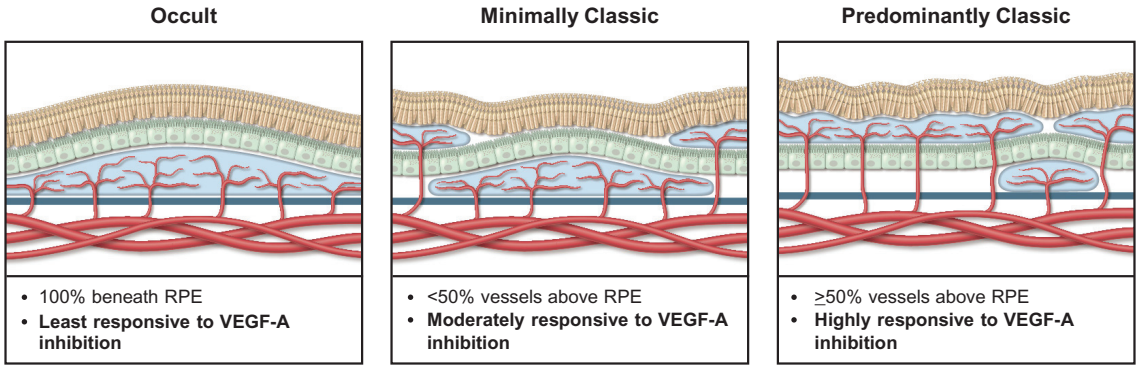
AMD is a chronic, progressive disease of the macula, a part of the retina containing the greatest concentration of light-sensing cells responsible for detailed, high visual acuity and central vision. The development of AMD is strongly associated with age, affecting up to 40% of individuals over the age of 75. There are two forms of AMD, dry AMD and wet AMD. Dry AMD is the most common form, representing approximately 85% to 90% of all AMD cases. However, dry AMD can develop into wet AMD, and wet AMD accounts for 90% of the severe vision loss associated with the disease.

Wet AMD is a rapidly progressing disease with loss of central vision developing over a period of weeks to months, and is the leading cause of vision loss for individuals over the age of 50. The most common symptoms of wet AMD are loss of central vision, distortion of objects or blurred vision. Peripheral vision usually remains intact. The disease typically affects patients initially in one eye, with a high likelihood of it occurring in the second eye over time. If left untreated, wet AMD can lead to rapid loss of visual acuity and blindness, adversely impacting the patient's ability to conduct daily activities, such as driving and reading.

Wet AMD occurs when new blood vessels in the choroid, or the vascular layer in the eye just under the retina, intrude into the retinal layers and leak fluid. The formation of these new blood vessels is referred to as CNV. These newly formed vessels are highly permeable, which can lead to fluid accumulation and adversely affect sensory cells in the retina.

Wet AMD can be classified as occult or classic, based on the neovascular pattern within lesions. In occult lesions, all of the blood vessels are below the retinal pigment epithelium, or RPE, and the areas on angiograms have a stippled appearance. Classic lesions, by contrast, appear as well-demarcated areas on angiograms due to neovascular blood vessels being located above the RPE. Classic lesions are further subdivided into predominantly classic if 50% or more of the blood vessels are above the RPE, and minimally classic, if greater than 0% and less than 50% of the blood vessels are above the RPE. Classic-containing lesions tend to be the most responsive to anti-VEGF-A therapies.

Classifications of Wet AMD Based on Neovascular Lesion Pattern



There is a further sub-type of wet AMD lesion referred to as retinal angiomatous proliferation, or RAP. RAP lesions are a type of CNV in which neovascularization in the retina protrudes into the sub-retinal space and connects to the choroidal circulation. Between 10% and 21% of wet AMD patients have RAP lesions which are more commonly found in older Caucasian patients. Although there are no therapies specifically approved to treat RAP lesions, patients are typically treated with VEGF-A inhibitors.

PCV is a further sub-type of wet AMD. PCV is an abnormality of inner choroidal vessels that causes dilations in the blood vessels in the retina that resemble polyps, known as polypoidal protrusions. PCV typically does not respond well to VEGF-A inhibitor therapies and many patients are diagnosed with PCV only after they fail to respond to these therapies. There is a high prevalence of PCV in Asian countries, with between 23% and 54% of patients with presumed cases of wet AMD in Japan having PCV. Prevalence rates of between 4% and 10% have been reported in Caucasian patients with presumed cases of wet AMD.

Current Treatments for Wet AMD and Their Limitations

There are four VEGF-A inhibitors approved by the Food and Drug Administration, or FDA, for the treatment of wet AMD, all of which are administered by regular intravitreal injections as monotherapy. These VEGF-A inhibitors include: the VEGF-A specific antibody ranibizumab, the antibody fragment brolucizumab (Beovu) and the VEGFR-based ligand trap aflibercept. The VEGF-A antibody, bevacizumab, an FDA approved therapy for colorectal and other cancers, is also used off-label by many physicians to treat wet AMD, comprising approximately 46% of anti-VEGF-A injections administered globally. In addition, pegaptanib sodium (Macugen) is an aptamer or antibody-like RNA construct that inhibits VEGF-A but is now infrequently administered following the approval of biologic VEGF-A inhibitors. Recent clinical development has focused on maintaining vision gains with a VEGF-A inhibitor whilst reducing the number of injections.

VEGF-A inhibitors stabilize loss vision in over 90% of wet AMD patients. However, the effectiveness of these therapies in many patients is limited. Improvements of ≥15 letters of visual acuity typically occur in less than 40% of treated patients. In addition, despite regular treatment with a VEGF-A inhibitor, many patients have insufficient gains in visual acuity to resume routine daily activities such as driving and reading. Chronic vision loss can also occur despite ongoing treatment with an anti-VEGF-A inhibitor. Retrospective and prospective analyses of patients treated with VEGF-A inhibitor therapies for five years have found that, after initial gains in visual function following one year of treatment, many patients then had a gradual decline in visual acuity in subsequent years, resulting in the eventual reversal of the majority of gains. In addition, in clinical settings, up to two-thirds of patients treated with VEGF-A inhibitor therapies continue to have retinal fluid following treatment and approximately 25% experience further vision loss 12 months following treatment. Treatment options are limited for patients who do not respond adequately or experience visual decline despite ongoing therapy with standard of care VEGF-A inhibitors, and typically involve switching treatment from one anti-VEGF-A monotherapy to another with minimal additional visual benefit achieved.

Market Opportunity for the Treatment of Wet AMD

Wet AMD affects approximately 1 million people in the United States and 2.5 million in Europe. As the risk of developing wet AMD increases with age, it is predicted that the overall aging of the population will result in a significant increase in the number of wet AMD cases, both in the United States and worldwide. Many wet AMD patients also experience suboptimal clinical responses despite receiving one or both of the leading standard of care treatments ranibizumab and aflibercept, which had combined annual worldwide sales of over US$11.9 billion in 2019. In addition, nearly half of wet AMD patients are treated with off-label bevacizumab as a lower cost alternative anti-VEGF-A therapy. As a result, we believe there is a significant and expanding market opportunity for novel therapies that can improve vision in patients with wet AMD, which has the potential to lead to sales greater than the combined annual sales of ranibizumab and aflibercept.

We believe that OPT-302, used in combination with standard of care VEGF-A inhibitors, can address the significant unmet need for wet AMD patients by providing improved outcomes over that which can be achieved by inhibiting VEGF-A alone.

Phase 1/2a Clinical Trial Results in Wet AMD

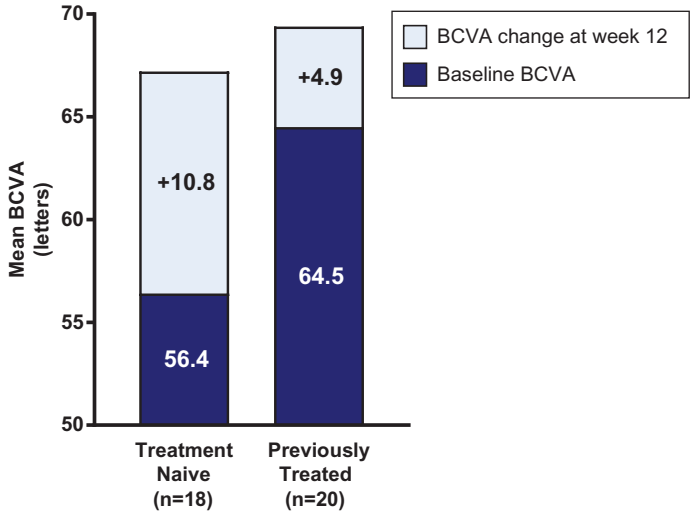
In 2017, we completed a Phase 1/2a clinical trial of OPT-302 in wet AMD patients under an investigational new drug, or IND, application accepted by the FDA in 2015. The trial was divided into two parts. Part 1 was a Phase 1 first-in-human 20-patient dose-escalation study in which OPT-302 was administered at three escalating

doses (0.3 mg, 1.0 mg or 2.0 mg), either in combination with 0.5 mg ranibizumab or alone as a 2.0 mg monotherapy, once every four weeks for a total of three doses, with a follow-up visit at week 12. Part 2 was a Phase 2a 31-patient dose-expansion trial in which 2.0 mg OPT-302 was administered in combination with ranibizumab or as a monotherapy once every four weeks for a total of three doses, with a follow-up visit at week 12. Of the 51 patients dosed, 49% were treatment naive and 51% were previously treated with anti-VEGF-A therapy. The previously-treated patients had received an average of 17 prior treatments, equating to prior treatment over an average of 1.3 years, of an intravitreal VEGF-A inhibitor prior to enrolling in the trial. The Phase 1/2a trial was conducted at 14 trial sites in the United States.

OPT-302 was well tolerated up to the highest dose tested both in combination with ranibizumab and as a monotherapy. No dose-limiting toxicities, or DLTs, were observed and the maximum tolerated dose, or MTD, was not reached. There were no treatment-related serious adverse events, or SAEs. The most common TEAEs were conjunctival hemorrhage, eye pain and corneal inflammation mainly related to the intravitreal injection procedure. TEAEs did not lead to permanent discontinuation of the study for any patient. The pharmacokinetic profile of OPT-302 was similar in the absence or presence of ranibizumab, and there was no evidence of OPT-302 immunogenicity in this clinical trial.

Although the focus of this trial was safety, we also observed preliminary signals of clinical benefit. Improvements in visual acuity were observed in treatment-naive patients as well as patients previously treated with anti-VEGF-A therapy, as measured by the number of letters that could be read on a standard eye chart following OPT-302 monotherapy and OPT-302 combination therapy. As illustrated in the figure below, after 12 weeks, in patients across all dose groups, the mean change in visual acuity from baseline increased by +10.8 letters in treatment-naive patients and +4.9 letters in previously treated patients who received OPT-302 combination therapy.

Mean Change in Visual Acuity from Baseline to Week 12 in Treatment-Naive and Previously-Treated Wet AMD Patients Administered OPT-302 in Combination with Ranibizumab

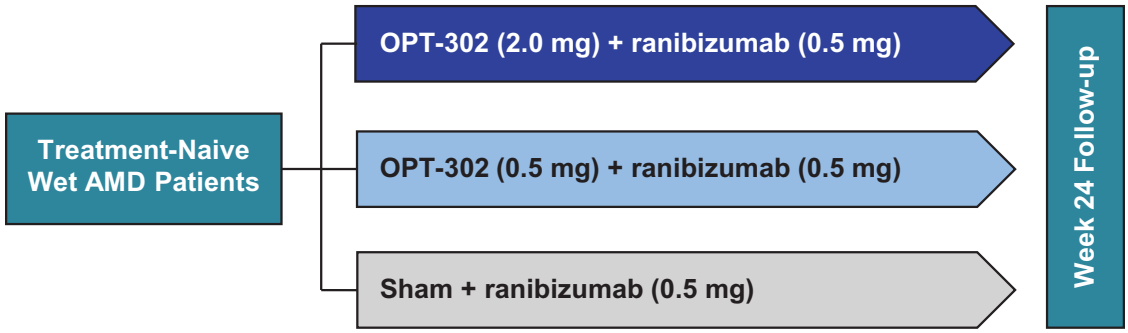


In addition, improvements in visual acuity following treatment with OPT-302 combination therapy were consistent with anatomical outcomes, such as reductions in intraretinal and subretinal fluid. Retinal thickness, which is assessed by spectral domain optical coherence tomography, or SD-OCT, using a standard criterion called central subfield thickness, or CST, was also reduced following OPT-302 combination therapy.

Phase 2b Clinical Trial Results in Wet AMD

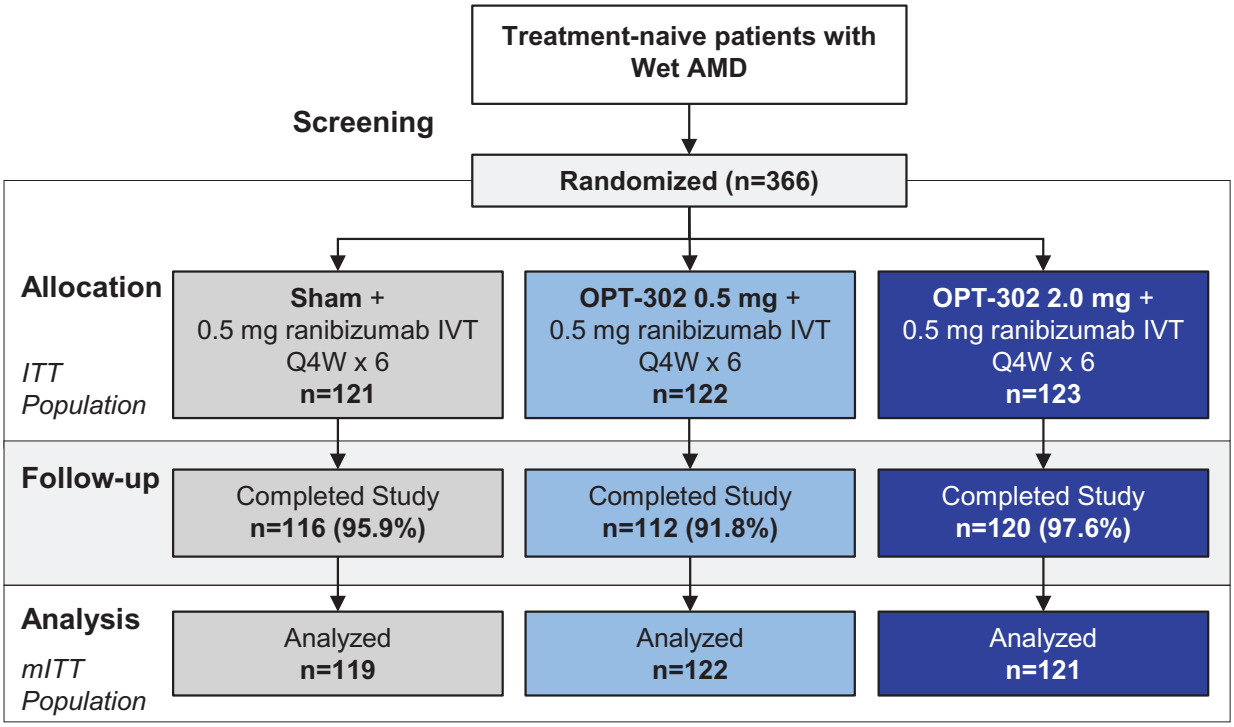
Based on the positive results of the Phase 1/2a trial, we completed an international, multi-center, double-masked Phase 2b clinical trial of OPT-302 in combination with ranibizumab in a total of 366 treatment-naive patients in August 2019. As illustrated in the figure below, patients were randomized into three groups to receive either 0.5 mg or 2.0 mg OPT-302 with 0.5 mg ranibizumab or ranibizumab monotherapy, which included a sham injection. A sham intravitreal injection involves pressing a syringe hub against the surface of the eye to mimic an intravitreal injection so that the patient remains masked to the treatment group to which they have been randomized. Administration was by intravitreal injection once every four weeks for 20 weeks (six treatments in total). The primary endpoint of the clinical trial was the mean change in BCVA from baseline on the ETDRS standardized eye chart at week 24. Secondary outcome measures included the proportion of patients gaining ≥15 letters in BCVA, changes in retinal thickness, change in intraretinal and subretinal fluid and proportion of patients losing ≥15 letters in BCVA.

Design of the Phase 2b Clinical Trial of OPT-302 with Ranibizumab in Wet AMD



As illustrated in the figure below, 366 treatment-naive patients were randomized 1:1:1 to each of the three treatment groups. We used data from the 362 patients who had a baseline assessment of their visual acuity and completed at least one post-dose visit as the modified intent to treat population, or mITT, in all analyses. Key inclusion criteria for patients in the trial included CNV classified as either occult, minimally classic or predominantly classic, and BCVA on the ETDRS standardized eye chart of ≥25 and ≤60 letters. The Phase 2b trial was conducted at 109 trial sites in the United States, Europe, Israel and the United Kingdom.

Patient Distribution in the Phase 2b Clinical Trial in Wet AMD



Q4W refers to administration every four weeks. IVT refers to administration by intravitreal injection.

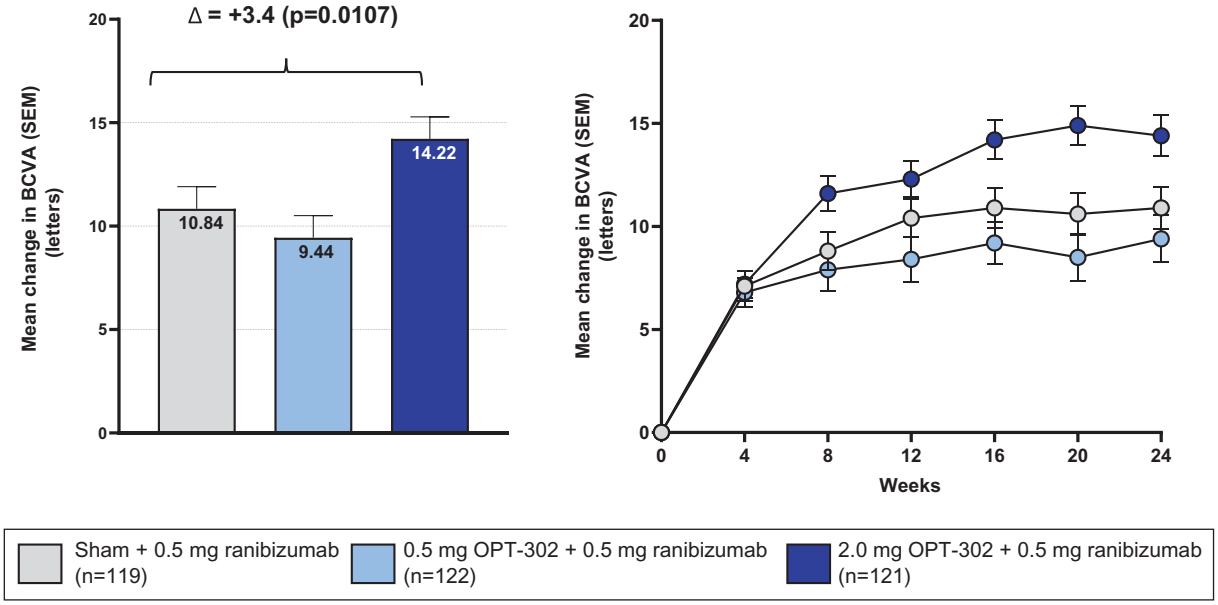
In presentations of statistical results in this prospectus, a p-value is a measure of statistical significance of the observed results, or the probability that the observed results were achieved purely by chance. By convention, a p-value of 0.05 or lower is commonly considered statistically significant. The FDA and comparable non-U.S. regulatory authorities utilize the reported statistical measures when evaluating the results of a clinical trial, including statistical significance as measured by p-value, to evaluate the reported evidence of a drug product's safety and efficacy.

Improvements in Visual Acuity

The Phase 2b clinical trial met the primary endpoint, demonstrating a statistically significant superior mean gain in visual acuity at week 24 compared to baseline in the 2.0 mg OPT-302 combination therapy group compared to the ranibizumab monotherapy group. The figure below illustrates patients in the 2.0 mg OPT-302 combination therapy group had a mean visual acuity improvement of +14.22 letters relative to baseline, compared to +10.84 letters for those treated with ranibizumab monotherapy at week 24 (p=0.0107). This represents a statistically significant benefit of +3.4 letters and a greater than 30% relative improvement in vision outcomes in the OPT-302 combination group compared to ranibizumab monotherapy. Evidence of improved visual acuity was observed beginning as early as week 8 and continued throughout the course of the trial to week 24. Mean visual acuity in the lower dose 0.5 mg OPT-302 combination therapy group was not significantly

different from the ranibizumab monotherapy group. However, evidence of a dose response was observed between the 2.0 mg and 0.5 mg OPT-302 combination therapy groups on several anatomical outcomes, such as retinal thickness and the proportion of patients with intraretinal and subretinal fluid at week 24.

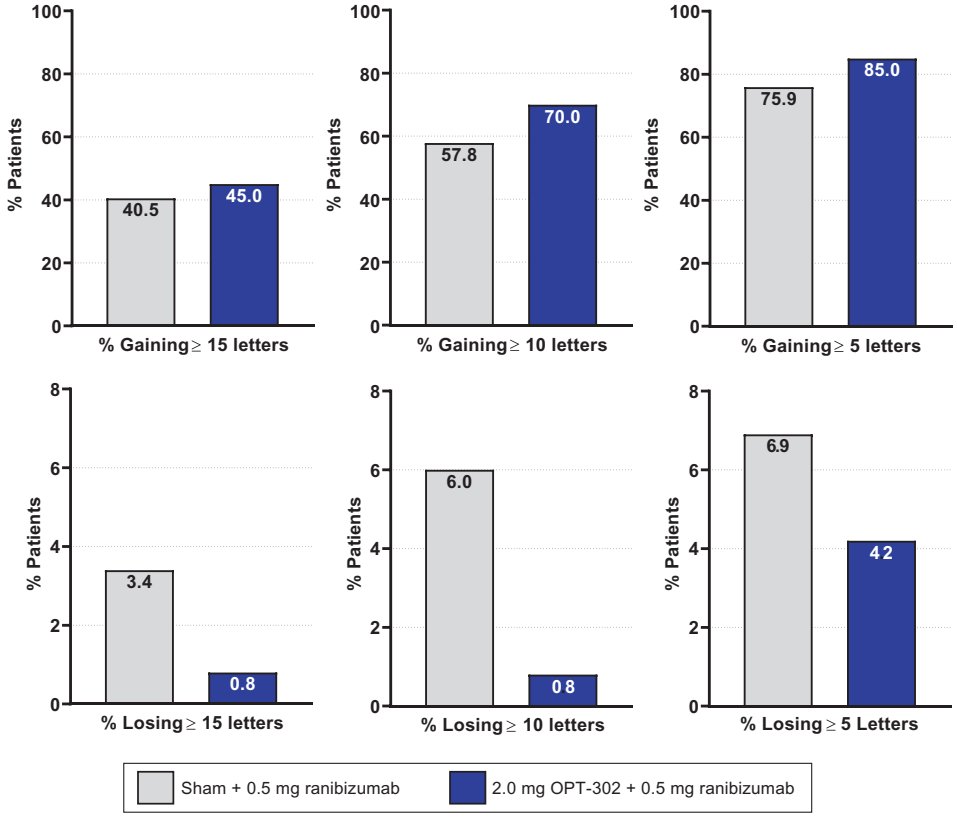
Mean Change in Visual Acuity from Baseline to Week 24 in Treatment-Naive Wet AMD Patients Administered Ranibizumab Monotherapy or OPT-302 Combination Therapy



Error bars shown in all figures represent the SEM, or the standard error of the mean.

Secondary outcome measurements from the trial were also supportive of the primary endpoint. As illustrated in the figure below, we observed a greater proportion of patients gaining ≥15, ≥10 and ≥5 letters in the 2.0 mg OPT-302 combination therapy group compared to the ranibizumab monotherapy group. In addition, the proportion of patients losing ≥15, ≥10 and ≥5 letters was lower in the 2.0 mg OPT-302 combination therapy group compared to the ranibizumab monotherapy group. The Phase 2b trial was not designed for statistical significance on secondary and exploratory endpoints and was not powered to detect statistically significant differences in secondary outcome measurements.

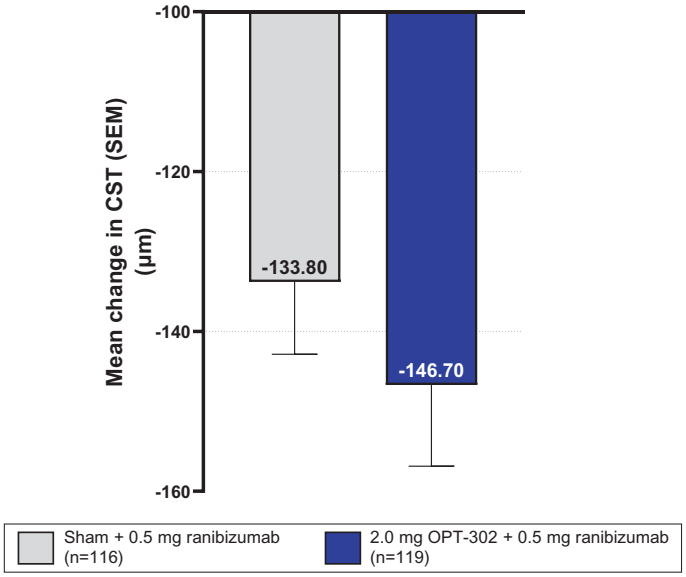
Greater Proportion of Patients Gaining, and Fewer Patients Losing, ≥15, ≥10 and ≥5 Letters with OPT-302 Combination Therapy Compared to Ranibizumab Monotherapy



Reductions in Retinal Thickness and Fluid

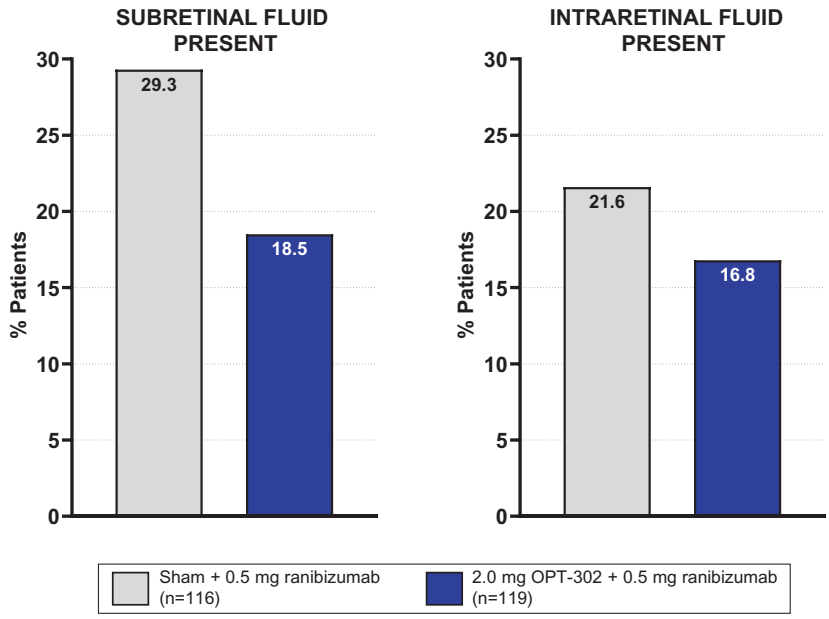
In addition to the statistically significant improvement in visual acuity, treatment with OPT-302 combination therapy led to greater reductions in retinal thickness. The reductions in retinal thickness in patients is consistent with less fluid accumulation in the retina and reduced disease severity as increased fluid accumulation in the retina is associated with the loss of visual acuity in wet AMD patients. The figure below depicts the greater mean reduction in retinal thickness in the OPT-302 combination therapy group compared to the ranibizumab monotherapy group at week 24.

Greater Reduction in Retinal Thickness from Baseline to Week 24 following OPT-302 Combination Therapy Compared to Ranibizumab Monotherapy



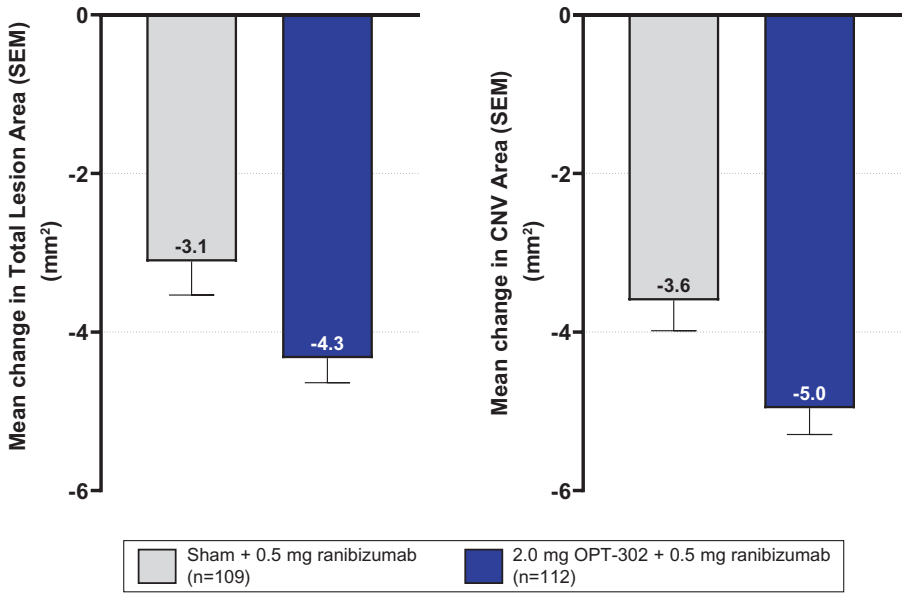
Fewer patients in the OPT-302 combination therapy group had subretinal fluid and intraretinal fluid present compared to the ranibizumab monotherapy group. The presence of subretinal fluid is a hallmark of wet AMD and its resolution is referred to as "drying" of the retina while intraretinal fluid is a prognostic biomarker for poor visual acuity and sub-optimal response to anti-VEGF-A therapies. As illustrated in the figure below, there were approximately 10% fewer patients with subretinal fluid and 5% fewer patients with intraretinal fluid following administration of OPT-302 combination therapy compared to ranibizumab monotherapy.

Fewer Patients with Subretinal and Intraretinal Fluid Present at Week 24 Following OPT-302 Combination Therapy Compared to Ranibizumab Monotherapy



Greater improvements in anatomical indicators of disease severity, including on exploratory endpoints of mean reduction in total lesion area and CNV area, were observed in the OPT-302 combination therapy group compared to ranibizumab monotherapy. As illustrated in the figure below, the patients treated with OPT-302 combination therapy had an approximately 39% further reduction in both total lesion area and CNV area compared to ranibizumab monotherapy.

Greater Reduction in Total Lesion Area and CNV Area from Baseline to Week 24 following OPT-302 Combination Therapy Compared to Ranibizumab Monotherapy

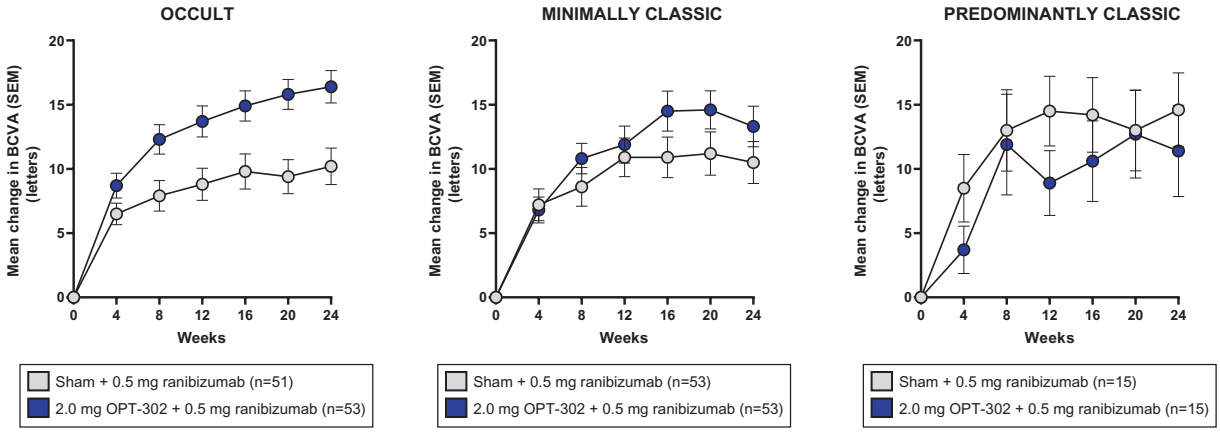


Improved Therapeutic Outcomes in Wet AMD Lesion Subtypes

A number of pre-specified subgroup and exploratory analyses were incorporated into the Phase 2b trial design in order to identify those wet AMD patients who may respond best to OPT-302. The Phase 2b trial randomized patients with a broad range of lesion morphologies including occult, minimally classic and predominantly classic lesions. In addition, the Phase 2b trial investigated efficacy in post-hoc analyses in other wet AMD subtypes, including PCV and RAP. This trial was not designed for statistical significance on these subgroup and exploratory analyses and was not powered to detect statistically significant differences in related measurements.

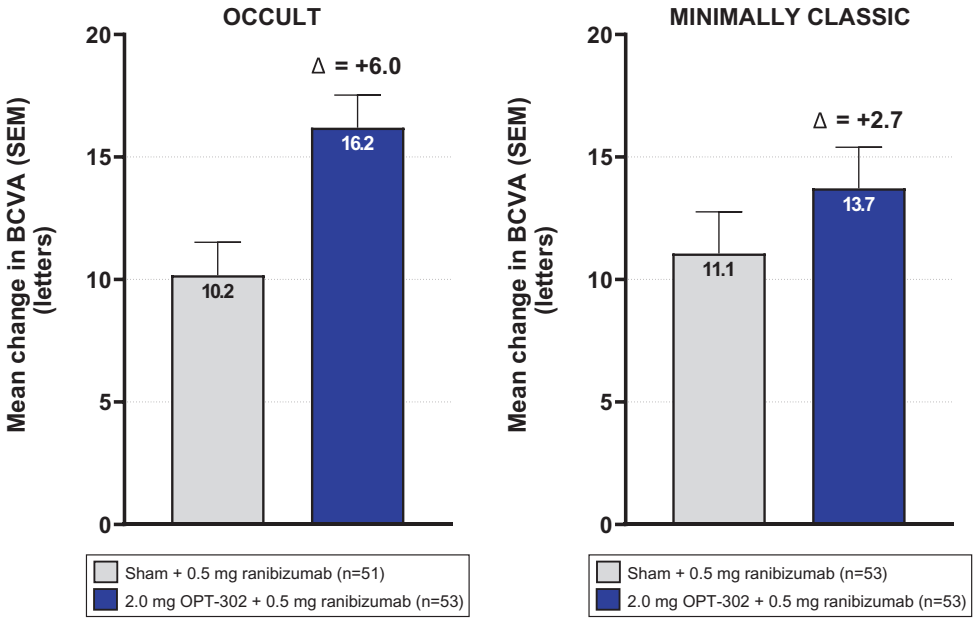
Patients enrolled in our Phase 2b trial consisted of 44% occult, 43% minimally classic and 13% predominantly classic lesion types, which is similar to the distribution reported in treatment-naive wet AMD patients. Predominantly classic patients typically respond well to VEGF-A inhibitor therapy and an additive benefit of OPT-302 combination therapy could not be discerned in this small patient group of only 15 patients per treatment arm. The majority of patients randomized in the Phase 2b trial had occult or minimally classic lesions. These patients did not respond as well to ranibizumab monotherapy as those with predominantly classic lesions. Patients with occult and minimally classic lesions treated with OPT-302 combination therapy experienced improvement in visual acuity beginning at week 8 and persisting through week 24 compared to ranibizumab monotherapy. The figure below illustrates the mean change in visual acuity over 24 weeks in each of the lesion classifications treated with OPT-302 combination therapy compared to ranibizumab monotherapy.

Mean Change in Visual Acuity from Baseline to Week 24 in Wet AMD Lesion Types Following OPT-302 Combination Therapy Compared to Ranibizumab Monotherapy



In a post-hoc analysis, in the occult lesion subgroup, the mean visual acuity gain from baseline to week 24 in the OPT-302 combination therapy group was +16.2 letters (n=53), compared to +10.2 letters in the ranibizumab monotherapy group (n=51), a benefit of +6.0 letters. In addition, in the minimally classic subgroup, the mean visual acuity gain from baseline to week 24 in the OPT-302 combination therapy group was +13.7 letters (n=53), compared to +11.1 letters in the ranibizumab monotherapy group (n=53), a benefit of +2.7 letters.

Gains in Visual Acuity from Baseline to Week 24 in Patients with Occult and Minimally Classic Lesions Following OPT-302 Combination Therapy Compared to Ranibizumab Monotherapy



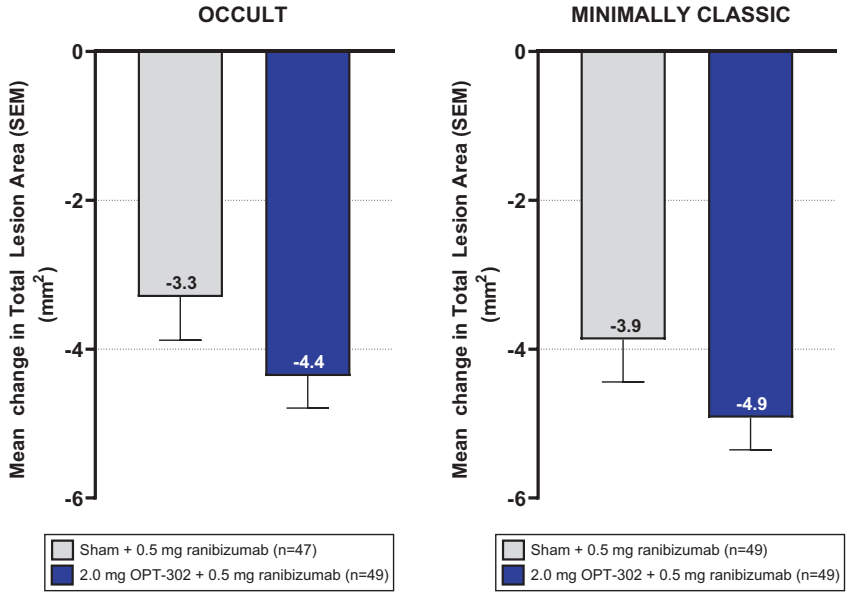
In particular, in the occult lesion subgroup, we observed a greater proportion of patients gaining ≥15 and ≥10 letters in the OPT-302 combination therapy group compared to the ranibizumab monotherapy group (approximately 22% and 19% over ranibizumab monotherapy, respectively). In the minimally classic subgroup, we observed a greater proportion of patients (approximately 10% over ranibizumab monotherapy) gaining ≥10 letters in the OPT-302 combination therapy group compared to the ranibizumab monotherapy group.

In patients with occult lesions, treatment with OPT-302 combination therapy also led to a greater mean reduction in retinal thickness of -134.6 µm from baseline compared to -103.5 µm for ranibizumab monotherapy. OPT-302 combination therapy did not have greater clinical benefit in the reduction of retinal thickness in minimally classic lesions, compared to the ranibizumab monotherapy group.

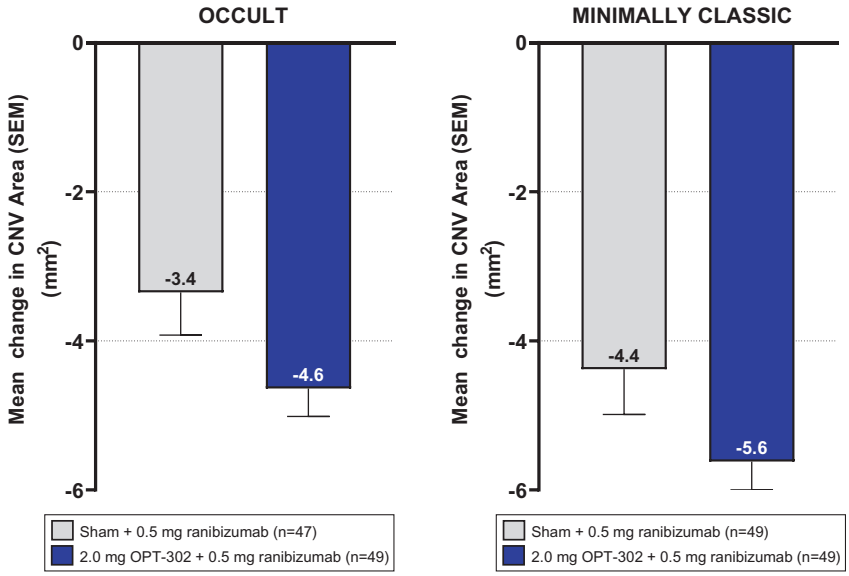
In patients with occult lesions, approximately 13% and 12% fewer patients in the OPT-302 combination group had subretinal fluid and intraretinal fluid, respectively, as compared to ranibizumab monotherapy at week 24. In patients with minimally classic lesions, approximately 2% fewer patients treated with OPT-302 combination therapy had subretinal fluid and intraretinal fluid compared to patients treated with ranibizumab monotherapy at week 24.

As shown in the figures below, by week 24, patients with occult and minimally classic lesions also had greater reductions in both wet AMD total lesion area and CNV area following OPT-302 combination therapy compared to patients receiving ranibizumab monotherapy.

Greater Reduction in Total Lesion Area from Baseline to Week 24 in Patients with Occult and Minimally Classic Lesions Following OPT-302 Combination Therapy Compared to Ranibizumab Monotherapy



Greater Reduction in CNV Area from Baseline to Week 24 in Patients with Occult and Minimally Classic Lesions Following OPT-302 Combination Therapy Compared to Ranibizumab Monotherapy



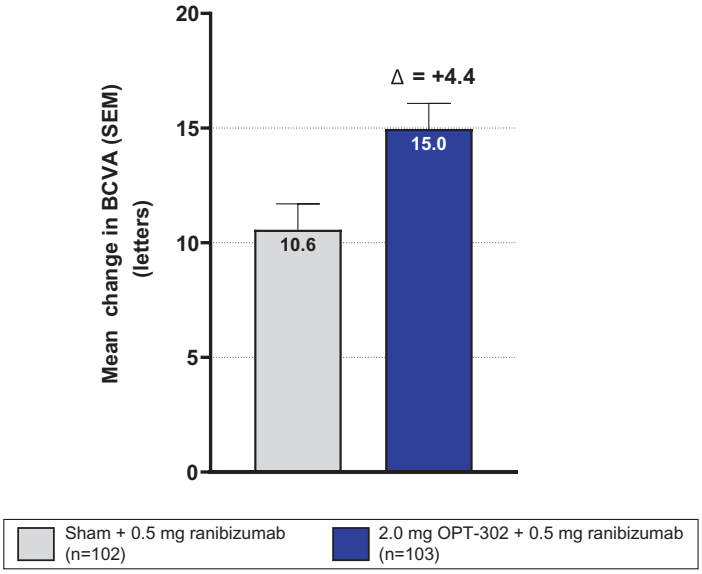
OPT-302 combination therapy improved visual acuity to the greatest extent in occult lesions compared to minimally classic or predominantly classic lesions, in each case compared to ranibizumab monotherapy. While these results were generated in treatment-naive wet AMD patients, classification of lesions following treatment with either OPT-302 combination therapy or ranibizumab monotherapy suggests that virtually all lesions shifted

toward an occult morphology. This suggests that OPT-302 combination therapy also has the potential to provide benefit to patients who have been previously treated with anti-VEGF-A monotherapy, given the predominantly occult morphology of their lesions following treatment.

RAP and PCV Lesion Subtypes

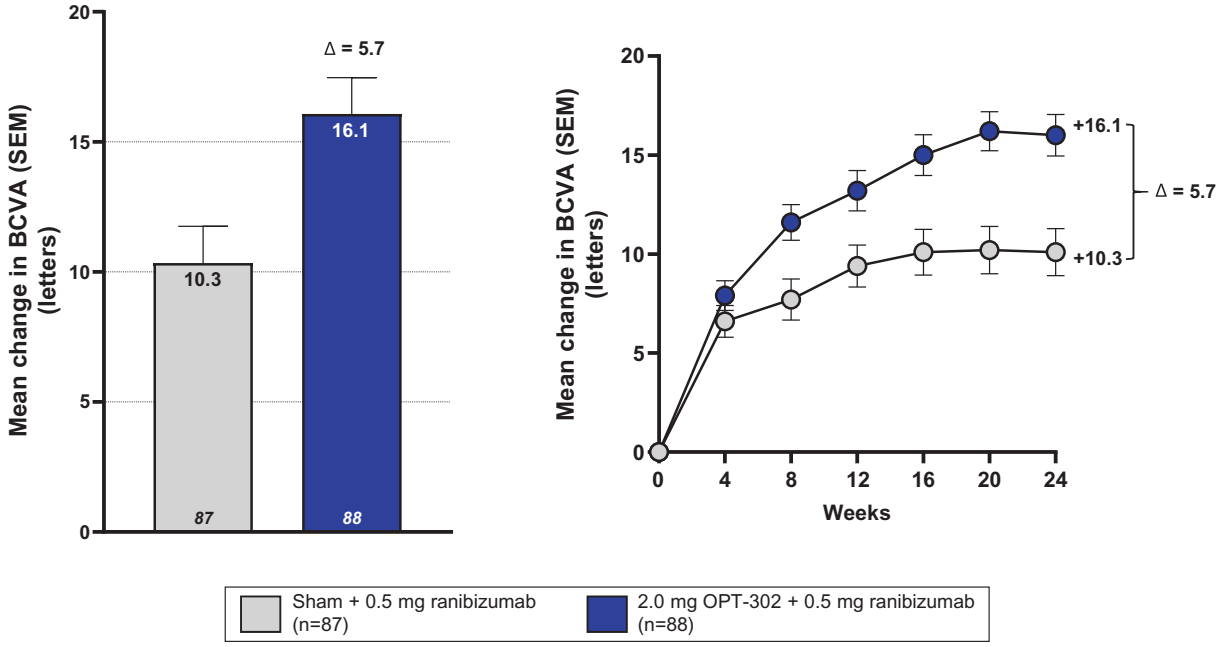
In our Phase 2b clinical trial, over 85% of patients enrolled did not have RAP lesions detected at randomization and these patients responded better to OPT-302 than patients with RAP lesions. In patients without RAP lesions, the mean visual acuity gain from baseline to week 24 was +15.0 letters (n=103) with OPT-302 combination therapy, compared to +10.6 letters for those treated with ranibizumab monotherapy (n=102), a benefit of +4.4 letters.

Mean Change in Visual Acuity from Baseline to Week 24 in Patients Without RAP Lesions Following OPT-302 Combination Therapy Compared to Ranibizumab Monotherapy



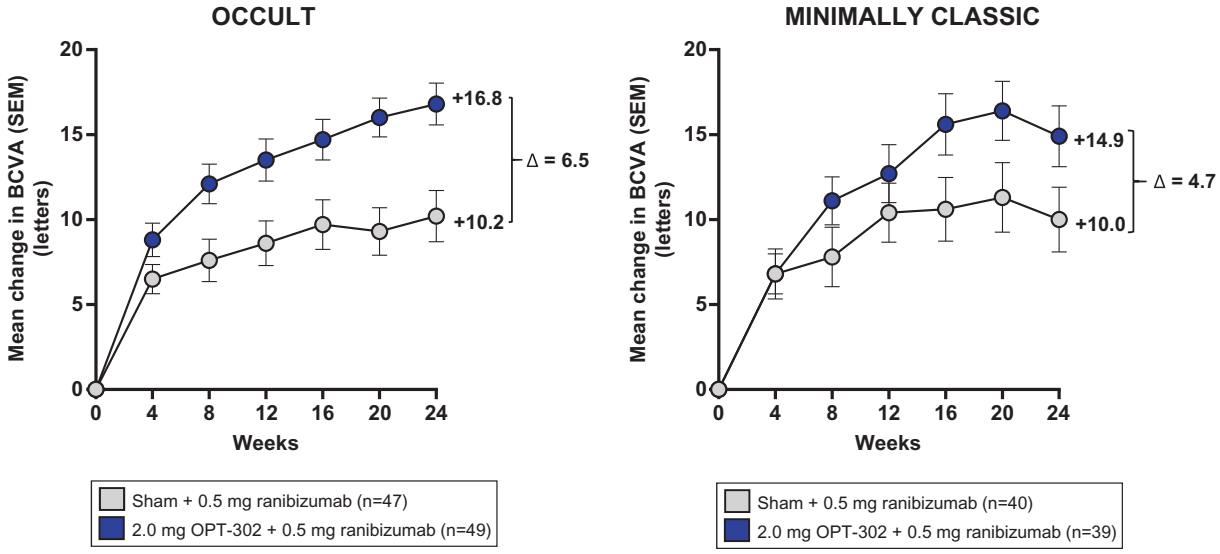
In patients without RAP lesions who had occult or minimally classic lesions, representing the majority of wet AMD patients, the mean visual acuity gain from baseline to week 24 was +16.1 letters with OPT-302 combination therapy (n=88) compared to +10.3 letters for those treated with ranibizumab monotherapy (n=87), a benefit of +5.7 letters. This represents the patient population for which the primary analysis of the primary endpoint of the planned Phase 3 trials of OPT-302 combination therapy for the treatment of wet AMD will be first conducted, followed by analysis of the total patient population and the every-eight week dosing groups.

Mean Change in Visual Acuity from Baseline to Week 24 in the combined group of RAP Absent Occult and Minimally Classic Lesions Following OPT-302 Combination Therapy Compared to Ranibizumab Monotherapy



Patients with RAP absent occult lesions demonstrated a mean visual acuity gain at week 24 of +16.8 letters with OPT-302 combination therapy (n=49) compared to +10.2 letters for those treated with ranibizumab monotherapy (n=47), a gain of +6.5 letters. Patients with RAP absent minimally classic lesions demonstrated a mean visual acuity gain at week 24 of +14.9 letters with OPT-302 combination therapy (n=39) compared to +10.0 letters for those treated with ranibizumab monotherapy (n=40), a gain of +4.7 letters.

Mean Change in Visual Acuity from Baseline to Week 24 in RAP Absent Occult and Minimally Classic Lesions Following OPT-302 Combination Therapy Compared to Ranibizumab Monotherapy



Improved Therapeutic Outcomes of OPT-302 in PCV Lesions

In patients with PCV lesions, the mean visual acuity gain from baseline to week 24 in the OPT-302 combination therapy group was +13.5 letters (n=22), compared to +6.9 letters in the ranibizumab monotherapy group (n=20). This equates to a benefit of +6.7 letters and is almost a two-fold improvement in visual acuity gain observed from baseline following OPT-302 combination therapy. Ranibizumab monotherapy was not observed to be as effective in patients with PCV compared to other wet AMD subtypes.

Safety and Tolerability

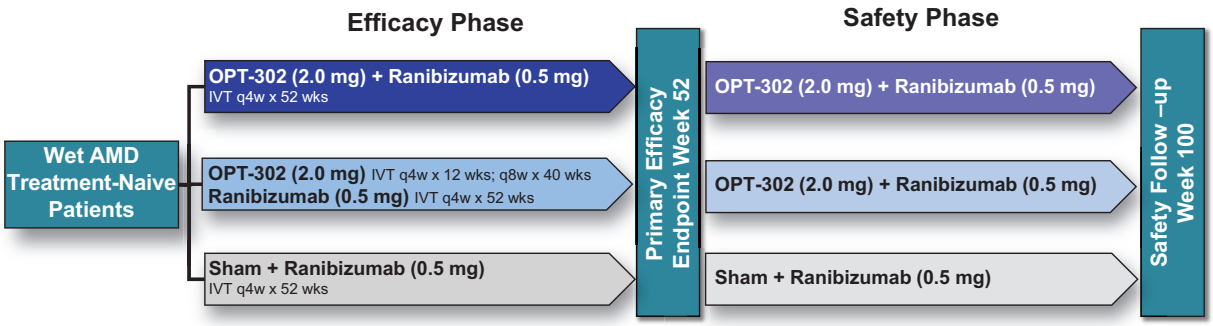
OPT-302 was well tolerated in this Phase 2b trial with a very low incidence of ocular inflammation and no safety issues identified with addition of OPT-302 to ranibizumab intravitreal therapy. The incidence of ocular TEAEs was similar in OPT-302 combination groups compared to the ranibizumab monotherapy group. TEAEs were considered potentially treatment related in approximately 15% of patients. The most common treatment-related TEAEs were eye pain, vitreous floaters, eye irritation and raised intraocular pressure. One patient discontinued from the trial due to a TEAE, which was not considered treatment related. Three patients treated with OPT-302 combination therapy had potentially treatment-related SAEs: one case each of vitritis, endophthalmitis and myocardial infarction.

Planned Pivotal Phase 3 Clinical Trials in Wet AMD

We are planning to initiate two concurrent pivotal Phase 3 clinical trials for the treatment of wet AMD. These double-masked, sham-controlled Phase 3 clinical trials will enroll treatment-naive patients and assess the efficacy and safety of 2.0 mg of OPT-302 in combination with anti-VEGF-A therapy for treatment-naive patients with wet AMD compared to a standard of care anti-VEGF-A monotherapy. In addition, to understand the durability of OPT-302 treatment effect with less frequent dosing, each trial will compare the clinical efficacy of OPT-302 administered in combination with the applicable VEGF-A inhibitor on an every 4-week and every 8-week dosing regimen. The primary endpoint of both trials will be the mean change in visual acuity from baseline at week 52. Patients will continue to be dosed until week 96 to further assess long-term safety at week 100. We expect to initiate the trials in the first half of 2021 and to report topline data in 2023. If the results at the completion of the primary efficacy phase at week 52 of the Phase 3 clinical trials are favorable, we intend to file for marketing approval for OPT-302 for the treatment of wet AMD in the United States, European Union and certain other territories.

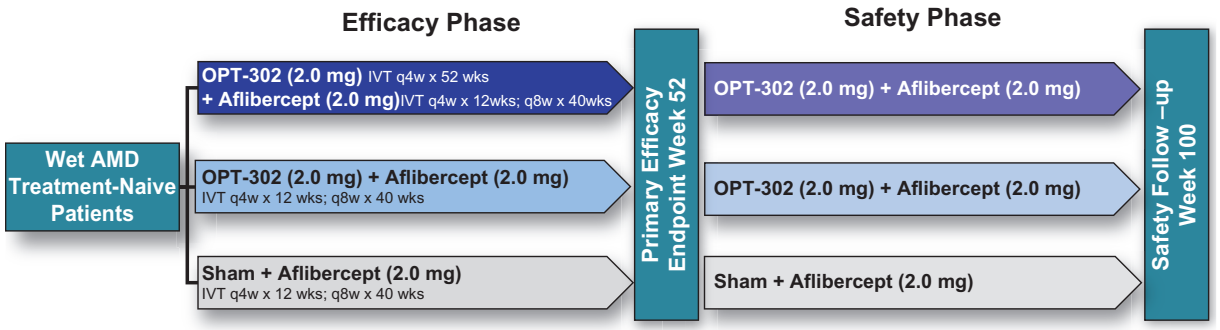
Study of OPT-302 in Combination with Ranibizumab (ShORe) Phase 3 Trial

In the Study of OPT-302 in combination with Ranibizumab, or ShORe, Phase 3 trial, treatment-naive patients with wet AMD will be randomized to one of three treatment groups. Patients randomized to the standard dosing arm will receive standard of care 0.5 mg ranibizumab every four weeks in combination with 2.0 mg OPT-302 on a standard every four weeks dosing regimen. In the extended dosing arm, 0.5 mg ranibizumab will be administered every four weeks to week 52, in combination with 2.0 mg OPT-302 administered every four weeks for three total doses over 12 weeks, followed by OPT-302 dosing every eight weeks to week 52, with a sham injection administered at visits where OPT-302 is not administered. Patients randomized to the control arm will receive 0.5 mg ranibizumab administered in combination with sham intravitreal injections administered every four weeks to week 52. The primary and secondary efficacy outcomes will be determined at the end of the efficacy phase at week 52. Each patient will then continue to be treated for an additional year in the safety phase to reach week 100 to evaluate safety and tolerability over a total two-year period.



Combination of OPT-302 with Aflibercept STudy (COAST) Phase 3 Trial

In the Combination OPT-302 with Aflibercept STudy, or COAST, Phase 3 trial, treatment-naive wet AMD patients will be randomized to one of three treatment groups. Patients randomized to the standard dosing arm will receive 2.0 mg aflibercept administered every four weeks for three total doses over 12 weeks, followed by aflibercept dosing every eight weeks to week 52, in combination with 2.0 mg OPT-302 administered every four weeks to week 52. In the extended dosing arm, 2.0 mg aflibercept in combination with 2.0 mg OPT-302 will be administered every four weeks for three total doses over 12 weeks, followed by dosing every eight weeks to week 52, with a sham injection administered at visits where OPT-302 and aflibercept are not administered. Patients randomized to the control arm, will receive 2.0 mg aflibercept administered every four weeks for three total doses over 12 weeks, followed by dosing every eight weeks to week 52, in combination with sham intravitreal injections administered every four weeks to week 52. Similar to the ShORe trial, the primary and secondary efficacy outcomes of the COAST trial will be assessed at the end of the efficacy phase at week 52. Each patient will then continue to be treated for an additional year in the safety phase to reach week 100 to evaluate the safety and tolerability over a total two-year period.



For consistency, the ShORe and COAST Phase 3 trials build upon and maintain key features of our Phase 2b clinical trial of OPT-302 combination therapy for the treatment of wet AMD, while evaluating the administration of OPT-302 combination therapy over a longer treatment period and in a greater number of patients. In addition, the results of our Phase 2b clinical trial has informed the design of the Phase 3 trials. Analysis of the Phase 2b trial demonstrated that OPT-302 combination therapy increased visual acuity by a further +5.7 letters over ranibizumab monotherapy in wet AMD patients with minimally classic and occult lesions, representing the majority of wet AMD patients. Based on these positive data, primary analysis of the primary endpoint of the Phase 3 trials will be first conducted in patients with minimally classic and occult lesions administered OPT-302 every four weeks, followed by analysis on the total patient population and the every-eight week dosing groups.

Development of Co-Formulation

OPT-302 is currently administered as a combination therapy consisting of a sequential injection of OPT-302 following intravitreal administration of a VEGF-A inhibitor. We plan to develop a co-formulation of OPT-302 with an approved and/or biosimilar anti-VEGF-A therapy to achieve VEGF-A, VEGF-C and VEGF-D inhibition following the administration of a single intravitreal injection of the co-formulated product. We believe that a co-formulated OPT-302 and VEGF-A inhibitor product could provide flexibility of treatment options for physicians and reduce the frequency and number of injections for patients.

We are currently assessing opportunities with multiple third parties to in-license and/or generate a biosimilar anti-VEGF-A therapy, which we intend to co-formulate with OPT-302 and advance through non-clinical studies, including IND-enabling safety and tolerability studies. We expect to file an IND for the co-formulated product in the second half of 2021 and subsequently investigate the co-formulated product in a Phase 1 clinical trial for the treatment of wet AMD.

Diabetic Macular Edema

Diabetic macular edema is a complication of DR, a disease affecting the blood vessels of the retina in diabetics. Chronically elevated blood glucose levels, or hyperglycemia, causes damage to the small blood vessels or capillaries in the retina in patients with diabetes. The consequent chronic decrease in oxygen supply to retinal cells results in tissue damage that is referred to as DR. Approximately one-third of patients with DR or up to 10% of diabetics develop DME, which is characterized by accumulation of fluid and retinal thickening within the macula and is responsible for most of the central visual loss experienced in the diabetic population. Central-involved DME is diagnosed when swelling or edema occurs from fluid leaking into the central fovea region of the macula.

Current Treatments for DME and Their Limitations

VEGF-A inhibitor therapy is the first-line standard of care therapy for DME. Both ranibizumab and aflibercept are approved for the treatment of DME, and similarly to wet AMD, many patients receive bevacizumab as an off-label, lower cost alternative VEGF-A inhibitor therapy. Many patients with central-involved DME require near-monthly administration of intravitreal VEGF-A inhibitors during the first 12 months of treatment, with fewer injections needed in subsequent years to maintain clinical benefit. VEGF-A inhibitors have largely replaced the use of laser photocoagulation as a treatment for DME.

The anti-inflammatory corticosteroid therapies dexamethasone (Ozurdex) and fluocinolone acetonide (Illuvian) are also approved for use in central-involved DME. These agents however, are rarely used as first-line therapy due to inferior visual acuity outcomes compared to anti-VEGF-A therapy. Patients with persistent DME and who are insufficiently responsive to anti-VEGF-A therapy have shown some treatment benefit with intravitreal corticosteroids. However, as intravitreal corticosteroids are associated with high rates of ocular adverse events including cataract progression and intraocular pressure elevation, switching to corticosteroids from an anti-VEGF-A therapy with a sub-optimal response needs to be carefully considered.

Despite the widespread use of treatments targeting VEGF-A in the management of DME, there is still a significant unmet need as many patients demonstrate a sub-optimal response, remain treatment refractory or require frequent injections for persistent leakage in the macula. Up to two-thirds of patients with central-involved DME treated with VEGF-A inhibitors do not show reductions in the fluid or clinically meaningful improvement in visual acuity. In addition, approximately 25% of DME patients treated with VEGF-A inhibitors continue to have macula thickening and swelling following treatment. This resistance may occur as treatment selective anti-VEGF-A monotherapies do not fully address all of the factors involved in the pathogenesis of DME. As such, combination therapies targeting alternative factors and pathways have the potential for improved clinical outcomes in DME patients.

Market Opportunity for the Treatment of DME

It is estimated that between 1.3 million and 2.0 million people worldwide, including 14% of Type 1 diabetics and 6% of Type 2 diabetics, have DME . The risk of developing DME increases with time. According to the Wisconsin Epidemiologic Study of Diabetic Retinopathy, after 10 years of follow-up, 20% of patients with Type 1 diabetes and 25% of those with Type 2 diabetes will have developed DME. Ranibizumab and aflibercept, two VEGF-A inhibitors approved for the treatment of DME, generated combined annual worldwide sales of over $11.9 billion in 2019. Approximately 22% of these sales are attributable to the treatment of DME.

Potential for OPT-302 in DME

We believe that as a potent inhibitor of VEGF-C and VEGF-D, OPT-302 has the potential to provide significant therapeutic benefit to patients affected by DME. Although the underlying causes of wet AMD and DME differ, members of the VEGF family play a role in the progression of both diseases. VEGF-C and VEGF-D and their receptors are specifically implicated in the progression of diabetes. For example, patients with diabetes have higher levels of VEGF-C and VEGF-A and increased expression of both VEGFR-2 and VEGFR-3 in the retina compared to non-diabetics. The VEGF-A inhibitors ranibizumab and aflibercept, originally approved for treatment of wet AMD patients, have also been approved for treatment of DME patients. Similar to wet AMD, bevacizumab is also frequently used off-label as a treatment for DME.

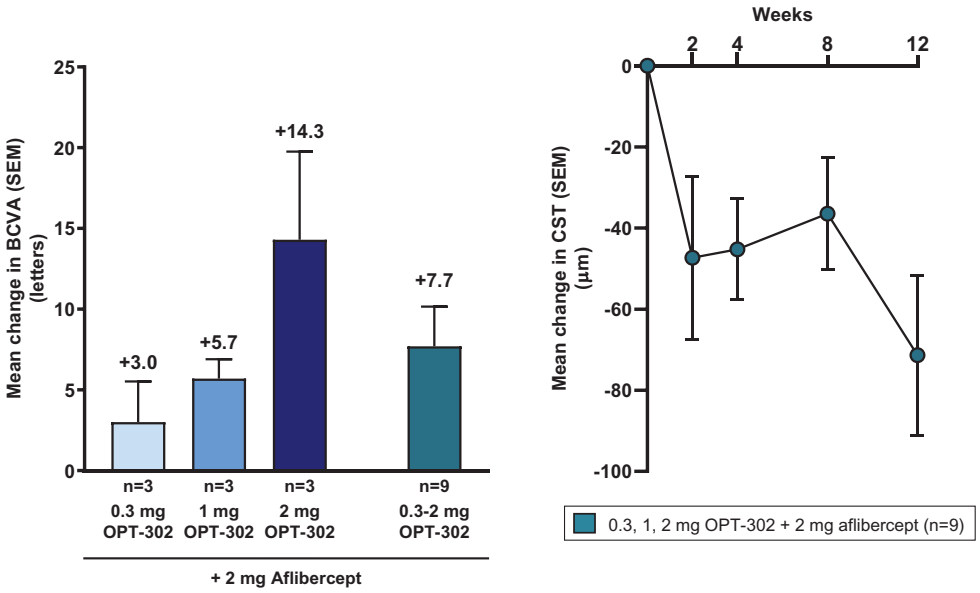
In our completed Phase 1b dose escalation clinical trial in patients with persistent DME, we observed promising evidence of a dose response of OPT-302 in combination with aflibercept, including further improvements in visual acuity despite patients' having been previously treated with anti-VEGF-A therapy. In our completed Phase 2a clinical trial, we observed improved visual acuity outcomes and evidence of a reduction in retinal thickness in treatment-refractory DME patients following OPT-302 combination therapy.

Phase 1b Clinical Trial of OPT-302 in DME

In 2018, we completed a Phase 1b dose-escalation clinical trial of OPT-302 in combination with aflibercept in nine patients with persistent DME that were previously treated with anti-VEGF-A therapies. Patients were administered three escalating doses (0.3 mg, 1.0 mg or 2.0 mg) of OPT-302 in combination with 2.0 mg aflibercept by intravitreal injections once every four weeks for a total of three doses. The primary analysis was conducted at week 12, four weeks after the final dose.

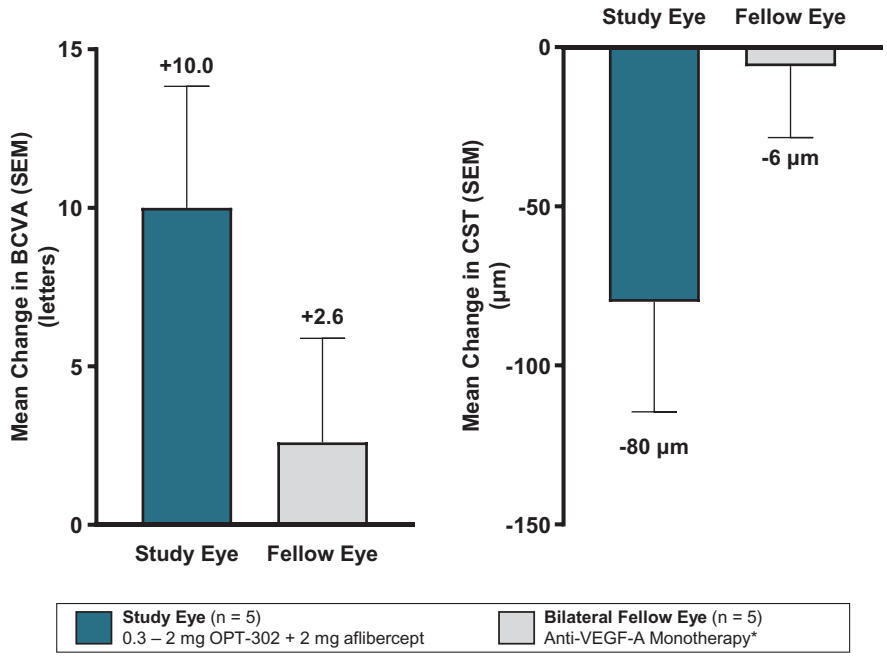
Across all nine patients in the Phase 1b trial, a mean gain in visual acuity of +7.7 letters from baseline to week 12 was observed across all dose groups, with a clear dose response of improved visual acuity with increasing doses of OPT-302. There was a corresponding mean decrease in retinal thickness at week 12 of -71 μm from baseline and six of nine (67%) patients had a ≥50% reduction in excess foveal thickness.

Dose-dependent Increases in Visual Acuity and Reduction in Retinal Thickness at Week 12 Following Treatment with OPT-302 in Combination with Aflibercept



Five of the nine patients in the Phase 1b trial had bilateral, persistent treatment-refractory DME. In these patients, study eyes received OPT-302 in combination with aflibercept, and fellow eyes received standard of care anti-VEGF-A monotherapy. In these bilateral disease patients, the mean change in visual acuity from baseline to week 12 was +10.0 letters in the study eye and +2.6 letters in the fellow eye. The corresponding reduction in retinal thickness from baseline to week 12 was -80 µm for OPT-302 combination treated study eyes, compared to -6 µm in fellow eyes that received anti-VEGF-A monotherapy.

In Patients with Bilateral DME, OPT-302 Combination Therapy Improved Visual Acuity and Reduced Retinal Thickness Compared to Fellow Eyes Treated with Anti-VEGF-A Monotherapy



* Patients with bilateral disease and persistent DME in the fellow eye receiving anti-VEGF-A (ranibizumab or aflibercept) monotherapy. Prior anti-VEGF-A therapy in Fellow Eyes BL to Week 12 (5 patients): 3x Aflibercept, 3x Ranibizumab, 1x Ranibizumab, 4x Ranibizumab, 3x Aflibercept.

OPT-302 in combination with aflibercept was well tolerated at all dose levels, with no DLTs and the MTD was not reached. There were no treatment-related clinically significant changes in intraocular pressure, electrocardiograms or vital signs. The most common AEs were related to the intravitreal injection procedure.

Phase 2a Clinical Trial of OPT-302 in DME

Based on the positive results of our Phase 1b trial, we reported outcomes from a Phase 2a trial in persistent DME patients refractory to anti-VEGF-A therapy in June 2020. Similar to the Phase 1b trial, this proof-of-concept trial was designed to investigate the ability of OPT-302 to improve outcomes in persistent DME patients. The primary endpoints were clinical response rate in visual acuity as well as safety and tolerability.

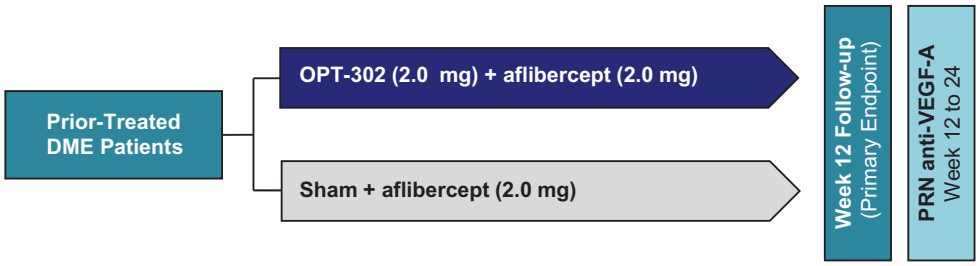
Clinical Trial Design

This Phase 2a trial was a randomized, double-masked, dose expansion trial that enrolled patients diagnosed with persistent center-involved DME despite regular administration of prior anti-VEGF-A monotherapy. These patients are considered to be a difficult-to-treat patient population since they have received prior anti-VEGF-A therapy and experienced a suboptimal clinical response. In our trial, these patients were defined as having visual acuity between 20/40 and 20/320 Snellen equivalent, or ≤73 and ≥24 BCVA letters on the ETDRS standardized eye chart, and retinal thickness of ≥320 µm on SD-OCT. In this Phase 2a trial, the mean number of prior intravitreal anti-VEGF-A injections was eight in each of the treatment groups, reflecting that the patients recruited into this trial were heavily pre-treated, with a mean of 39 days since the immediate prior injection to the start of the trial.

The Phase 2a trial was conducted at 53 trial sites in the United States, Israel, Australia and Latvia. Of the 144 patients randomized in the trial, 115 patients conformed sufficiently with the trial protocol and were included in our analyses of clinical efficacy. Patients were randomized 2:1 to receive either 2.0 mg OPT-302 in

combination with 2.0 mg aflibercept or a sham injection and 2.0 mg aflibercept. Patients received intravitreal injections once every four weeks for a total of three doses. The primary analysis was conducted at week 12, four weeks after the final dose.

Design of the Phase 2a Clinical Trial of OPT-302 in Combination with Aflibercept in Persistent Diabetic Macular Edema



PRN refers to *pro re nata*, or treatment on an as needed basis.

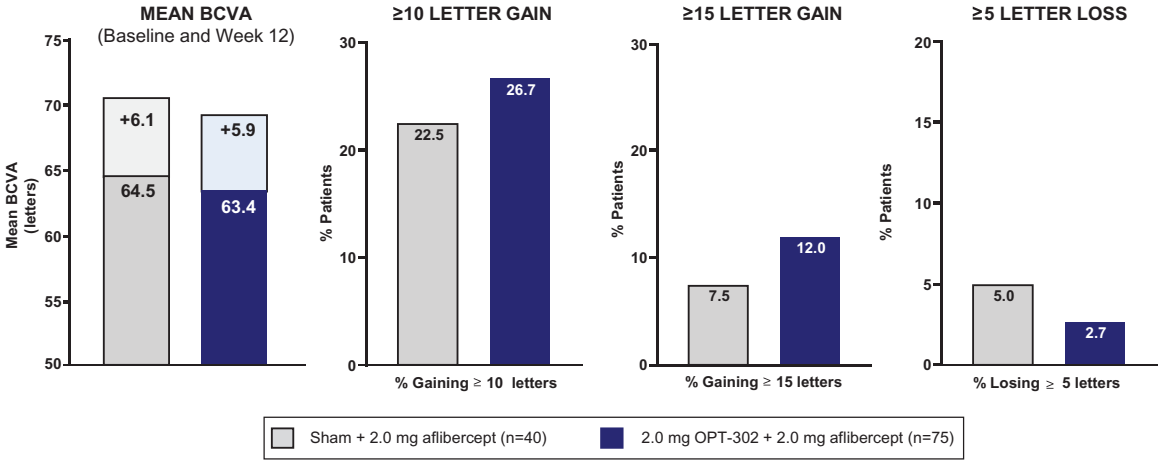
Improvements in Visual Acuity

The primary efficacy endpoint of the trial was the clinical response rate, defined as the proportion of patients receiving OPT-302 combination therapy that achieved a ≥5 letter gain in visual acuity at week 12 compared to baseline. Our predefined measure of success was a response rate of greater than or equal to 38%, based on historical observations that show limited ability to achieve a ≥5 letter improvement in DME patients on long-term anti-VEGF-A monotherapy. As an exploratory trial, this Phase 2a was not powered to detect statistical significance of OPT-302 combination therapy compared to aflibercept monotherapy.

We observed that 52.8% of patients treated with OPT-302 combination therapy achieved a ≥5 letter improvement in visual acuity at week 12 compared to baseline, meeting the pre-specified primary efficacy endpoint for this trial.

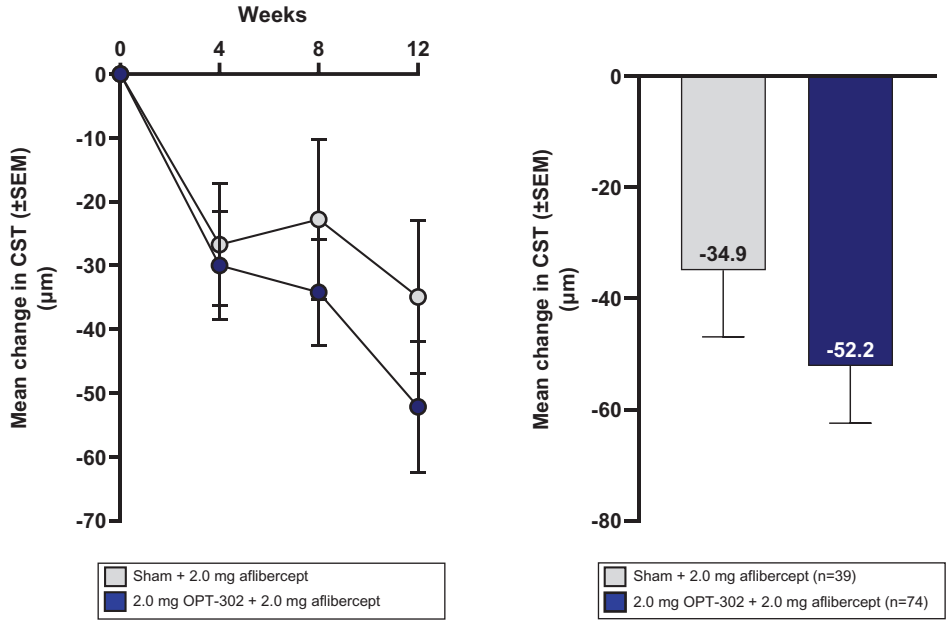
The mean change in visual acuity at week 12 compared to baseline was +5.9 letters in patients receiving OPT-302 combination therapy and +6.1 letters in the aflibercept monotherapy group. In the OPT-302 combination therapy group, the percentage of patients with visual acuity gains of ≥10 and ≥15 letters was higher, and the percentage of patients who lost ≥5 letters was lower than that in the aflibercept monotherapy group. These measures of visual function are shown in the figure below.

Measures of Visual Acuity at Week 12 Following OPT-302 Combination Therapy and Aflibercept Monotherapy



Patients treated with OPT-302 combination therapy also had decreased retinal thickness compared to aflibercept monotherapy, as shown in the figure below.

Greater Reduction in Retinal Thickness from Baseline to Week 12 following OPT-302 Combination Therapy Compared to Aflibercept Monotherapy



Prior Treatment History in Persistent DME Patients

Prior studies have shown that DME patients with mild visual acuity loss of 20/40 or better at baseline, show similar outcomes to any of the VEGF-A therapies: ranibizumab, aflibercept and bevacizumab. However, in patients with poorer baseline vision of 20/50 or worse, aflibercept has better outcomes compared to ranibizumab and bevacizumab over the first 12 months of treatment. It has also been shown that DME patients who experience inadequate responses to ranibizumab have achieved further anatomical and functional improvements upon switching to aflibercept.

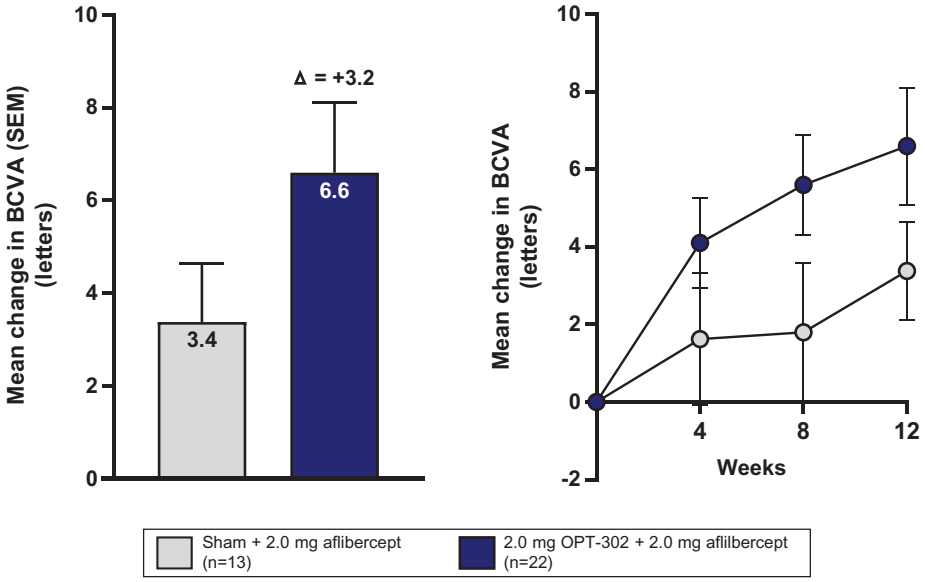
Due to the challenge of enrolling a large group of patients with identical prior treatment histories, we designed our Phase 2a trial to accelerate enrollment by randomizing patients with variable prior treatment histories. This strategy allowed us to more broadly understand the prior treatment history in persistent DME patients, which will inform the design of our future trials in DME.

In order to explore the importance of differences in prior treatment history, we collected detailed anti-VEGF-A treatment histories for patients enrolled in our Phase 2a DME trial. Patients randomized into our Phase 2a trial had variable prior treatment histories which included infrequent or irregular dosing and/or therapy with aflibercept, ranibizumab and bevacizumab. Approximately one third of patients had a prior treatment history of having received only aflibercept, or aflibercept for their three anti-VEGF-A treatments immediately before trial enrollment. Approximately 11% of patients had a prior treatment history of having received only ranibizumab, or ranibizumab for their three anti-VEGF-A treatments immediately before trial enrolment, whereas approximately 44% of patients had received only bevacizumab prior to trial enrollment. Patients with a prior treatment history of bevacizumab were required to receive at least one injection of either aflibercept or ranibizumab immediately prior to randomization in to the trial. Post-hoc analyses of the results from our Phase 2a trial suggest that some patients may have benefitted from the increased efficacy of aflibercept and/or from the switch to aflibercept therapy as administered in our trial on an every four-week dosing cycle. In the subset of

patients who had only received aflibercept, or received aflibercept for their three anti-VEGF-A treatments immediately before trial enrollment, referred to as treatment history of prior aflibercept, the mean improvement in visual acuity observed for the aflibercept monotherapy group was +3.4 letters (n=13), compared to a mean improvement of +7.4 letters for those patients with more variable prior treatment history who received aflibercept monotherapy (n=27) following randomization into the trial. This suggests that the majority of patients enrolled in the trial had not achieved a maximal response to all anti-VEGF-A therapies prior to enrolling in the trial.

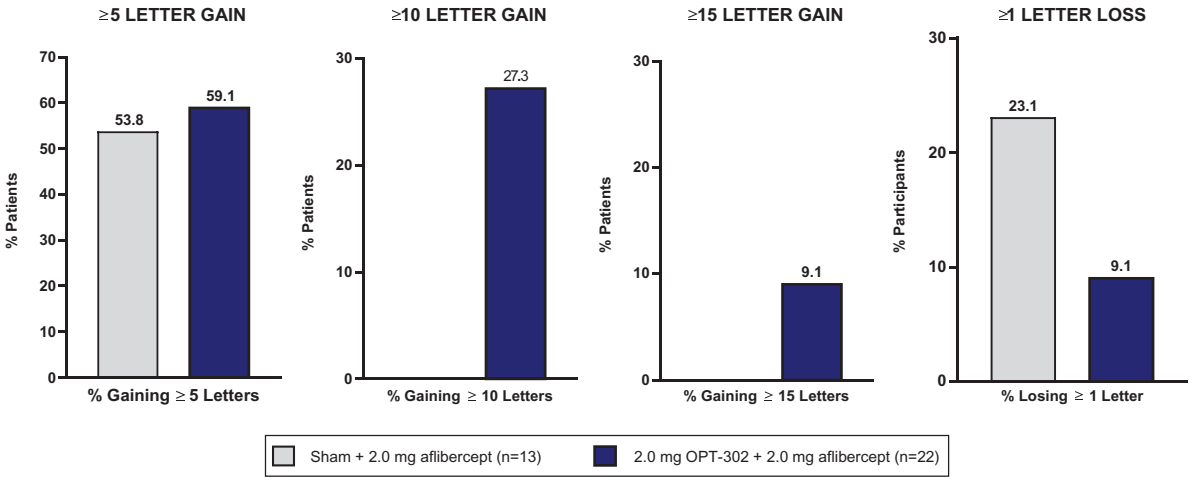
Due to the observed increase in treatment benefit for patients with a variable treatment history who then received aflibercept every four weeks in the trial, the subset of patients with a treatment history of prior aflibercept may represent the most stringent and least variable patient population in which to test the ability of OPT-302 to provide additional benefit. In this more homogeneous patient population, as shown in the figure below, patients administered OPT-302 combination therapy demonstrated a mean improvement in visual acuity of +6.6 letters (n=22) from baseline to week 12, compared to +3.4 letters (n=13) in the aflibercept monotherapy group.

Greater Gains in Visual Acuity following OPT-302 Combination Therapy in Patients with a Treatment History of Prior Aflibercept



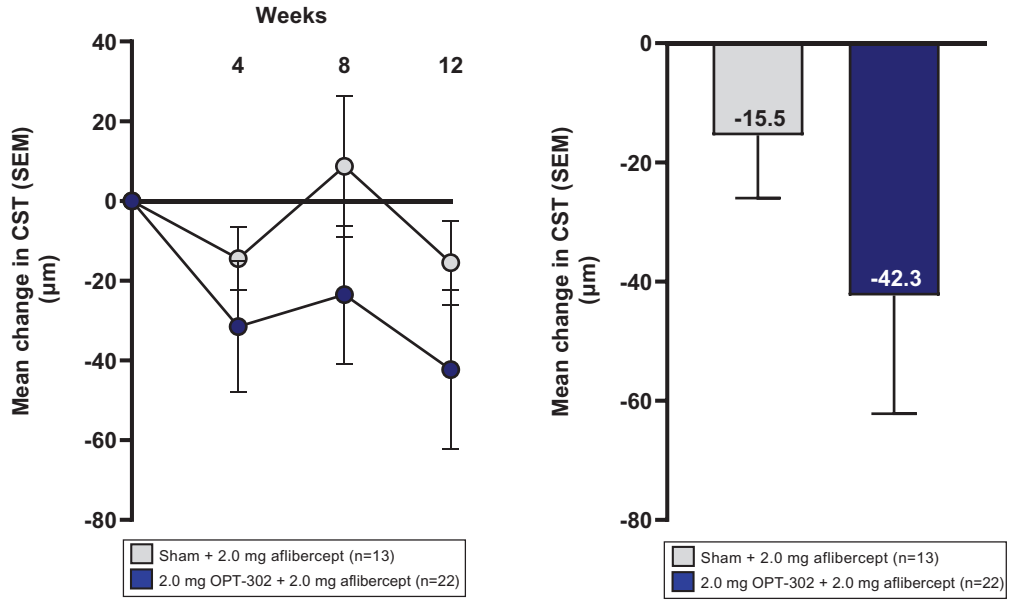
In addition, 27.3% of patients gained ≥10 letters and 9.1% gained ≥15 letters of visual acuity from baseline to week 12 following OPT-302 combination therapy. There were no patients with a treatment history of prior aflibercept that gained ≥10 letters of visual acuity in the aflibercept monotherapy group. Furthermore, the proportion of patients who lost ≥1 letters was 9.1% in the OPT-302 combination therapy group and 23.1% in the aflibercept monotherapy group. We believe that these results, as shown in the figures below, strongly support the potential of OPT-302 to improve the visual acuity in patients with persistent DME despite prior treatment with anti-VEGF-A monotherapy.

Proportion of Patients with a Treatment History of Prior Aflibercept Who Gained and Lost Visual Acuity from Baseline to Week 12



In this subgroup of patients with a treatment history of prior aflibercept, anatomical changes were consistent with functional visual acuity outcomes. As shown in the figure below, a greater mean reduction in retinal thickness was observed in the OPT-302 combination therapy group compared to the aflibercept monotherapy group at week 12. In particular, 22.7% of patients in the OPT-302 combination therapy group experienced at least a 300 µm reduction in retinal thickness at week 12, compared to 7.7% of patients in the aflibercept monotherapy group.

Greater Mean Reduction in Retinal Thickness following OPT-302 Combination Therapy in Patients with a Treatment History of Prior Aflibercept



Safety and Tolerability

OPT-302 combination therapy was well tolerated. There was one potentially treatment-related SAE of cerebrovascular accident, or stroke, resulting in one patient discontinuing treatment and withdrawing from the trial. The most common TEAEs were conjunctival hemorrhage and increased intraocular pressure and were mainly related to the intravitreal injection procedure. TEAEs did not lead to discontinuation of the trial for any patient. The incidence of intra-ocular inflammation was low, occurring in one patient for each treatment group, and the observed events were manageable and able to be resolved.

We now have extensive global clinical dosing experience demonstrating a favorable tolerability profile following repeated intravitreal administration of OPT-302 in 399 patients, with over 1,800 doses of OPT-302 administered across three international clinical studies in two disease indications and in combination with the two leading standard of care anti-VEGF-A therapies, ranibizumab and aflibercept. In particular, across our clinical trials, the incidence of intra-ocular inflammation was similar across all treatment groups.

Retinal Vein Occlusion

Based on the positive clinical data from our clinical trials of OPT-302 in wet AMD and DME, we intend to prioritize future development in these two indications while exploring potential opportunities to develop OPT-302 in other ophthalmic indications such as RVO, DR and other diseases involving aberrant CNV.

RVO is a sight-threatening visual disorder resulting from blockage of one of the veins carrying blood out of the retina. This blocked vein can leak blood and fluid resulting in swelling that can cause macular edema. Persistent, inadequately-treated macular edema associated with RVO can blur vision, cause significant loss in visual acuity and eventually lead to blindness. Macular edema is the most common cause of vision loss in people who suffer from RVO.

Similar to wet AMD and DME, the first-line standard of care to treat macular edema associated with RVO is intravitreal anti-VEGF-A monotherapy. VEGF-A inhibitors however, are only effective in significantly improving vision in approximately 30% to 40% of patients with macular edema associated with RVO above sham control. The prevalence of RVO in people over the age of 50 has been reported to be 0.7%, or approximately 1.8 million people in the United States and Europe. Over 500,000 individuals in the United States and Europe have macular edema associated with RVO. We believe that OPT-302 has the potential to bring therapeutic benefit to patients suffering from macular edema secondary to RVO.

Competition

The biotechnology and pharmaceutical industries, and the ophthalmic disease subsector, are characterized by rapidly advancing technologies, evolving understanding of disease etiology, intense competition and a strong emphasis on intellectual property. While we believe that OPT-302 and our knowledge and experience provide us with certain competitive advantages, we face substantial potential competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions and governmental agencies and public and private research institutions. Many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, pre-clinical studies, conducting clinical trials and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Accordingly, our competitors may be more successful than we may be in developing, commercializing and achieving widespread

market acceptance. In addition, our competitors' products may be more effective or more effectively marketed and sold than any treatment we or our development partners may commercialize and may render our product candidates obsolete or noncompetitive before we can recover the expenses related to developing and commercializing our product candidates.

We are developing OPT-302 for the treatment of wet AMD and additional retinal disease indications, such as DME and RVO, together with certain combination agents. Companies that have products that may compete with OPT-302 include Roche Group, Regeneron Pharmaceuticals, Inc. and Novartis AG, which have marketed anti-VEGF-A therapies including ranibizumab (Lucentis) and aflibercept (Eylea), each a standard of care treatment for wet AMD, and brolucizumab (Beovu), as well as Ocugen, Inc., Kodiak Sciences Inc. and Graybug Vision, Inc., which have product candidates in development for the treatment of wet AMD and DME. We are also aware of other companies that are working on therapies for the whole eye, including Santen, Inc. and Ocular Therapeutix, Inc. In addition, bevacizumab (Avastin), marketed by Genentech, Inc., is used off-label to treat wet AMD.

It is possible that our competitors will succeed in developing technologies that are more effective than our product candidates or that would render our technology obsolete or noncompetitive, or will succeed in developing biosimilar or interchangeable products for our product candidates. We anticipate that we will continue to face increasing competition in the future as new companies enter our market and scientific developments surrounding biosimilars and other retinal therapies continue to accelerate, particularly once ranibizumab and aflibercept approach loss of exclusivity. We cannot predict to what extent the entry of biosimilars or other competing products will impact potential future sales of our products or our product candidates.

With respect to our current and potential future product candidates, we believe that our ability to compete effectively and develop products that can be manufactured cost-effectively and marketed successfully will depend on our ability to:

- advance the development of OPT-302 and any other product candidates;
- license additional technology;
- complete clinical trials which position our products for regulatory and commercial success;
- maintain a proprietary position in our products;
- obtain required government and other public and private approvals on a timely basis;
- attract and retain key personnel;
- commercialize effectively;
- obtain reimbursement for our products in approved indications;
- establish efficient manufacturing processes and supply chain;
- comply with applicable laws, regulations and regulatory requirements and restrictions with respect to our business, including the commercialization of our products, including with respect to any changed or increased regulatory restrictions; and
- enter into additional collaborations to advance the development and commercialization of our product candidates.

Our Commercial License Arrangement with Selexis SA

In October 2013, we entered into a commercial license agreement, or the Selexis Agreement, with Selexis SA, or Selexis, under which Selexis granted us a non-exclusive, worldwide, sublicensable license under certain patents, know-how and other intellectual property controlled by Selexis to use certain cell lines, deliverables and

materials provide by Selexis to manufacture OPT-302 and related products and to use, sale and otherwise exploit such products.

We paid Selexis a nominal upfront payment upon entering into the Selexis Agreement. We are also required to make certain payments under the Selexis Agreement totaling approximately US$1.3 million upon the achievement of certain development and commercial milestones. We are also obligated to pay a low single-digit running royalty on worldwide net sales of the licensed products. Our royalty obligations will continue, on a product-by-product and country-by-country basis, until the expiration of the relevant patents, but will not extend beyond October 2024 in any event. After the expiration of the royalty term, our license will continue and become full paid, perpetual and irrevocable.

The Selexis Agreement will expire on the date of expiration of the last-to-expire of the license patents. Either party may terminate the Selexis Agreement for the other party's uncured material breach or bankruptcy. We may also terminate the Selexis Agreement at any time upon prior notice to Selexis.

Intellectual Property

As of June 30, 2020, we have rights to over 22 issued U.S. patents, over four U.S. patent applications, over 75 issued non-U.S. patents and over eight pending non-U.S. applications. All of our current issued patents and patent applications are projected to expire between August 2021 and November 2034.

With respect to soluble forms of VEGFR-3, we own and have licensed rights to patent families including issued patents in the United States, Europe, Canada and Australia, which are expected to expire between 2022 and 2031. These patents cover composition of matter and/or method of use claims, including claims directed at the treatment of eye diseases associated with abnormal blood vessel growth, such as wet AMD.

With respect to OPT-302, we own a patent family with two issued U.S. patents, an issued European patent validated in 38 countries and over eight issued non-U.S. patents granted in jurisdictions such as Japan, Australia, South Africa, Mexico, Malaysia, New Zealand, Colombia, Singapore and Russia. Patent applications are pending in the United States and in over eight other non-U.S. jurisdictions, including Europe, China, Brazil, South Korea and India. The two issued U.S. patents have claims covering the composition of matter of OPT-302 and its use and/or nucleic acids, vectors, and host cells for producing it. These issued patents and pending patent applications, if issued, are expected to expire in 2034, without taking into account any patent term extension.

The actual protection afforded by a patent, which can vary from country to country, depends on the type of patent, the scope of its coverage as determined by the patent office or courts in the country, and the availability of legal remedies in the country. The information in the above list is based on our current assessment of patents that we own or control or have exclusively licensed. The information is subject to revision, for example, in the event of changes in the law or legal rulings affecting our patents or if we become aware of new information. Significant legal issues remain unresolved as to the extent and scope of available patent protection for biotechnology products and processes in the United States and other important markets outside the United States. We expect that litigation will likely be necessary to determine the term, validity, enforceability and/or scope of certain of our patents and other proprietary rights. An adverse decision or ruling with respect to one or more of our patents could result in the loss of patent protection for a product and, in turn, the introduction of competitor products or follow-on biologics to the market earlier than anticipated.

Patents expire, on a country by country basis, at various times depending on various factors, including the filing date of the corresponding patent application(s), the availability of patent term adjustment, patent term extension and supplemental protection certificates and requirements for terminal disclaimers. In most countries, including the United States, the patent term is 20 years from the earliest claimed filing date of a non-provisional

patent application or its foreign equivalent in the applicable country. In the United States, a patent's term may, in certain cases, be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over a commonly owned patent or a patent naming a common inventor and having an earlier expiration date. In the United States, a patent may also be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended, with extended rights limited to the approved product, its approved uses, and/or its manufacture.

Although we believe our owned and licensed patents and patent applications provide us with a competitive advantage, the patent positions of biotechnology and pharmaceutical companies can be uncertain and involve complex legal and factual questions. We may not be able to develop patentable products or processes or obtain patents from pending patent applications. In the event of patent issuance, the patents may not be sufficient to protect the proprietary technology owned by or licensed to us or our partners. Our current patents, or patents that issue on pending applications, may be challenged, invalidated, infringed or circumvented. In addition, changes to patent laws in the United States or in other countries may limit our ability to defend or enforce our patents, or may apply retroactively to affect the term and/or scope of our patents. Our patents have been and may in the future be challenged by third parties in post-issuance administrative proceedings or in litigation as invalid, not infringed or unenforceable under U.S. or foreign laws, or they may be infringed by third parties. As a result, we are or may be from time to time involved in the defense and enforcement of our patent or other intellectual property rights in a court of law and administrative tribunals, such as in USPTO *inter partes* review or reexamination proceedings, foreign opposition proceedings or related legal and administrative proceedings in the United States and elsewhere. The costs of defending our patents or enforcing our proprietary rights in post-issuance administrative proceedings or litigation may be substantial and the outcome can be uncertain. An adverse outcome may allow third parties to use our proprietary technologies without a license from us.

Furthermore, we rely upon trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, by using confidentiality and invention assignment agreements with its commercial partners, collaborators, employees and consultants. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant it ownership of technologies that are developed through a relationship with a third party. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our commercial partners, collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Our commercial success will also depend in part on not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter its development or commercial strategies for our product candidates or processes, or to obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that it may require to develop or commercialize its future products may have an adverse impact on us. If third parties prepare and file patent applications in the United States that also claim technology to which we have rights, we may have to participate in interference or derivation proceedings in the USPTO to determine priority of invention.

As of June 30, 2020, we or our subsidiary have registered and own "Opthea" as a trademark in nine jurisdictions, including the United States and Europe. Other than the registered trademark listed above, we currently rely on our unregistered trademarks, trade names and service marks, as well as our domain names and logos, as appropriate, to market our brands and to build and maintain brand recognition.

Government Regulation

The FDA and other regulatory authorities at federal, state, and local levels, as well as in non-U.S. countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring, and post-approval reporting of biologics such as those we are developing. We, along with third-party contractors, will be required to navigate the various nonclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of OPT-302 or any future product candidate.

U.S. Biological Product Development

In the United States, the FDA regulates biologics under both the Federal Food, Drug and Cosmetic Act and the Public Health Services Act and their implementing regulations. Both drugs and biologics also are subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state and local statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or post-market may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, license revocation, a clinical hold, untitled or warning letters, product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Our product candidates and any future biological product candidates we develop must be approved by the FDA through a biologics license application, or BLA, process before they may be legally marketed in the United States. The BLA is a request for approval to market the biologic for one or more specified indications and must contain proof of safety, purity and potency. The FDA review and approval process generally involves the following:

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's current Good Laboratory Practices regulations;
- submission to the FDA of an IND, which must become effective before clinical trials may begin and must be updated annually or when significant changes are made;
- approval by an institutional review board, or IRB, or ethics committee at each clinical site before the trial is commenced;
- performance of adequate and well-controlled human clinical trials to establish the safety, purity and potency of the proposed biologic product candidate for its intended purpose;
- preparation of and submission to the FDA of a BLA after completion of all pivotal clinical trials that includes substantial evidence of safety, purity and potency from results of nonclinical testing and clinical trials; satisfactory completion of an FDA advisory committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with current good manufacturing practices, or cGMP, and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with GCP; and
- FDA review and approval, or licensure, of the BLA to permit commercial marketing of the product for particular indications for use in the United States.

Nonclinical Studies and IND

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as in vitro and animal studies to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for safety/toxicology studies.

Prior to beginning the first clinical trial with a product candidate in the United States, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and in vitro studies assessing the toxicology, PK, pharmacology, and PD characteristics of the product candidate; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold until the IND sponsor and the FDA resolve the outstanding concerns or questions. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical Trials

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. For new indications, a separate new IND may be required. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site, and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries. For purposes of BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap.

A sponsor who wishes to conduct a clinical trial outside of the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of a BLA. The FDA will accept a well-designed and well-conducted foreign clinical study not conducted under an IND if the study was conducted in accordance with GCP requirements, and the FDA is able to validate the data through an onsite inspection if deemed necessary.

- Phase 1 — The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism, distribution and elimination of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.
- Phase 2 — The investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to

identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

- Phase 3 — The investigational product is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval and product labeling.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a condition to approval of the BLA. Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate, and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product, or for biologics, the safety, purity and potency. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

BLA Submission, Review and Approval

Assuming successful completion of the clinical trials, the results of product development, nonclinical studies and clinical trials are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications. The BLA must include all relevant data available from pertinent preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. The submission of a BLA requires payment of a substantial application user fee to FDA, unless a waiver or exemption applies.

Once a BLA has been submitted, the FDA's goal is to review standard applications within ten months after it accepts the application for filing (a 60-day process), or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. In both standard and priority reviews, the review process can be significantly extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed, or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may convene an advisory committee to provide clinical insight on application review questions. Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response letter will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the

application are inadequate to support approval, the FDA may issue the Complete Response letter without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the Complete Response letter, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with a Risk Evaluation and Mitigation Strategy, or REMS, to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

Expedited Development and Review Programs

Any marketing application for a biologic submitted to the FDA for approval may be eligible for FDA programs intended to expedite the FDA review and approval process, such as priority review, fast track designation, breakthrough therapy and accelerated approval.

A product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or to provide a significant improvement in the treatment, diagnosis or prevention of a serious disease or condition compared to marketed products. For products containing new molecular entities, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date (compared with ten months under standard review).

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need by providing a therapy where none exists or a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. Fast track designation provides opportunities for frequent interactions with the FDA review team to expedite development and review of the product. The FDA may also review sections of the BLA for a fast track product on a rolling basis before the complete application is submitted, if the sponsor and FDA agree on a schedule for the submission of the application sections, and the sponsor pays any required user fees upon submission of the first section of the BLA. The review clock does not begin until the final section of the BLA is submitted.

In addition, a sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs or biologics designated as breakthrough therapies are also eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy. The benefits of breakthrough therapy designation include the same benefits as fast track designation, plus intensive guidance from the FDA to ensure an efficient drug development program.

Additionally, products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review and approval will not be shortened. Furthermore, priority review, fast track designation, breakthrough therapy designation, and accelerated approval do not change the standards for approval but may expedite the development or approval process.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or 200,000 or more individuals in the United States for which there is no reasonable expectation that the cost of developing and making available in the United States a drug or biologic for this type of disease or condition will be recovered from sales in the United States for that drug or biologic. Orphan designation must be requested before submitting a BLA. After the FDA grants orphan designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. The orphan drug designation does not convey any advantage in, or automatically shorten the duration of, the regulatory review or approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan exclusivity does not prevent FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application fee. A designated orphan product may not receive orphan exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Post-Approval Requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to quality control and quality assurance, record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing user fee requirements, under which FDA assesses an annual program fee for each product identified in an approved BLA. Biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by

the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including AEs of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of a product, mandated modification of promotional materials or issuance of corrective information, issuance by FDA or other regulatory authorities of safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product, or complete withdrawal of the product from the market or product recalls;
- fines, warning or untitled letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of existing product approvals;
- product seizure or detention, or refusal of the FDA to permit the import or export of products; or
- injunctions, consent decrees or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

Biosimilars and Reference Product Exclusivity

The Affordable Care Act signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-approved reference biological product. To date, a number of biosimilars have been licensed under the BPCIA, and numerous biosimilars have been approved in Europe. The FDA has issued several guidance documents outlining its approach to the review and approval of biosimilars.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an

individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. Complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and impact of the BPCIA is subject to significant uncertainty.

Other U.S. Healthcare Laws and Compliance Requirements

In the United States, our current and future operations are subject to regulation by various federal, state and local authorities in addition to the FDA, including but not limited to, CMS other divisions of the U.S. Department of Health and Human Services, or HHS (such as the Office of Inspector General, Office for Civil Rights and the Health Resources and Service Administration), the U.S. Department of Justice, or DOJ, and individual U.S. Attorney offices within the DOJ, and state and local governments. For example, our clinical research, sales, marketing and scientific/educational grant programs may have to comply with the anti-fraud and abuse provisions of the Social Security Act, the false claims laws, transparency and price reporting laws, the privacy and security provisions of HIPAA and similar state laws, each as amended, as applicable. Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors and customers may be subject to healthcare laws, regulations and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security, price reporting, and transparency laws. Some of our pre-commercial activities are subject to some of these laws.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between therapeutic product manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor.

Additionally, the intent standard under the Anti-Kickback Statute was amended by the Affordable Care Act to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Further, courts have found that if "one purpose" of remuneration is to induce referrals, the federal Anti-Kickback statute is violated. Violations of the Anti-Kickback Statute can result in significant civil and criminal fines and penalties for each violation, imprisonment, and exclusion from federal healthcare programs. In addition, the Affordable Care Act codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act, or the FCA, as discussed below.

The federal false claims laws, including the FCA, which can be enforced by private citizens through civil qui tam actions, and civil monetary penalty laws, prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false or fraudulent claim for payment to, or approval by, the federal government, including federal healthcare programs, such as Medicare and Medicaid, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. Pharmaceutical and other healthcare companies have been, and continue to be, prosecuted under these laws, among other things, for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product and for causing false claims to be submitted because of the companies' marketing of the product for unapproved, off-label, and thus generally non-reimbursable, uses.

HIPAA created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the Anti-Kickback Statute, the Affordable Care Act amended the intent standard for certain healthcare fraud statutes under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. When an entity is determined to have violated the FCA, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs.

We may be subject to data privacy and security regulations by both the federal government and the states in which we conduct our business. HIPAA, as amended by HITECH, and its implementing regulations, imposes requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates and their subcontractors relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates, which are independent contractors or agents of covered entities that create, maintain, transmit, receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, many state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways, are often not pre-empted by HIPAA, and may have a more prohibitive effect than HIPAA, thus complicating compliance efforts.

Additionally, the federal Physician Payments Sunshine Act, or the Sunshine Act, within the Affordable Care Act, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually to CMS information related to certain payments or other transfers of value made or distributed to physicians, as defined by such law, and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members. Failure to report accurately could result in penalties. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made in the previous year to certain non-physician providers such as physician assistants and nurse practitioners.

Many states have similar statutes or regulations to the above federal laws that may be broader in scope and may apply regardless of payor. We may also be subject to state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, and/or state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, drug pricing or marketing expenditures. Certain state and local laws also require the registration of pharmaceutical sales representatives. We may be subject to state and foreign laws governing the privacy and security of health information, some of which may be more stringent than those in the United States (such as the GDPR, which was adopted by the EU and subsequently became effective in May 2018). These laws may differ from each other in significant ways and may not have the same effect, further complicating compliance efforts.

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of drug and biological products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical and biotechnology companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical and biotechnology companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws. Additionally, to the extent that we have business operations in foreign countries or sell any of our products in foreign countries and jurisdictions, including Canada or the EU, we may be subject to additional regulation.

Ensuring business arrangements with third parties comply with applicable healthcare laws and regulations is a costly endeavor. If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other current or future governmental regulations that apply to us, we may be subject to penalties, including without limitation, significant civil, criminal and/or administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private "qui tam" actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect its ability to operate our business and results of operations. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we may obtain regulatory approval. In the United States and in foreign markets, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage and establish adequate reimbursement levels for such products. In the United States, third-party payors include federal and state healthcare programs, private managed care providers, health insurers and other organizations. Third-party payors decide which medications they will pay for and establish reimbursement levels. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid in the United States, and commercial payors are critical to new product acceptance.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from third-party payors, which decide which therapeutics they will pay for and establish reimbursement levels. In the United States, the principal decisions about reimbursement for new medicines are typically made by CMS, an agency within HHS. CMS decides whether and to what extent our products will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a therapeutic is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

We cannot be sure that coverage or reimbursement will be available for any product that we commercialize and, if coverage and reimbursement are available, what the level of reimbursement will be. Coverage may also be more limited than the purposes for which the product is approved by the FDA or comparable foreign regulatory authorities. Reimbursement may impact the demand for, or the price of, any product for which we obtain regulatory approval.

We may develop products that, once approved, may be administered by a physician. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization.

Third-party payors are increasingly challenging the price, examining the medical necessity, and reviewing the cost-effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. Obtaining reimbursement for our products may be particularly difficult because of the higher prices often associated with branded drugs and drugs administered under the supervision of a physician. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA approvals. Our product candidates may not be considered medically necessary or cost-effective. Obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our product on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Adequate third-party reimbursement may not be available to enable us to

maintain price levels sufficient to realize an appropriate return on its investment in product development. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize any product candidate that we successfully develops.

Different pricing and reimbursement schemes exist in other countries. In the EU, governments influence the price of biopharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to establish their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any product candidates for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care, the increasing influence of health maintenance organizations, and additional legislative changes in the United States has increased, and we expect will continue to increase, the pressure on healthcare pricing. The downward pressure on the rise in healthcare costs in general, particularly prescription medicines, medical devices and surgical procedures and other treatments, has become very intense. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare Reform

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect the ability to profitably sell product candidates for which marketing approval is obtained. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

For example, the Affordable Care Act has substantially changed healthcare financing and delivery by both governmental and private insurers. Among the Affordable Care Act provisions of importance to the pharmaceutical and biotechnology industries, in addition to those otherwise described above, are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23% and 13% of the average manufacturer price for most branded and generic drugs, respectively, and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, or BBA, effective as of January 2019) point-of-sale discounts off negotiated prices of applicable branded drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;

- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the 340B Drug Discount Program;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- expansion of healthcare fraud and abuse laws, including the FCA and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected;
- requirements to report certain financial arrangements with certain healthcare providers and teaching hospitals;
- a requirement to annually report certain information regarding drug samples that manufacturers and distributors provide to physicians;
- establishment of a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending; and
- a licensure framework for follow on biologic products.

Since its enactment, there have been executive, legal and political challenges to certain aspects of the Affordable Care Act. By way of example, the TCJA included a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas ruled that the individual mandate is a critical and inseverable feature of the Affordable Care Act, and therefore, because it was repealed as part of the TCJA, the remaining provisions of the Affordable Care Act are invalid as well. On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit ruled that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. On March 2, 2020, the U.S. Supreme Court granted the petitions for writs of certiorari to review the case, although it is unclear when a decision will be made or how the Supreme Court will rule. In addition, there may be other efforts to challenge, repeal or replace the Affordable Care Act.

Further legislation or regulation could be passed that could harm our business, financial condition and results of operations. Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. For example, in August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect beginning on April 1, 2013 and will stay in effect through 2030 unless additional Congressional action is taken. These Medicare sequester reductions have been suspended from May 1, 2020 through December 31, 2020 due to the COVID-19 pandemic. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. In addition, the BBA amended the Affordable Care Act, effective January 1, 2019, by increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole."

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the Trump administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. Further, the Trump administration previously released a "Blueprint," or plan, to lower drug prices and reduce out of pocket costs of drugs that contained proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. HHS has solicited feedback on some of these measures and has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019.

While some of these and other measures may require additional authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative or administrative measures to control drug costs. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control biopharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions on coverage or access could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates that we successfully commercialize or put pressure on our product pricing.

We expect that these and other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that we receive for any approved product. It is possible that additional governmental action is taken in response to the COVID-19 pandemic. For example, on August 6, 2020, the Trump administration issued another executive order that instructs the federal government to develop a list of "essential" medicines and then buy them and other medical supplies from U.S. manufacturers instead of from companies around the world, including China. The order is meant to reduce regulatory barriers to domestic pharmaceutical manufacturing and catalyze manufacturing technologies needed to keep drug prices low and the production of drug products in the United States. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

European Union Regulation

In the European Union, a clinical trial application must be submitted to each country's national regulatory authority in which the clinical trial is to take place, together with an independent ethics committee, much like the FDA and IRB, respectively. It is expected, however, that the Clinical Trials Regulation 536/2014 shall start to

apply during the course of 2020. This new Regulation takes direct effect in each European Union Member State and seeks to simplify and streamline the approval of clinical trials in the European Union, for example, by allowing the clinical trial sponsor to submit a single application for approval of a clinical trial across the EU via a new EU Portal. The new Regulation also aims to streamline and simplify the rules on safety reporting, and introduces enhanced transparency requirements such as mandatory submission of a summary of the clinical trial results to a new EU Database.

Medicinal products can only be commercialized in the European Economic Area after a marketing authorization, or MA, has been obtained. There are two types of marketing authorizations:

- The centralized MA, which is issued by the European Commission through the Centralised Procedure, based on the opinion of the Committee for Medicinal Products for Human Use of the European Medicines Agency, or EMA, and which is valid throughout the entirety of the EEA. The Centralised Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto immune and viral diseases. The Centralised Procedure is optional for products containing an active substance not authorized in the EEA before 20 May 2004, for products that constitute a significant therapeutic, scientific or technical innovation or for which a centralized authorization would be in the interest of patients.
- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralised Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member State through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

The European Union also provides opportunities for market exclusivity. For example, in the European Union, upon receiving marketing authorization, innovative medicinal products generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic or biosimilar application. During the additional two-year period of market exclusivity, a generic or biosimilar marketing authorization can be submitted, and the innovator's data may be referenced, but no generic or biosimilar product can be marketed until the expiration of the market exclusivity. Products receiving orphan designation, can receive ten years of market exclusivity, during which time no similar medicinal product for the same indication may be placed on the market. An orphan product's market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the criteria for orphan drug designation are no longer met, in other words, when it is shown on the basis of available evidence that the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if:

- the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- the applicant consents to a second orphan medicinal product application; or
- the applicant cannot supply sufficient quantities of the orphan medicinal product.

In the EU, companies developing a new medicinal product must agree to a Paediatric Investigation Plan, or a PIP, with the EMA and must conduct pediatric clinical trials in accordance with that PIP, unless a deferral or

waiver applies (for example, because the relevant disease or condition occurs only in adults). The MA application for the product must include the results of pediatric clinical trials conducted in accordance with the PIP, unless a waiver applies, or a deferral has been granted, in which case the pediatric clinical trials must be completed at a later date. Products that are granted a marketing authorization on the basis of the pediatric clinical trials conducted in accordance with the PIP are eligible for a six month extension of the protection under a supplementary protection certificate (if any is in effect at the time of approval) or, in the case of orphan medicinal products, a two year extension of the orphan market exclusivity. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

Coverage, Pricing and Reimbursement

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost effectiveness of a particular drug candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross border imports from low priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

Advertising Regulation

All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the European Union. Although general requirements for advertising and promotion of medicinal products are established under European Union directives, the details are governed by regulations in each European Union Member State and can differ from one country to another.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Pharmacovigilance System

The holder of a European MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance, or QPPV, who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

All new European MA applications must include a risk management plan, or RMP, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies. RMPs and PSURs are routinely available to third parties requesting access, subject to limited redactions.

Rest of the World Regulation

For other countries outside of the EU and the United States, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Additionally, the clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom, or UK, voted in favor of leaving the EU, commonly referred to as "Brexit" and the United Kingdom officially withdrew from the EU on January 31, 2020. The United Kingdom and the EU are currently in a transition period during which the United Kingdom and the EU are negotiating additional arrangements, including their future trading arrangement. The United Kingdom has stated that it wants the transition period to expire, and the future trading terms to be agreed, by December 31, 2020.

Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from EU directives and regulations, immediately following Brexit, it is expected that the United Kingdom's regulatory regime will remain aligned with EU regulations. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom. In the longer term, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom.

The Foreign Corrupt Practices Act

The FCPA prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Additional Regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

Other Regulations

We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control, and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

In addition to regulation in the United States and Europe, a variety of foreign regulations govern clinical trials, commercial sales and distribution of drugs. Pharmaceutical firms who wish to market their medicinal drugs outside the European Union and the United States must submit marketing authorization application to the national authorities of the concerned countries, such as the Pharmaceutical and Medical Device Agency, or PMDA in Japan. The approval process varies from jurisdiction to jurisdiction and the time to approval may be longer or shorter than that required by the FDA or European Commission.

Manufacturing and Supply

We are dependent on specialized third parties, who are subject to cGMP requirements and regulations, for the supply and manufacture of OPT-302 drug substance and drug product. We do not have any internal manufacturing and control capabilities. We source the drug substance for OPT-302 and our clinical trials on a purchase order basis. However, we believe that competitive pricing is achieved because there are a number of potential long-term replacements for our suppliers of drug substance.

In October 2013, we entered into a biopharmaceutical manufacturing agreement, or the Patheon Agreement, with Patheon Biologics Company, Austria Pty Ltd. and Patheon Biologics Company B.V., or collectively Patheon. The Patheon Agreement establishes the general terms and conditions pursuant to which Patheon or its affiliates will manufacture OPT-302 drug product for us in accordance with cGMP requirements. Under the Patheon Agreement, Patheon granted us a perpetual, royalty-free, fully paid-up, non-exclusive, worldwide, transferable and sublicensable license, under all of Patheon's intellectual property rights embedded in the development and manufacture process to the extent necessary for developing, making, using and selling OPT-302.

The Patheon Agreement will expire on the date that all of the manufacturing services to be performed by Patheon are completed. We may terminate the Patheon Agreement for any reason upon prior written notice. Patheon may terminate the Patheon Agreement upon prior written notice if Patheon has not performed any activities under the Patheon Agreement for certain period of time or if, despite Patheon's commercially reasonably best efforts, Patheon determines that the services cannot be completed according to specifications approved by us or within a reasonable time after the originally planned timeframe. Either party may terminate the Patheon Agreement for the other party's uncured material breach or bankruptcy. In addition, the Patheon Agreement will terminate if the parties are unable to reach agreement regarding necessary changes to the services based on the results of individual stage of development work. Upon termination of the Patheon Agreement, we are required to pay Patheon for services properly performed, including non-cancelable costs. Based upon the timing of the termination, we may also be required to pay Patheon certain close out cost for canceled services

Employees

As of June 30, 2020, we had eight full-time employees, four of whom had an M.D. or Ph.D. degree. None of our employees are represented by collective bargaining agreements. We believe that our management maintains good relations with our employees. As of June 30, 2020, all of our employees were based in Australia, with four employees in our research and development department and four employees in our general and administrative department.

Facilities

We occupy approximately 591 square feet of office space in South Yarra, Victoria, Australia under a lease that expires in July 2022. We believe that our existing facilities are adequate to meet our current needs and that suitable additional alternative facilities will be available in the future on commercially reasonable terms to meet our future needs.

Legal Proceedings

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. We are currently not a party to any material legal proceedings.

MANAGEMENT

Directors and Senior Management

The following table sets forth information relating to our directors, senior management and key employees as of September 30, 2020.

Name	Age	Position
Senior Management and Key Employees		
Megan Baldwin, Ph.D.	46	Chief Executive Officer and Managing Director
Michael Tonroe	54	Chief Financial Officer and Company Secretary
Richard Chadwick, Ph.D.	54	Head of Intellectual Property
Michael Gerometta, Ph.D.	56	Head of Chemistry, Manufacturing and Controls Development
Clare Price	52	Director of Clinical Development
Annette Leahy	45	Director of Clinical Research
Ian Leitch, Ph.D.	57	Director of Clinical Research
Non-Employee Directors		
Jeremy Levin, D.Phil, MB BChir[(1)]	67	Chairperson
Lawrence Gozlan	41	Director
Michael Sistenich	45	Director
Daniel Spiegelman	62	Director

(1) Dr. Levin joined our board of directors as Chairperson effective as of October 12, 2020. On the same date, Geoffrey Kempler retired from our board of directors.

The business addresses for our senior management and board of directors is Opthea Limited, Suite 0403, Level 4, 650 Chapel Street, South Yarra, VIC 3141, Australia.

Senior Management and Key Employees

Megan Baldwin, Ph.D., has served as our Chief Executive Officer and Managing Director since February 2014. Since joining our company in 2008, Dr. Baldwin has held various positions, including Head of Preclinical R&D from February 2009 to November 2012 and Chief Executive Officer of Opthea Pty Ltd., previously a wholly-owned subsidiary, from November 2012 to December 2015. Dr. Baldwin has over 20 years of experience focusing on angiogenesis and therapeutic strategies for ophthalmic and cancer indications. Prior to joining our company, Dr. Baldwin was employed at Genentech, Inc. (now a subsidiary of the Roche Group), a leader in the field of angiogenesis-based therapies for cancer and other diseases. Dr. Baldwin earned a Bachelor of Science Honours and Ph.D. in Medicine from the University of Melbourne. We believe that Dr. Baldwin's business expertise and her daily insight into corporate matters as our Chief Executive Officer qualify her to serve on our board of directors.

Michael Tonroe has served as our Chief Financial Officer and Company Secretary since May 2014. From March 2011 to April 2014, Mr. Tonroe served as the Chief Financial Officer and Company Secretary of the Australian Synchrotron Co. Ltd. in Melbourne. Mr. Tonroe has over 20 years of experience in financial management serving in board-level positions for private and listed companies in Australia, the United Kingdom, the United States and Canada. Mr. Tonroe is a fellow of the Institute of Chartered Accountants in England and Wales and earned a Bachelor of Science in Business Studies from Buckingham University.

Richard Chadwick, Ph.D., has served as our Head of Intellectual Property since February 2008. From April 2003 to December 2007, Dr. Chadwick was a patent attorney at FB Rice & Co., a private law firm. Prior to FB Rice & Co., Dr. Chadwick was a patent attorney at Wynne-Jones, Laine & James, a private law firm, and also worked as an in-house attorney at Dow Corning Limited, a materials science company, and Unilever plc, a consumer goods company. Dr. Chadwick earned a Bachelor of Science in Biochemistry with Microbiology from the University of St. Andrews and a Ph.D. in Biochemistry and Molecular Biology from the University of Manchester.

Michael Gerometta, Ph.D., has served as our Head of Chemistry, Manufacturing and Controls Development since December 2008. Dr. Gerometta has over 30 years of experience in the Australian biotechnology industry, working with numerous contract manufacturing organizations overseas and locally in all facets of translational CMC from concept through to Phase 2 studies. Dr. Gerometta earned a Bachelor of Science in Chemistry from the University of Technology, Sydney, and a Ph.D. in Biotechnology from the Queensland University of Technology.

Clare Price has served as our Director of Clinical Development since July 2016. From February 2016 to July 2016, Ms. Price served as the Director of Clinical Development at Commercial Eyes Pty Ltd., a pharmaceutical consulting firm. From January 2007 to January 2016, Ms. Price served in various roles, most recently as the Clinical Programme Director, at Starpharma Holdings Ltd, an Australian biotechnology company. Ms. Price earned a Bachelor of Pharmacy from Bath Spa University.

Annette Leahy has served as one of our Directors of Clinical Research since August 2017. From May 2016 to August 2017, she was the Clinical Trials Manager at Swisse Wellness Pty Ltd., an Australian wellness company. From September 2014 to May 2016, she served in various roles, most recently as Senior Manager, Learning and Development, at Novotech (Australia) Pty Ltd., an Australian clinical research organization. Ms Leahy earned a Bachelor of Health Information Management from La Trobe University.

Ian Leitch, Ph.D., has served as one of our Directors of Clinical Research since September 2011. From September 2006 to September 2011, Dr. Leitch was a member of the Medical Sciences group at Amgen Inc., a biopharmaceutical company, and had responsibility for the design and management of clinical studies in oncology. From 1998 to 2006, Dr. Leitch was Senior Program Manager for Cardiovascular Research and Clinical Study Director for Ophthalmology at Miravant Medical Technologies Inc., a biopharmaceutical company. He earned a Bachelor of Science with Honours and a Ph.D. from the Department of Pharmacology, Faculty of Medicine, at Monash University and completed part of the doctoral studies at the University of California, Santa Barbara.

Non-Employee Directors

Lawrence Gozlan has served as a member of our board of directors since July 2020. Since 2007, Mr. Gozlan has served as the Life Sciences Investment Manager of Jagen Pty Ltd., an international investment organization. Mr. Gozlan has also served as a member of the board of directors of Alterity Therapeutics Ltd., a drug development company, since 2011. Mr. Gozlan earned a Bachelor of Science in Microbiology and Immunology from the University of Melbourne. We believe Mr. Gozlan's extensive investment experience in biotechnology and life sciences companies qualify him to serve on our board of directors.

Jeremy Levin, D.Phil., MB BChir has served as the Chairperson of our board of directors since October 2020. Since March 2015, Dr. Levin has served as the Chief Executive Officer, and since April 2014, as the chairperson of the board of directors, of Ovid Therapeutics Inc., a biopharmaceutical company. From May 2012 to October 2013, Dr. Levin served as the President and Chief Executive Officer of Teva Pharmaceutical Industries Ltd., a publicly held pharmaceutical company. From September 2007 to December 2012, Dr. Levin held several roles at Bristol-Myers Squibb Company, a publicly held pharmaceutical company, ultimately serving as the Senior Vice President of Strategy, Alliances and Transactions. Dr. Levin also served as a member

of the executive committee at Bristol-Myers Squibb Company. Dr. Levin earned a Bachelor of Arts in Zoology, Master of Arts in Cell Biology and D.Phil. in Chromatin Structure, all from University of Oxford, and a Bachelor of Medicine, Bachelor of Surgery from the University of Cambridge. We believe Dr. Levin's extensive experience in the global biotechnology and pharmaceutical industry qualify him to serve on our board of directors.

Michael Sistenich has served as a member of our board of directors since November 2015. Since May 2017, Mr. Sistenich has served as a co-founder and partner of Aurenda Partners Pty Ltd., an investment firm. From August 2016 to February 2017, Mr. Sistenich served as the interim Chief Executive Officer of Nohla Therapeutics, Inc., a cellular therapy company, and has also served as a member of the board of directors of Nohla Therapeutics, Inc. from March 2017 to June 2019. Mr. Sistenich has advised a wide range of global institutions, high net worth individuals and companies on healthcare investments over the past 20 years. He is a healthcare specialist in international investment management and investment banking. Mr. Sistenich earned a Master of Science in Biochemistry from the University of Oxford. We believe Mr. Sistenich's financial experience and his service on the boards of directors of several biotechnology companies qualify him to serve on our board of directors.

Daniel Spiegelman has served as a member of our board of directors since September 2020. Since July 2020, Mr. Spiegelman has served as interim President of Recardia Therapeutics Inc., a pharmaceutical development company. From May 2012 to January 2020, Mr. Spiegelman served as Executive Vice President, Chief Financial Officer and a member of the board of directors of BioMarin Pharmaceutical Inc., a biotechnology company. From October 2008 to March 2018, Mr. Spiegelman served as a member of the board of directors of Cascadian Therapeutics, Inc., a publicly held biotechnology company that was acquired by Seattle Genetics, Inc. in 2018. From October 2008 to March 2018, Mr. Spiegelman served as a member of the board of directors of Cascadian Therapeutics, Inc., a publicly held biotechnology company that was acquired by Seattle Genetics, Inc. in 2018. From May 2009 to May 2012, Mr. Spiegelman served as a consultant to provide strategic financial management support to a portfolio of public and private life science companies. Mr. Spiegelman has also served as a member of the board of directors of Myriad Genetics, a molecular diagnostic company, since May 2020. Mr. Spiegelman earned a Bachelor of Arts from Stanford University and a Master of Business Administration from the Stanford Graduate School of Business. We believe Mr. Spiegelman's extensive leadership experience in biotechnology and pharmaceutical companies qualify him to serve on our board of directors.

Board of Directors

Our board of directors currently consists of five members, including Dr. Baldwin, our Chief Executive Officer and Managing Director. Directors are elected at our annual general meeting of shareholders. Under our Constitution, at the close of each annual general meeting one-third of the directors, other than the Managing Director, or if their number is not a multiple of three, then the number nearest to but not more than one-third of the directors must retire. In addition, a director, other than the managing director, must retire from office at the conclusion of the third annual general meeting of shareholders after the director was last elected, even if his or her retirement results in more than one-third of all directors retiring from office. A retiring director remains in office until the end of such shareholder meeting and will be eligible for re-election at that meeting.

The membership of our board of directors is directed by the following requirements as set forth in our Constitution and our Board Charter, as applicable:

- there will be a minimum of three directors and a maximum of 10, and our board of directors may determine the number of directors within those limits;
- the majority of our board of directors should be independent;
- our board of directors has the power to appoint any person to be a director, either to fill a vacancy or as an additional director (provided that the total number of directors does not exceed the maximum number of directors permitted), and any director so appointed will hold office until the end of the next annual general meeting when he or she may be re-elected; and

- our board of directors should, collectively, have the appropriate level of personal qualities, skills, experience and time commitment to properly fulfill its responsibilities.

Our board of directors has delegated responsibility for the management of our businesses to the Chief Executive Officer and Managing Director but remains responsible for overseeing the performance of management. The principal roles and responsibilities of our board of directors include the following:

- review, evaluate, provide input into and approve our business plan;
- monitor senior management's performance and implementation of strategy, and ensure appropriate resources are available;
- review, evaluate and approve and monitor major resource allocations and capital investments, and acquisitions and divestitures;
- review, evaluate, approve and monitor major resource allocations and capital investments, and acquisitions and divestitures;
- review and monitor our financial and operating results;
- review, evaluate and approve the overall corporate organizational structure, the assignment of senior management responsibilities and plans for senior management development and succession;
- review, evaluate and approve compensation strategy as it relates to our senior management; and
- review and ratify systems of risk management and internal compliance and control, codes of conduct and legal compliance.

Our board of directors has established delegated limits of authority, which define the matters that are delegated to management and those that require board of director approval. Under the Corporations Act, at least two of our directors must be resident Australians. None of our non-employee directors have any service contracts with us that provide for benefits upon termination of employment. Under our Board Charter, the board of directors is required to meet at least six times per year.

Board Committees

To assist with the effective discharge of its duties, the board of directors has established an Audit and Risk Committee, a Remuneration Committee and a Nomination Committee. Each committee operates under a charter approved by our board of directors, which sets forth the purposes and responsibilities of the committees as well as qualifications for committee membership, committee structure and operations and committee reporting to the board of directors.

Audit and Risk Committee

The members of our Audit and Risk Committee are Messrs. Lawrence Gozlan, Michael Sistenich and Daniel Spiegelman. Our board of directors has determined that each of Messrs. Gozlan, Sistenich and Spiegelman satisfies the independence requirements under Nasdaq listing standards and Rule 10A-3(b)(1) of the Exchange Act. The chairperson of our Audit and Risk Committee is Mr. Spiegelman. Our board of directors has determined that Mr. Spiegelman is an "audit committee financial expert" within the meaning of SEC regulations. Each member of our Audit and Risk Committee can read and understand fundamental financial statements in accordance with applicable requirements. In arriving at these determinations, our board of directors has examined each member's scope of experience and the nature of his or her employment.

The charter for our Audit and Risk Committee requires the committee to consist of at least three directors, each of whom must be non-employee directors and a majority of which must be independent directors. The chairperson of our Audit and Risk Committee must be an independent director and cannot be the chairperson of our board of directors. The Audit and Risk Committee is required to hold at least one regular meeting per fiscal quarter and must review its charter at least annually.

The role of the Audit and Risk Committee is to advise our board of directors in discharging responsibilities of our board of directors with respect to our financial reporting including accounting standards, internal control integrity and compliance, external audit activities including auditor appointment, independence, terms of engagement and fees and business risk management. Specific responsibilities of our Audit and Risk Committee include:

- reviewing accounting standards and quarterly and annual financial statements prior to referral to the board of directors;
- monitor developments likely to affect financial reporting including legislative pronouncements or disclosure requirements, as they affect both current and future years;
- review any unusual transactions, pending litigation, outstanding claims or contingencies which the management, auditors or legal counsel believe may have a material effect on the financial position or operations and the manner in which these matters are disclosed in financial statements;
- evaluating internal control policies and procedures;
- making recommendations to the board of directors on the appointment, reappointment or replacement of external auditors;
- evaluating the independence and effectiveness of external auditors and preapprove all audit and material non-audit services provided by external auditors;
- reviewing the results of the external audit and assess remedial action taken or proposed in audit reports;
- reviewing all representation letters signed by management to ensure that the information presented is complete and appropriate;
- monitoring risks and establish risk management policies;
- making recommendations to the board of directors regarding proposed changes to our risk management framework; and
- reviewing the schedule of insurance annually.

Remuneration Committee

The members of our Remuneration Committee are Messrs. Gozlan, Sistenich and Spiegelman. The chairperson of our Remuneration Committee is Mr. Sistenich. The objectives of the Remuneration Committee are to link remuneration to the creation of shareholder value, to offer competitive and appropriate remuneration for the business performance delivered and to put into place a remuneration framework that reflects the responsibilities of senior management while being sufficiently competitive to attract and retain high caliber performers. The charter of our Remuneration Committee requires the committee to consist of at least three directors, a majority of whom must be independent. The chairperson of our Remuneration Committee must be an independent director. The Remuneration Committee is required to hold at least one regular meeting each year. Specific responsibilities of our Remuneration Committee include:

- overseeing our remuneration strategy;
- ensuring remuneration policies and practices enable us to attract, motivate and retain a diverse mix of directors and senior management;
- fairly and responsibly remunerating directors and senior management;
- at least annually, reviewing and reporting on diversity of our employee base; and
- seeking information it considers necessary to fulfill its duties, including external advice.

Nomination Committee

The members of our Nomination Committee are Messrs. Gozlan, Sistenich and Spiegelman. The chairperson of our Nomination Committee is Mr. Gozlan. The role of the Nomination Committee is to assist our board of directors by identifying, reviewing and evaluating individuals qualified to become members of our board of directors, reviewing and recommending the nomination of directors and assisting the board of directors with other related tasks. The charter of our Nomination Committee requires the committee to consist of at least three directors, the majority of whom must meet the independence recommendations of the ASX Corporate Governance Council (as well as all applicable laws and regulations) and each of whom must be free of any relationship that, in the opinion of the board of directors, would interfere with his or her exercise of independent judgment. The members of the Nomination Committee will be appointed annually by the board of directors. The Nomination Committee is required to hold at least one regular meeting each year. Specific responsibilities of our Nomination Committee include:

- assisting in identifying, interviewing and recruiting candidates for the board of directors;
- reviewing potential director qualifications;
- preparing a description of the role and capabilities required for a particular role;
- at least annually, presenting to the board of directors a list of individuals recommended for nomination for election to the board of directors at the annual meeting of shareholders;
- planning succession of our directors;
- inducting and coordinating professional development programs for our directors;
- developing and implementing a process for evaluating the performance of the board of directors and its committees;
- managing the succession of our senior management;
- reviewing and making recommendations about changes to the charter of the Nomination Committee as required in the Committee's opinion; and
- annually review its own performance.

Foreign Private Issuer Exemption

We qualify as a "foreign private issuer" as defined in Section 405 of the Securities Act of 1933, as amended. As a foreign private issuer, we are exempt from certain rules under the Exchange Act that impose disclosure requirements as well as procedural requirements for proxy solicitations under Section 14 of the Exchange Act. In addition, the members of our board of directors and senior management are not subject to short-swing profit and insider trading reporting obligations under Section 16 of the Exchange Act. They will, however, be subject to the obligations to report changes in share ownership under Section 13 of the Exchange Act and related SEC rules, to the extent applicable.

The foreign private issuer exemption will also permit us to follow home country corporate governance practices or requirements instead of certain Nasdaq listing requirements, including the following:

- We expect to rely on an exemption from the requirement that our independent directors meet regularly in executive sessions under Nasdaq listing rules. The ASX Listing Rules and the Corporations Act do not require the independent directors of an Australian company to have such executive sessions.
- We expect to rely on an exemption from the quorum requirements applicable to meetings of shareholders under Nasdaq listing rules. In compliance with Australian law, our Constitution provides that three shareholders present, in person or by proxy, attorney or a representative, shall constitute a quorum for a general meeting. Nasdaq listing rules require that an issuer provide for a quorum as specified in its by-laws for any meeting of the holders of ordinary shares, which quorum may not be less than 33 1/3% of the outstanding voting ordinary shares.

- We expect to follow applicable Australian law and the ASX Listing Rules regarding prior shareholder approval in lieu of the requirement prescribed by Nasdaq listing rules that issuers obtain shareholder approval prior to the issuance of securities in connection with certain acquisitions, private placements of securities, or the establishment or amendment of certain stock option, purchase or other compensation plans. Applicable Australian law and the ASX Listing Rules differ from Nasdaq requirements, with the ASX Listing Rules requiring prior shareholder approval for issuance of equity securities in a number of circumstances, including (i) issuance of equity securities exceeding 15% of our issued share capital in any 12-month period (but, in determining the 15% limit, securities issued under certain exceptions to the rule or with shareholder approval are not counted), (ii) subject to certain exceptions, issuance of equity securities to related parties (as defined in the ASX Listing Rules) and (iii) issuances of securities to directors or their associates under an employee incentive plan.
- We expect to rely on an exemption from the requirement to disclose third-party director and director nominee compensation under Nasdaq listing rules. The ASX Listing Rules and the Corporations Act do not have a similar requirement.

These exemptions do not modify the independence requirements for our Audit and Risk Committee, and we intend to comply with the requirements of the Sarbanes-Oxley Act and the Nasdaq listing rules, which require that our Audit and Risk Committee be composed of at least three independent members. Rule 10A-3 under the Exchange Act provides that the Audit and Risk Committee must have direct responsibility for the nomination, compensation and choice of our auditors, as well as control over the performance of their duties, management of complaints made, and selection of consultants. Under Rule 10A-3, if the laws of a foreign private issuer's home country require that any such matter be approved by the board of directors or the shareholders of the Company, the Audit and Risk Committee's responsibilities or powers with respect to such matter may instead be advisory.

We intend to take all actions necessary for us to maintain compliance as a foreign private issuer under the applicable corporate governance requirements of the Sarbanes-Oxley Act, the rules adopted by the SEC and the listing rules of Nasdaq.

Code of Conduct

We have adopted a Code of Conduct applicable to all of our directors, officers and employees. Our Code of Conduct is available on our website at www.opthea.com. We post on our website all disclosures that are required by law or the listing standards of Nasdaq concerning any amendments to, or waivers from, any provision of the Code of Conduct. The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website, and you should not consider it to be a part of, this prospectus.

Family Relationships

There are no family relationships among any of the members of our board of directors and our senior management.

Remuneration

Overview

Our remuneration policy is to align director and senior management objectives with shareholder and business objectives by providing a fixed remuneration component and typically offering long-term incentives based on key performance areas. Our board of directors believes the remuneration policy to be appropriate and effective in its ability to attract and retain the best executives and directors to run and manage the consolidated entity, as well as create goal congruence between directors, executives and shareholders. Our board of directors and the Remuneration Committee are responsible for determining the appropriate remuneration package for our senior management, including our Chief Executive Officer.

Australian executives and directors receive a superannuation guarantee contribution required under Australian law and do not receive any other retirement benefits.

Remuneration of Senior Management

For the fiscal year ended June 30, 2020, the aggregate cash remuneration paid to our senior management was A$942,855.

Our senior management receive fixed compensation and performance-linked remuneration. The level of fixed remuneration is set to provide a base level of compensation which is both appropriate to the applicable position and is competitive in the marketplace. The Remuneration Committee accesses external advice independent of senior management if required. Fixed compensation is comprised of base salary and superannuation contribution and is reviewed every 12 months by the Remuneration Committee.

Performance-linked remuneration consists of short-term and long-term incentives. The objective of short-term incentives is to link the achievement of our operational targets with the remuneration received by our senior management charged with meeting those targets. Total potential short-term incentives are set at a level that we believe provides sufficient incentive to our senior management to achieve the operational targets at a cost to us that is reasonable under the circumstances. Short-term incentives may include cash bonuses based on the extent to which specific targets set at the beginning of each fiscal year are met. The targets consist of a number of key performance indicators covering corporate objectives and individual measures of performance. Individual performance indicators are linked to our development plans. Our Remuneration Committee determines, on an annual basis and after consideration of performance against the key performance indicators, the amount, if any, of short-term incentives payable to our senior management. Payments of short-term incentive bonuses are made in the following reporting period.

We also provide long-term incentives through option grants under our Long Term Incentive Plan. The objective of the Long Term Incentive Plan is to reward our management and key employees in a manner that aligns this element of compensation with the creation of shareholder wealth. Long Term Incentive Plan grants are made to senior management and employees who are able to influence the generation of shareholder wealth and have a direct impact on our performance and development. Option vesting conditions are based on continued service to us.

In making remuneration determinations for our senior management, the Remuneration Committee considers operational contributions by our senior management as well as the following performance indicators: revenue, loss before tax, tax benefit, loss after tax, basic loss per ordinary share, net tangible assets per share and changes in prevailing trading prices of our ordinary shares on the ASX.

Remuneration of Non-Employee Directors

Our non-employee directors receive a fixed fee annually, which is reviewed by our board of directors on an annual basis. Messrs. Sistenich and Gozlan are each entitled to an annual fixed fee of A$65,700 (inclusive of superannuation contributions). Mr. Spiegelman is entitled to an annual fixed fee of US$70,000 (inclusive of superannuation contributions and fees for his service as chairperson of the audit and risk committee), plus an annual fixed fee of US$10,000 for service as Chair of any other committees and US$5,000 for service on any other committee in a non-Chair role. Dr. Levin is entitled to an annual fixed fee of US$75,000 (inclusive of superannuation contributions and fees for his service as chairperson of the board of directors), plus an annual fixed fee of US$5,000 for service on any committee of the board of directors. Unless otherwise noted, the fixed fees cover both service on the board of directors and committees of the board of directors. The remuneration of our non-employee directors is reviewed by our board of directors on an annual basis. Non-employee directors are not provided with retirement benefits apart from statutory superannuation, which is only applicable to Australian resident directors. Non-employee directors are reimbursed for costs directly related to conducting business related to their service on our board of directors.

We implemented a non-executive director share and option plan, or the NED Plan, in 2014. Under the NED Plan, present and future non-executive directors may:

- elect to receive ordinary shares or options to purchase ordinary shares in lieu of receiving some or all of their annual fixed fee;
- be awarded ordinary shares or options to purchase ordinary shares in lieu of additional cash remuneration in respect of services provided to the Company which in the opinion of the board of directors are outside the scope of the ordinary duties of the relevant director; and
- otherwise be awarded ordinary shares or options to purchase ordinary shares as part of the directors' remuneration in addition to any existing cash remuneration paid to directors (if any).

The NED Plan is designed to assist us in preserving our cash for use toward advancing the clinical development of our product candidate and provide our non-employee directors an opportunity to demonstrate their commitment and support for us through sacrificing some or all of their cash fees for ordinary shares or options. The NED Plan also provides us with further flexibility in the design of the directors' remuneration packages and in turn assists us with retaining existing directors and attracting new additional directors with the relevant experience and expertise.

On October 12, 2020, we granted an option to purchase 2,000,000 ordinary shares to each of Messrs. Gozlan and Spiegelman under the NED Plan. The option granted to Mr. Gozlan has an exercise price per ordinary share of A$4.49, and the option granted to Mr. Spiegelman has an exercise price per ordinary share of A$2.29. In addition, our board of directors has approved an option to purchase 3,000,000 ordinary shares for Dr. Levin, which we expect to grant under the NED Plan following approval of such grant by our shareholders at an extraordinary general meeting of shareholders to be convened following the completion of this offering. The exercise price per ordinary share for Dr. Levin's option will be A$2.99. For each of the options described above, 25% of the ordinary shares underlying such option will vest immediately on the applicable grant date, and 25% of the ordinary shares will vest annually thereafter over the following three years.

In addition, if a change in control of our company (as defined in the NED Plan) occurs prior to the grant of Dr. Levin's option upon receipt of shareholder approval, we have agreed to pay Dr. Levin a cash amount equal to the value Dr. Levin would have received had his option been granted prior to the change in control and accelerated in full in connection with the change in control.

For the fiscal year ended June 30, 2020, the aggregate cash remuneration paid to our non-employee directors was A$167,441, including A$2,747 in cash reimbursements.

Employment Agreements with Senior Management

The key provisions of the employment agreements are set out below for each member of our senior management. None of these employment agreements have termination dates. The base salary under the employment agreements may be increased by the board of directors from time to time, including by 3% for the fiscal year ending June 30, 2021.

Officer	Date of Agreement	Base Salary	Termination without Cause	Benefits upon Termination without Cause
Megan Baldwin, Ph.D. *Chief Executive Officer and Managing Director*	April 23, 2014	A$440,000 per year	Not less than three months' notice (if by employee) Not less than three months' notice or payment in lieu of notice period (if by us)	Upon notice of termination by us, any options that have vested or will vest during the notice period will be released; all other options will lapse at the discretion of our board of directors.
Michael Tonroe *Chief Financial Officer and Company Secretary*	May 8, 2014	A$256,844 per year	Not less than three months' notice (if by employee) Not less than three months' notice or payment in lieu of notice period (if by us)	Not applicable.

Upon termination of employment, our senior management are entitled to receive their statutory entitlements of accrued annual and long service leave, together with any superannuation benefits.

Remuneration of Our Non-Employee Directors and Senior Management During the Fiscal Year Ended June 30, 2020

Details of the remuneration of our non-employee directors and senior management for the fiscal year ended June 30, 2020 are set forth below. During the fiscal year ended June 30, 2020, no options to purchase ordinary shares were granted to any of our non-employee directors or senior management.

	Salary/Fees[1]	Short-Term Incentive Cash Bonus[2]	Post-Employment Superannuation	Total
Non-Employee Directors[3]				
Geoffrey Kempler[4]	A$ 90,405	A$ —	A$ 8,589	A$ 98,994
Michael Sistenich	60,000	—	5,700	65,700
Senior Management				
Megan Baldwin, Ph.D.	440,000	100,000	51,300	591,300
Michael Tonroe	256,844	64,211	30,500	351,555

(1) For our non-employee directors, amounts set forth in this column include our reimbursement of expenses incurred in connection with performance of services relating to board service.

(2) Bonuses are paid in the fiscal year following the year in which they were earned.

(3) Messrs. Gozlan and Spiegelman joined our board of directors in July 2020 and September 2020, respectively, and are not presented in the table. Dr. Levin joined our board of directors effective as of October 12, 2020 and is not presented in the table. See "—Remuneration of Non-Employee Directors" for information regarding options granted to each of Messrs. Gozlan and Spiegelman and expected to be granted to Dr. Levin.

(4) Mr. Kempler retired from our board of directors effective as of October 12, 2020.

Details of options held by our non-employee directors and senior management as of June 30, 2020 are set forth below. None of our non-employee directors or senior management exercised any options to purchase ordinary shares during the fiscal year ended June 30, 2020.

	Number of Options	Grant Date	Exercise Price	Percentage Vested[1]	Last Vesting Date	Expiration Date
Non-Employee Directors[2]						
Geoffrey Kempler[3]	2,000,000	3/7/16	A$0.480	100%	3/7/18	3/7/21
	1,500,000	11/29/18	0.855	100	11/29/19	11/29/22
Michael Sistenich	1,000,000	3/7/16	0.480	100	3/7/18	3/7/21
	1,500,000	11/29/18	0.855	100	11/29/19	11/29/22
Senior Management						
Megan Baldwin, Ph.D.	4,000,000	3/7/16	0.480	100	3/7/18	3/7/21
	3,000,000	11/29/18	0.855	100	11/29/19	11/29/22
Michael Tonroe	800,000	3/7/16	0.480	100	1/1/19	1/1/22
	600,000	4/3/19	0.855	100	4/3/20	4/3/23

(1) No options lapsed or were forfeited during the fiscal year ended June 30, 2020.

(2) Messrs. Gozlan and Spiegelman joined our board of directors in July 2020 and September 2020, respectively, and are not presented in the table. Dr. Levin joined our board of directors effective as of October 12, 2020 and is not presented in the table.

(3) Mr. Kempler retired from our board of directors effective as of October 12, 2020.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Other than compensation arrangements which are described under "Management—Remuneration" or as disclosed below, from July 1, 2017 through the date of this prospectus, we did not enter into any transactions or loans with any: (i) enterprises that directly or indirectly, through one or more intermediaries, control, are controlled by or are under common control with us; (ii) associates; (iii) individuals owning, directly or indirectly, an interest in our voting power that gives them significant influence over us, and close members of any such individual's family; (iv) key management personnel and close members of such individuals' families; or (v) enterprises in which a substantial interest in our voting power is owned, directly or indirectly, by any person described in (iii) or (iv) or over which such person is able to exercise significant influence.

Ordinary Share Private Financing

In December 2019, we issued and sold to certain institutional investors, including Regal Funds Management Pty Ltd., approximately 18.9 million ordinary shares at a purchase price of A$2.65 per share for an aggregate purchase price of A$50.0 million. Regal Funds Management Pty Ltd., a holder of over 10% of our outstanding ordinary shares as of June 30, 2020, purchased approximately 2.8 million shares for A$7.5 million.

Director and Senior Management Compensation

See "Management—Remuneration" for information regarding compensation of our senior management and directors.

Indemnification Agreements

Our Constitution provides that, except to the extent prohibited by law including under the Corporations Act and, to the extent that an officer is not otherwise indemnified by us pursuant to an indemnity, we will indemnify every person who is or has been an officer of the company against any liability (other than legal costs that are unreasonable) incurred by that person as an officer. This includes any liability incurred by that person in their capacity as an officer of our subsidiary where we requested that person to accept that appointment.

We have entered into Deeds of Indemnity, Insurance and Access, or Indemnity Deeds, with Megan Baldwin, Ph.D., Michael Tonroe, Lawrence Gozlan, Jeremy Levin, Michael Sistenich and Daniel Spiegelman, each a non-employee director, or executive officer. Under the Indemnity Deeds, we have agreed to indemnify (to the maximum extent permitted under Australian law and our Constitution, subject to certain specified exceptions) each director and executive officer against all liabilities incurred in their capacity as our or our subsidiaries' director or officer and any and all costs and expenses relating to such a claim or to any notified event incurred by such director or executive officer, including costs and expenses reasonably and necessarily incurred to mitigate any liability for such a claim or any claim which may arise from such a notified event. The Indemnity Deeds provide that the indemnities are unlimited as to amount, continuous and irrevocable.

Separately, we have obtained insurance for our directors and executive officers, as required by the Indemnity Deeds.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling us pursuant to the foregoing provisions, we have been informed that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Related Person Transaction Policy

We comply with Australian law and the rules and regulations of the ASX regarding approval of transactions with related parties. Prior to the closing of this offering, we intend to adopt a related person transaction policy

that sets forth our procedures for the identification, review, consideration and approval or ratification of related person transactions. The policy will become effective upon the execution of the underwriting agreement for this offering. For purposes of our policy, a related person transaction is a transaction, arrangement or similar contractual relationship, or any series of similar transactions, arrangements or relationships, in which we and any related person are, were or will be participants and the amount involved in the transaction exceeds $120,000, with the exception of usual transactions concluded under normal conditions. A related person is any member of our board of directors, our senior management or any beneficial owner of more than 5% of any class of our ordinary shares, including any of their immediate family members and any entity owned or controlled by such persons.

Under the policy, if a transaction has been identified as a related person transaction, including any transaction that was not a related person transaction when originally consummated or any transaction that was not initially identified as a related person transaction prior to consummation, our senior management must present information regarding the related person transaction to the board of directors for review, consideration and approval or ratification. The presentation must include a description of, among other things, the material facts, the interests, direct and indirect, of the related persons, the benefits to us of the transaction and whether the transaction is on terms that are comparable to the terms available to or from, as the case may be, an unrelated third party or to or from employees generally. Under the policy, we will collect information that we deem reasonably necessary from each member of our board of directors and, to the extent feasible, significant shareholder to enable us to identify any existing or potential related-person transactions and to effectuate the terms of the policy.

All of the transactions described above were entered into prior to the adoption of the written policy, but our board of directors evaluated and approved all transactions that were considered to be related party transactions under Australian law and the rules and regulations of the ASX at the time at which they were consummated.

PRINCIPAL SHAREHOLDERS

The following table sets forth information with respect to the beneficial ownership of our ordinary shares as of September 30, 2020, for:

- each person or group of affiliated persons known by us to beneficially own more than 5% of our ordinary shares;
- each member of our senior management;
- each of our directors; and
- all of our directors and senior management as a group.

To our knowledge, as of September 30, 2020, approximately 371,334 ordinary shares, or 0.14% of our ordinary shares, were held of record by five residents of the United States.

We have determined beneficial ownership in accordance with the rules and regulations of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Except as indicated by the footnotes below, we believe, based on information furnished to us, that the persons and entities named in the table below have sole voting and sole investment power with respect to all shares that they beneficially own.

Applicable percentage ownership before the offering is based on 269,157,769 ordinary shares outstanding as of September 30, 2020. Applicable percentage ownership after the offering is based on ordinary shares outstanding immediately after the closing of this offering (after giving effect to the sale and issuance of 8,563,300 ADSs representing 68,506,400 ordinary shares at an ADS-to-ordinary share ratio of 1-to-8), assuming no exercise by the underwriters of their option to purchase additional ADSs and no exercise of any pre-funded warrants offered and sold in this offering. In computing the number of shares beneficially owned by a person or entity and the percentage ownership of such person or entity, we deemed to be outstanding all shares subject to options and warrants held by the person or entity that are currently exercisable, or exercisable within 60 days of September 30, 2020. However, except as described above, we did not deem such shares outstanding for the purpose of computing the percentage ownership of any other person or entity. The information contained in the following table is not necessarily indicative of beneficial ownership for any other purpose, and the inclusion of any shares in the table does not constitute an admission of beneficial ownership of those shares. Each of our shareholders is entitled to one vote per ordinary share. None of the holders of our shares will have different voting rights from other holders of shares after the closing of this offering. We are not aware of any arrangement that may, at a subsequent date, result in a change of control of our company. For further information regarding options to purchase ordinary shares held by our directors and senior management, see “Management—Remuneration.”

Unless otherwise indicated, the address of each beneficial owner listed below is c/o Opthea Limited, Suite 0403, Level 4, 650 Chapel Street, South Yarra, VIC 3141, Australia.

	Shares Beneficially Owned before this Offering		Shares Beneficially Owned after this Offering	
Name of Beneficial Owner	**Number**	**Percent**	**Number**	**Percent**
Principal Shareholders				
Funds affiliated with Regal Funds Management Pty Ltd.[1]	28,726,324	10.7%	28,726,324	8.5%
Funds affiliated with Baker Bros. Advisors L.P.[2]	26,526,759	9.9	34,020,359	9.9
Entities affiliated with the Liberman Family[3]	19,228,128	7.1	19,228,128	5.7
KiFin Ltd.[4]	16,275,227	6.0	16,275,227	4.8
Directors, Director Nominees and Senior Management				
Megan Baldwin, Ph.D.[5]	7,987,723	2.9	7,987,723	2.3
Michael Tonroe[6]	1,400,000	*	1,400,000	*
Geoffrey Kempler[7]	4,400,960	1.6	4,400,960	1.3
Lawrence Gozlan[8]	500,000	*	500,000	*
Jeremy Levin, DPhil, MB BChir[9]	—	*	—	*
Michael Sistenich[10]	3,020,178	1.1	3,020,178	*
Daniel Spiegelman[11]	500,000	*	500,000	*
All directors and senior management as a group (seven persons)[12]	17,808,861	6.3%	17,808,861	5.0%

* Represents beneficial ownership of less than 1%.

(1) Consists of 28,726,324 ordinary shares held by funds affiliated with Regal Funds Management Pty Ltd., referred to together as the Regal Funds. Regal Funds Management Pty Ltd. is the investment manager for each of such funds holding our ordinary shares. Philip King and Craig Collie are the Chief Investment Officer and portfolio manager, respectively, of Regal Funds Management Pty Ltd. and, as such, they may be deemed to have voting and dispositive power with respect to the ordinary shares held by the affiliated funds. Philip King and Craig Collie disclaim beneficial ownership of the ordinary shares held by the Regal Funds except to the extent of their pecuniary interest. The address for Regal Funds Management Pty Ltd. is Level 47, Gateway, 1 Macquarie Place, Sydney, NSW 2000, Australia.

(2) Consists of (i) 2,166,666 ordinary shares held by 667, L.P., (ii) 24,360,093 ordinary shares held by Baker Brothers Life Sciences, L.P., (iii) 551,720 ordinary shares underlying ADSs represented by pre-funded warrants purchased by 667, L.P. in this offering and (iv) 6,941,880 ordinary shares underlying ADSs represented by pre-funded warrants purchased by Baker Brother Life Sciences, L.P. in this offering. The pre-funded warrants may not be exercised if, upon giving effect to such exercise, the aggregate number of ordinary shares beneficially owned by the holders and their respective affiliates and any persons who are members of a group (as defined in Section 13(d) of the Exchange Act) with such affiliates exceeds 9.99% of the number of ordinary shares (including ordinary shares underlying ADSs) outstanding immediately after giving effect to the exercise. We refer to 667, L.P. and Baker Brothers Life Sciences, L.P. together as the Baker Funds. Baker Bros. Advisors LP is the manager and investment advisor of the Baker Funds and has sole voting and dispositive power with respect to the ordinary shares held by the Baker Funds. Baker Bros. Advisors (GP) LLC is the sole general partner of Baker Bros. Advisors LP. The managing members of Baker Bros. Advisors (GP) LLC are Julian C. Baker and Felix J. Baker and, as such, they may be deemed to have voting and dispositive power with respect to the ordinary shares held by the Baker Funds. Julian C. Baker and Felix J. Baker disclaim beneficial ownership of the ordinary shares held by the Baker Funds except to the extent of their pecuniary interest therein. The address for Baker Bros. Advisors LP, Baker Bros. Advisors (GP) LLC, Julian C. Baker, Felix J. Baker and the Baker Funds is 860 Washington Street, 3rd Floor, New York, New York 10014.

(3) Consists of 19,228,128 ordinary shares held by entities affiliated with the Liberman Family, including 13,520,540 ordinary shares held by Jagen Pty Ltd., for which Lawrence Gozlan, a member of our board of directors, serves as founder and Chief Investment Officer. Bori Liberman, Helen Liberman, Laini Liberman,

Justin Liberman and Nic Liberman share voting and dispositive power with respect to the ordinary shares held by the entities affiliated with the Liberman Family. The address for the entities affiliated with the Liberman Family is 8 Oxford Street, South Yarra, VIC 3141, Australia.

(4) Consists of 16,275,227 ordinary shares held by KiFin Ltd. KiFin Ltd. is managed by its sole director, Guardian Corporate Services Limited, or GCSL. The directors of GCSL are Ritchie Linden, Conrad Rademeyer, Gregoire Lartigue, Abacus Managers Limited, Abacus Management Limited and Abacus Corporate Services Limited. Meade Malone and Rajiv Balleram are the two directors of the three Abacus entities acting as corporate directors of GCSL. The directors of GCSL have shared and equal voting rights with respect to decisions of GCSL, as sole director of KiFin Ltd., and as such may be deemed to have shared voting and dispositive power with respect to the ordinary shares held by KiFin Ltd. Each director of GCSL disclaims beneficial ownership of the ordinary shares held by KiFin Ltd. except to the extent of their pecuniary interest. The address for KiFin Ltd. is Geneva Place, 333 Waterfront Drive, Road Town, Tortola, British Virgin Islands.

(5) Consists of (i) 987,723 ordinary shares beneficially owned and (ii) 7,000,000 ordinary shares issuable upon the exercise of options that are exercisable within 60 days of September 30, 2020.

(6) Consists of 1,400,000 ordinary shares issuable upon the exercise of options that are exercisable within 60 days of September 30, 2020.

(7) Consists of (i) 900,960 ordinary shares directly held by Mr. Kempler and (ii) 3,500,000 ordinary shares issuable upon the exercise of options that are exercisable within 60 days of September 30, 2020. Mr. Kempler retired from our board of directors effective as of October 12, 2020.

(8) Mr. Gozlan joined our board of directors in July 2020. Consists of 500,000 ordinary shares that will vest and become issuable upon the exercise of an option within 60 days of September 30, 2020, which option was granted on October 12, 2020.

(9) Dr. Levin joined our board of directors as Chairperson effective as of October 12, 2020.

(10) Consists of (i) 520,178 ordinary shares directly held by Mr. Sistenich and (ii) 2,500,000 ordinary shares issuable upon the exercise of options that are exercisable within 60 days of September 30, 2020.

(11) Mr. Spiegelman joined our board of directors in September 2020. Consists of 500,000 ordinary shares that will vest and become issuable upon the exercise of an option within 60 days of September 30, 2020, which option was granted on October 12, 2020.

(12) Consists of (i) 2,408,861 ordinary shares beneficially owned and (ii) 15,400,000 ordinary shares issuable upon the exercise of options that are exercisable within 60 days of September 30, 2020.

DESCRIPTION OF SHARE CAPITAL

General

The following description of our ordinary shares is only a summary. We encourage you to read our Constitution, which is included as an exhibit to this registration statement, of which this prospectus forms a part.

We are a public company limited by shares incorporated under the Corporations Act by the Australian Securities and Investments Commission, or ASIC. Our corporate affairs are principally governed by our Constitution, the Corporations Act and the Australian Securities Exchange, or ASX, Listing Rules. Our ordinary shares trade on the ASX.

The Australian law applicable to our Constitution is not significantly different than a U.S. company's charter documents except we do not have a limit on our authorized share capital, the concept of par value is not recognized under Australian law and as further discussed under "—Our Constitution."

Subject to any restrictions on the issue of securities in our Constitution, the Corporations Act and the ASX Listing Rules and any other applicable law, we may from time to time issue shares and grant options on any terms, with the rights and restrictions and for the consideration that our board of directors determine. The rights and restrictions attaching to ordinary shares are derived through a combination of our Constitution, the common law applicable in Australia, the ASX Listing Rules, the Corporations Act and other applicable law. A general summary of some of the rights and restrictions attaching to our ordinary shares are summarized below. Each ordinary shareholder is entitled to receive notice of, and to be present, vote and speak at, general meetings.

Changes to Our Share Capital

As of June 30, 2020, we had (i) 269,157,769 ordinary shares outstanding and (ii) outstanding options to purchase 18,044,000 ordinary shares at a weighted-average exercise price of A$0.68 per share.

From July 1, 2017, through the date of this prospectus, the following events have changed the number of our issued and outstanding ordinary shares:

- In December 2019, we issued 18,867,930 ordinary shares to institutional shareholders at an issue price of A$2.65 per share.
- We issued the following ordinary shares upon the exercise of options over the following periods:
    - from July 1, 2017 through June 30, 2018, 2,063,518 ordinary shares upon the exercise of options granted in connection with capital raise transactions;
    - from July 1, 2018 through June 30, 2019, 46,776,951 ordinary shares upon the exercise of options granted in connection with capital raise transactions; and
    - from July 1, 2019 through June 30, 2020, 875,000 ordinary shares upon the exercise of options granted to officers and employees.

On October 12, 2020, we granted an option to purchase 2,000,000 ordinary shares to each of Messrs. Gozlan and Spiegelman under the NED Plan. The option granted to Mr. Gozlan has an exercise price per ordinary share of A$4.49, and the option granted to Mr. Spiegelman has an exercise price per ordinary share of A$2.29. We also expect to grant an option to purchase 3,000,000 ordinary shares to Dr. Levin under the NED Plan upon approval by our shareholders at a future meeting of shareholders following the closing of this offering (see "Management—Remuneration of Non-Employee Directors").

Our Constitution

Our Constitution is similar in nature to the bylaws of a U.S. corporation. It does not provide for or prescribe any specific objectives or purposes of our company. Our Constitution is subject to the terms of the Corporations

Act. It may be amended or repealed and replaced by special resolution of shareholders, which is a resolution passed by at least 75% of the votes cast by shareholders (in person or by proxy) entitled to vote on the resolution.

Under Australian law, a company has the legal capacity and powers of an individual both within and outside Australia. The material provisions of our Constitution are summarized below. This summary is not intended to be complete nor to constitute a definitive statement of the rights and liabilities of our shareholders, and is qualified in its entirety by reference to the complete text of our Constitution, a copy of which is on file with the Securities and Exchange Commission.

Interested Directors

A director or that director's alternate who has a material personal interest in a matter that is being considered at a directors' meeting must not be present while the matter is being considered at the meeting or vote in respect of that matter according to our Constitution unless permitted to do so by the Corporations Act, in which case such director may (i) be counted in determining whether or not a quorum is present at any meeting of directors considering that contract or arrangement or proposed contract or arrangement; (ii) sign or countersign any document relating to that contract or arrangement or proposed contract or arrangement; and (iii) vote in respect of, or in respect of any matter arising out of, the contract or arrangement or proposed contract or arrangement.

Unless a relevant exception applies, the Corporations Act requires our directors to provide disclosure of any material personal interest, and prohibits directors from voting on matters in which they have a material personal interest and from being present at the meeting while the matter is being considered, unless directors who do not have a material personal interest in the relevant matter have passed a resolution that identifies the director, the nature and extent of the director's interest in the matter and its relation to our affairs and states that those directors are satisfied that the interest should not disqualify the director from voting or being present. In addition, the Corporations Act and the ASX Listing Rules may require shareholder approval of any provision of related party benefits to our directors, unless a relevant exception applies.

Directors' Compensation

Our non-employee directors are paid remuneration for their services as directors. Subject to the ASX Listing Rules, non-employee directors as a whole may be paid or provided remuneration for their services a total amount or value not to exceed $500,000 per annum. Subject to the ASX Listing Rules, the aggregate, capped sum for non-employee directors' remuneration is to be divided among the directors in such proportion as the directors themselves agree and in accordance with our Constitution. The capped sum remuneration for non-employee directors may not be increased except at a general meeting of shareholders and the particulars of the proposed increase are required to have been provided to shareholders in the notice convening the meeting. In addition, our board of directors may fix the remuneration of each executive director, which may comprise salary or commission on or participation in our profits (or comprising a combination of each) as our directors determine.

Fees payable to our non-employee directors must be by way of a fixed sum and not by way of a commission on or a percentage of profits or operating revenue. Remuneration paid to our executive directors must also not include a commission or percentage of operating revenue.

Pursuant to our Constitution, any director who performs extra services or makes any special exertions, whether in going or residing abroad or otherwise for any of the purposes of the Company, that director may be paid an additional sum for those services and exertions.

In addition to other remuneration provided in our Constitution, all of our directors are entitled to be paid by us for all travelling and other expenses properly incurred by the directors in attending general meetings, board meetings, committee meetings or otherwise in connection with our business.

In addition, in accordance with our Constitution, a director may be paid a retirement benefit as determined by our board of directors subject to the requirements of the Corporations Act.

Borrowing Powers Exercisable by Directors

Pursuant to our Constitution, the management and control of our business affairs are vested in our board of directors. Our board of directors has the power to raise or borrow money or obtain other financial accommodation for the purposes of the Company, and may grant security for the repayment of that sum or sums or the payment, performance or fulfilment of any debts, liabilities, contracts or obligations incurred or undertaken by the Company in any manner and upon any terms and conditions as our board of directors deems appropriate.

Retirement of Directors

Pursuant to our Constitution, one-third of our directors, other than the managing director, must retire from office at every annual general meeting. If the number of directors is not a multiple of three, then the number nearest, to but not exceeding, one-third must retire from office. The directors who retire in this manner are required to be the directors or director longest in office since last being elected. A director, other than the managing director, must retire from office at the conclusion of the third annual general meeting after which the director was elected. A retiring director remains in office until the end of the meeting and will be eligible for re-election at the meeting.

Rights and Restrictions on Classes of Shares

The rights attaching to our ordinary shares are detailed in our Constitution. Our Constitution provides that, subject to the Corporations Act, the ASX Listing Rules and our Constitution, our directors may issue shares with preferential, deferred or special rights, privileges or conditions or with any restrictions, whether in relation to dividends, voting, return of share capital, or otherwise as our board of directors may determine. Subject to the Corporations Act, the ASX Listing Rules and our Constitution (see "—Change of Control"), we may issue further shares on such terms and conditions as our board of directors resolve. We may only issue preference shares if the rights attaching to the preference shares relating to repayment of capital, participation in surplus assets and profits, cumulative and non-cumulative dividends, voting and priority of payment of capital and dividends in respect of other shares (including ordinary shares) are set out in our constitution or otherwise approved by special resolution passed at a general meeting. Our outstanding share capital consists of only one class of ordinary shares.

Dividend Rights

Under the Corporations Act, a company must not pay a dividend unless (a) the company's assets exceed its liabilities immediately before the dividend is declared and the excess is sufficient for the payment of the dividend; (b) the payment of the dividend is fair and reasonable to the company's shareholders as a whole; and (c) the payment of the dividend does not materially prejudice the company's ability to pay its creditors. Subject to this requirement, our board of directors may from time to time determine to pay and declare dividends to shareholders. All dividends unclaimed for one year after the time for payment has passed may be invested or otherwise made use of by our board of directors for our benefit until claimed or until dealt with under any law relating to unclaimed moneys.

Voting Rights

Under our Constitution, and subject to any voting exclusions imposed under the ASX Listing Rules (which typically exclude parties from voting on resolutions in which they have an interest), the rights and restrictions attaching to a class of shares, each shareholder has one vote on a show of hands at a meeting of the shareholders unless a poll is demanded under the Constitution or the Corporations Act. On a poll vote, each shareholder shall have one vote for each fully paid share and a fractional vote for each share held by that shareholder that is not

fully paid, such fraction being equivalent to the proportion of the amount that has been paid to such date on that share. Shareholders may vote in person or by proxy, attorney or representative. Under Australian law, shareholders of a public company are generally not permitted to approve corporate matters by written consent. Our Constitution does not provide for cumulative voting.

Under Australian law, an ordinary resolution is passed if a majority of the votes cast on the resolution (in person or by proxy) by members entitled to vote on the resolution are in favor of the resolution. Under Australian law, a special resolution is passed if at least 75% of the votes cast on the resolution (in person or by proxy) are in favor of the resolution.

ADS holders may not directly vote at a meeting of the shareholders but may instruct the depositary to vote the number of deposited ordinary shares their ADSs represent.

Right to Share in Our Profits

Pursuant to our Constitution, our shareholders are entitled to participate in our profits only by payment of dividends. Our board of directors may from time to time determine to pay dividends to the shareholders. However, any such dividend may only be payable in accordance with the requirements set out in the Corporations Act described above.

Rights to Share in the Surplus in the Event of Winding Up

Our Constitution provides for the right of shareholders to participate in a surplus in the event of our winding up, subject to the rights attaching to a class of shares,.

No Redemption Provision for Ordinary Shares

There are no redemption provisions in our Constitution in relation to ordinary shares. Under our Constitution, shares may be issued and allotted, which are liable to be redeemed. Under the Corporations Act, redeemable preference shares may only be redeemed if those preference shares are fully paid-up and payment in satisfaction of redemption is out of profits or the proceeds of a new issue of shares made for the purposes of the redemption.

Variation or Cancellation of Share Rights

Subject to the Corporations Act, the ASX Listing Rules and the terms of issue of shares of that class, the rights and privileges attached to shares in a class of shares may only be varied or cancelled by a special resolution, together with either:

- a special resolution passed at a meeting of members holding shares in the class; or
- the written consent of members with at least 75% of the shares in the class.

Directors May Make Calls

Our Constitution provides that subject to compliance with the Corporations Act and the terms on which partly paid shares are issued, directors may make calls on the holders of the shares for any money unpaid on them.

General Meetings of Shareholders

General meetings of shareholders may be called by our board of directors. Except as permitted under the Corporations Act, shareholders may not convene a meeting. The Corporations Act requires the directors to call and arrange to hold a general meeting on the request of shareholders with at least 5% of the votes that may be

cast at a general meeting. Notice of the proposed meeting of our shareholders is required at least 28 days prior to such meeting under the Corporations Act.

Foreign Ownership Regulation

Our Constitution does not impose specific limitations on the rights of non-residents to own securities. However, acquisitions and proposed acquisitions of securities in Australian companies may be subject to review and approval by the Australian Federal Treasurer under the Foreign Acquisitions and Takeovers Act 1975 (Cth), or the FATA, which generally applies to acquisitions or proposed acquisitions:

- by a foreign person (as defined in the FATA) or associated foreign persons that would result in such persons having an interest in 20% or more of the issued shares of, or control of 20% or more of the voting power in, an Australian company; and
- by non-associated foreign persons that would result in such foreign persons having an aggregate interest in 40% or more of the issued shares of, or control of 40% or more of the voting power in, an Australian company, where the Australian company is valued above the monetary threshold prescribed by FATA.

Due to the impacts of the COVID-19 pandemic, the monetary thresholds for foreign investment proposals covered by the FATA and its associated regulations have been reduced to zero. This regime may revert in the future to the previous regime, which, in general terms, provided that in respect of proposals for investment in non-sensitive sectors, no such review or approval under the FATA is required if the foreign acquirer is a U.S. entity or an entity from certain other countries and the value of the Australian target is less than A$1,192 million.

The Australian Federal Treasurer may prevent a proposed acquisition in the above categories or impose conditions on such acquisition if the Treasurer is satisfied that the acquisition would be contrary to the national interest. If a foreign person acquires shares or an interest in shares in an Australian company in contravention of the FATA, the Australian Federal Treasurer may make a range of orders including an order the divestiture of such person's shares or interest in shares in that Australian company.

Ownership Threshold

There are no specific provisions in our Constitution that require a shareholder to disclose ownership above a certain threshold. The Corporations Act, however, requires a shareholder to notify us and the ASX once it, together with its associates, acquires a 5% interest in our ordinary shares, at which point the shareholder will be considered to be a "substantial" shareholder. Further, once a shareholder owns (alone or together with associates) a 5% interest in us, such shareholder must notify us and the ASX of any increase or decrease of 1% or more in its holding of our ordinary shares, and must also notify us and the ASX on its ceasing to be a "substantial" shareholder.

Issues of Shares and Change in Capital

Subject to our Constitution, the Corporations Act, the ASX Listing Rules and any other applicable law, we may at any time issue shares and give any person a call or option over any shares on any terms, with preferential, deferred or other special rights, privileges or conditions or with restrictions and for the consideration and other terms that the directors determine. We may only issue preference shares if the rights attaching to the preference shares relating to repayment of capital, participation in surplus assets and profits, cumulative and non-cumulative dividends, voting and priority of payment of capital and dividends in respect of other shares (including ordinary shares) are set out in our Constitution or otherwise approved by special resolution passed at a general meeting of shareholders.

Subject to the requirements of our Constitution, the Corporations Act, the ASX Listing Rules and any other applicable law, including relevant shareholder approvals, we may consolidate or divide our share capital into a larger or smaller number by resolution, reduce our share capital in any manner (provided that the reduction is fair

and reasonable to our shareholders as a whole, does not materially prejudice our ability to pay creditors and obtains the necessary shareholder approval) or buy back our ordinary shares whether under an equal access buy-back or on a selective basis.

Change of Control

Takeovers of listed Australian public companies, including us, are regulated by the Corporations Act, which prohibits the acquisition of a "relevant interest" in issued voting shares in a listed company if the acquisition will lead to that person's or someone else's voting power in our company increasing from 20% or below to more than 20% or increasing from a starting point that is above 20% and below 90%, which we refer to as the Takeovers Prohibition, subject to a range of exceptions.

Generally, a person will have a relevant interest in securities if the person:

- is the holder of the securities (other than if the person holds those securities as a bare trustee);
- has power to exercise, or control the exercise of, a right to vote attached to the securities; or
- has the power to dispose of, or control the exercise of a power to dispose of, the securities.

If, at a particular time,

- a person has a relevant interest in issued securities; and
- the person (whether before or after acquiring the relevant interest) has:
    - entered or enters into an agreement with another person with respect to the securities;
    - given or gives another person an enforceable right, or has been or is given an enforceable right by another person, in relation to the securities (whether the right is enforceable presently or in the future and whether or not on the fulfillment of a condition); or
    - granted or grants an option to, or has been or is granted an option by, another person with respect to the securities; and
- the other person would have a relevant interest in the securities if the agreement were performed, the right enforced or the option exercised,

then the other person is taken to have a relevant interest in the relevant securities.

There are a number of exceptions to the Takeover Prohibition. In general terms, some of the more significant exceptions include:

- when the acquisition results from the acceptance of an offer under a formal takeover bid;
- when the acquisition is conducted on market by or on behalf of the bidder during the bid period for a full takeover bid that is unconditional or only conditional on certain 'prescribed' matters set out in the Corporations Act;
- when the acquisition has been previously approved by our shareholders by resolution passed at general meeting;
- an acquisition by a person if, throughout the six months before the acquisition, that person or any other person has had voting power in our company of at least 19% and, as a result of the acquisition, none of the relevant persons would have voting power in our company more than three percentage points higher than they had six months before the acquisition;
- when the acquisition results from the issue of securities under a rights issue;
- when the acquisition results from the issue of securities under a dividend reinvestment scheme or bonus share plan;

- when the acquisition results from the issue of securities under certain underwriting arrangements;
- when the acquisition results from the issue of securities through a will or through operation of law;
- an acquisition that arises through the acquisition of a relevant interest in another listed company which is listed on a prescribed financial market or a financial market approved by ASIC;
- an acquisition arising from an auction of forfeited shares conducted on-market; or
- an acquisition arising through a compromise, arrangement, liquidation or buy-back.

Breaches of the takeovers provisions of the Corporations Act are criminal offenses. ASIC and the Australian Takeover Panel have a wide range of powers relating to breaches of takeover provisions, including the ability to make orders, canceling contracts, freezing transfers of, and rights attached to, securities and forcing a party to dispose of securities. There are certain defenses to breaches of the Takeover Prohibition provided in the Corporations Act.

Access to and Inspection of Documents

Inspection of our records is governed by our Constitution and the Corporations Act. Any member of the Company has the right to inspect or obtain copies of our share register on the payment of a prescribed fee. Our books containing the minutes of general meetings will be kept at our registered office and will be open to inspection of members at all times when the office is required to be open to the public. Other corporate records, including minutes of directors' meetings, financial records and other documents, are not open for inspection by shareholders (who are not directors). Where a shareholder is acting in good faith and an inspection is deemed to be made for a proper purpose, a shareholder may apply to the court to make an order for inspection of our books.

Legal Name; Formation; Registered Office

We were incorporated under the laws of Australia in 1984 under the name Circadian Technologies Limited. In 1985, we completed an initial public offering of our ordinary shares and the listing of our ordinary shares on the Australian Securities Exchange, or the ASX. In December 2015, we changed the name of our company to Opthea Limited. Our headquarters and registered offices are located at Suite 0403, Level 4, 650 Chapel Street, South Yarra, VIC 3141, Australia. Our agent for service of process in the United States is Corporation Service Company, located at 1180 Avenue of the Americas, Suite 210, New York, New York 10036. Our website address is www.opthea.com. The reference to our website is an inactive textual reference only and information contained in, or that can be assessed through, our website is not part of this prospectus.

Listing

The ADSs have been approved for listing on the Nasdaq Global Select Market under the symbol "OPT." Our ordinary shares are listed on the ASX under the symbol "OPT."

Transfer Agent and Registrar

Upon the closing of this offering, the transfer agent and registrar for the ADSs will be National Australia Bank Ltd. Computershare Investor Services Pty Limited is our transfer agent and registrar for our ordinary shares and currently maintains our share register for our ordinary shares. The share register reflects only record owners of our ordinary shares. Holders of the ADSs will not be treated as one of our shareholders and their names will therefore not be entered in our share register. The depositary, the custodian or their nominees will be the holder of the shares underlying the ADSs. Holders of the ADSs have a right to receive the ordinary shares underlying their ADSs. See "Description of American Depositary Shares."

DESCRIPTION OF AMERICAN DEPOSITARY SHARES

American Depositary Shares

The Bank of New York Mellon, as depositary, will register and deliver American Depositary Shares, or ADSs. Each ADS will represent eight ordinary Shares (or a right to receive eight ordinary shares) deposited with HSBC Bank Australia Limited, as custodian for the depositary in Australia. Each ADS will also represent any other securities, cash or other property that may be held by the depositary. The deposited shares together with any other securities, cash or other property held by the depositary are referred to as the deposited securities. The depositary's office at which the ADSs will be administered and its principal executive office are located at 240 Greenwich Street, New York, New York 10286.

In June 2011, we sponsored a Level I American Depositary Receipt, or ADR, facility and filed a registration statement on Form F-6 with the SEC to issue ADSs to requesting holders of our ordinary shares, which ADSs could be traded on the over-the-counter market in the United States. Under this Level I facility, ADSs were issued under an existing deposit agreement with The Bank of New York Mellon as depositary. In connection with this offering, we are amending the terms of the existing ADR facility and the related deposit agreement, including to change the ADS-to-ordinary share ratio from 1-to-5 to 1-to-8, which will take effect prior to the execution of the underwriting agreement for this offering, and have filed a new registration statement on Form F-6 (File No. 333-249327) relating to the existing ADSs and the ADSs offered and sold in this offering as well as the amended and restated deposit agreement.

You may hold ADSs either (A) directly (i) by having an ADR, which is a certificate evidencing a specific number of ADSs, registered in your name, or (ii) by having uncertificated ADSs registered in your name, or (B) indirectly by holding a security entitlement in ADSs through your broker or other financial institution that is a direct or indirect participant in The Depository Trust Company, or DTC. If you hold ADSs directly, you are a registered ADS holder, or an ADS holder. This description assumes you are an ADS holder. If you hold the ADSs indirectly, you must rely on the procedures of your broker or other financial institution to assert the rights of ADS holders described in this section. You should consult with your broker or financial institution to find out what those procedures are.

Registered holders of uncertificated ADSs will receive statements from the depositary confirming their holdings.

As an ADS holder, we will not treat you as one of our shareholders and you will not have shareholder rights. Australian law governs shareholder rights. The depositary will be the holder of the shares underlying your ADSs. As a registered holder of ADSs, you will have ADS holder rights. The amended and restated deposit agreement among us, the depositary, ADS holders and all other persons indirectly or beneficially holding ADSs sets out ADS holder rights as well as the rights and obligations of the depositary. New York law governs the deposit agreement and the ADSs.

The following is a summary of the material provisions of the deposit agreement. For more complete information, you should read the entire deposit agreement and the form of ADR. For directions on how to obtain copies of those documents, see "Where You Can Find More Information."

Dividends and Other Distributions

How will you receive dividends and other distributions on the shares?

The depositary has agreed to pay or distribute to ADS holders the cash dividends or other distributions it or the custodian receives on shares or other deposited securities, upon payment or deduction of its fees and expenses. You will receive these distributions in proportion to the number of shares your ADSs represent.

Cash. After completion of this offering, we do not expect to declare or pay any cash dividends or cash distributions on our ordinary shares for the foreseeable future. The depositary will convert any cash dividend or

other cash distribution we pay on the shares into U.S. dollars, if it can do so on a reasonable basis and can transfer the U.S. dollars to the United States. If that is not possible or if any government approval is needed and cannot be obtained, the deposit agreement allows the depositary to distribute the foreign currency only to those ADS holders to whom it is possible to do so. It will hold the foreign currency it cannot convert for the account of the ADS holders who have not been paid. It will not invest the foreign currency and it will not be liable for any interest.

Before making a distribution, any withholding taxes, or other governmental charges that must be paid will be deducted. See "Material United States Federal Income and Australian Tax Considerations." The depositary will distribute only whole U.S. dollars and cents and will round fractional cents to the nearest whole cent. *If the exchange rates fluctuate during a time when the depositary cannot convert the foreign currency, you may lose some of the value of the distribution.*

Shares. The depositary may distribute additional ADSs representing any shares we distribute as a dividend or free distribution. The depositary will only distribute whole ADSs. It will sell shares which would require it to deliver a fraction of an ADS (or ADSs representing those shares) and distribute the net proceeds in the same way as it does with cash. If the depositary does not distribute additional ADSs, the outstanding ADSs will also represent the new shares. The depositary may sell a portion of the distributed shares (or ADSs representing those shares) sufficient to pay its fees and expenses in connection with that distribution.

Rights to purchase additional shares. If we offer holders of our securities any rights to subscribe for additional shares or any other rights, the depositary may (i) exercise those rights on behalf of ADS holders, (ii) distribute those rights to ADS holders or (iii) sell those rights and distribute the net proceeds to ADS holders, in each case after deduction or upon payment of its fees and expenses. To the extent the depositary does not do any of those things, it will allow the rights to lapse unexercised. *In that case, you will receive no value for them.* The depositary will exercise or distribute rights only if we ask it to and provide satisfactory assurances to the depositary that it is legal to do so. If the depositary will exercise rights, it will purchase the securities to which the rights relate and distribute those securities or, in the case of shares, new ADSs representing the new shares, to subscribing ADS holders, but only if ADS holders have paid the exercise price to the depositary. U.S. securities laws may restrict the ability of the depositary to distribute rights or ADSs or other securities issued on exercise of rights to all or certain ADS holders, and the securities distributed may be subject to restrictions on transfer.

Other Distributions. The depositary will send to ADS holders anything else we distribute on deposited securities by any means it thinks is legal, fair and practical. If it cannot make the distribution in that way, the depositary has a choice. It may decide to sell what we distributed and distribute the net proceeds, in the same way as it does with cash. Or, it may decide to hold what we distributed, in which case ADSs will also represent the newly distributed property. However, the depositary is not required to distribute any securities (other than ADSs) to ADS holders unless it receives satisfactory evidence from us that it is legal to make that distribution. The depositary may sell a portion of the distributed securities or property sufficient to pay its fees and expenses in connection with that distribution. U.S. securities laws may restrict the ability of the depositary to distribute securities to all or certain ADS holders, and the securities distributed may be subject to restrictions on transfer.

The depositary is not responsible if it decides that it is unlawful or impractical to make a distribution available to any ADS holders. We have no obligation to register ADSs, shares, rights or other securities under the Securities Act. We also have no obligation to take any other action to permit the distribution of ADSs, shares, rights or anything else to ADS holders. *This means that you may not receive the distributions we make on our shares or any value for them if it is illegal or impractical for us to make them available to you*.

Deposit, Withdrawal and Cancellation

How are ADSs issued?

The depositary will deliver ADSs if you or your broker deposits shares or evidence of rights to receive shares with the custodian. Upon payment of its fees and expenses and of any taxes or charges, such as stamp

taxes or stock transfer taxes or fees, the depositary will register the appropriate number of ADSs in the names you request and will deliver the ADSs to or upon the order of the person or persons that made the deposit.

How can ADS holders withdraw the deposited securities?

You may surrender your ADSs to the depositary for the purpose of withdrawal. Upon payment of its fees and expenses and of any taxes or charges, such as stamp taxes or stock transfer taxes or fees, the depositary will deliver the shares and any other deposited securities underlying the ADSs to the ADS holder or a person the ADS holder designates at the office of the custodian. Or, at your request, risk and expense, the depositary will deliver the deposited securities at its office, if feasible. However, the depositary is not required to accept surrender of ADSs to the extent it would require delivery of a fraction of a deposited share or other security. The depositary may charge you a fee and its expenses for instructing the custodian regarding delivery of deposited securities.

How do ADS holders interchange between certificated ADSs and uncertificated ADSs?

You may surrender your ADR to the depositary for the purpose of exchanging your ADR for uncertificated ADSs. The depositary will cancel that ADR and will send to the ADS holder a statement confirming that the ADS holder is the registered holder of uncertificated ADSs. Upon receipt by the depositary of a proper instruction from a registered holder of uncertificated ADSs requesting the exchange of uncertificated ADSs for certificated ADSs, the depositary will execute and deliver to the ADS holder an ADR evidencing those ADSs.

Voting Rights

How do you vote?

ADS holders may instruct the depositary how to vote the number of deposited shares their ADSs represent. If we request the depositary to solicit your voting instructions (and we are not required to do so), the depositary will notify you of a shareholders' meeting and send or make voting materials available to you. Those materials will describe the matters to be voted on and explain how ADS holders may instruct the depositary how to vote. For instructions to be valid, they must reach the depositary by a date set by the depositary. The depositary will try, as far as practical, subject to the laws of the Commonwealth of Australia and the provisions of our articles of association or similar documents, to vote or to have its agents vote the shares or other deposited securities as instructed by ADS holders. If we do not request the depositary to solicit your voting instructions, you can still send voting instructions, and, in that case, the depositary may try to vote as you instruct, but it is not required to do so. In any event, the depositary will not exercise any discretion in voting deposited securities and it will only vote or attempt to vote as instructed.

We cannot assure you that you will receive the voting materials in time to ensure that you can instruct the depositary to vote your shares. In addition, the depositary and its agents are not responsible for failing to carry out voting instructions or for the manner of carrying out voting instructions. *This means that you may not be able to exercise voting rights and there may be nothing you can do if your shares are not voted as you requested.*

In order to give you a reasonable opportunity to instruct the depositary as to the exercise of voting rights relating to Deposited Securities, if we request the Depositary to act, we agree to give the depositary notice of any such meeting and details concerning the matters to be voted upon at least 30 days in advance of the meeting date.

Except by instructing the depositary as described above, you will not be able to exercise voting rights unless you surrender your ADSs and withdraw the shares. However, you may not know about the meeting enough in advance to withdraw the shares.

Fees and Expenses

Pursuant to the terms of the deposit agreement, the persons depositing or withdrawing ordinary shares or holders of ADSs will be required to pay the following fees:

Persons depositing or withdrawing shares or ADS holders must pay:	For:
US$5.00 (or less) per 100 ADSs (or portion of 100 ADSs)	Issuance of ADSs, including issuances resulting from a distribution of shares or rights or other property Cancellation of ADSs for the purpose of withdrawal, including if the deposit agreement terminates
US$0.05 (or less) per ADS	Any cash distribution to ADS holders
A fee equivalent to the fee that would be payable if securities distributed to you had been shares and the shares had been deposited for issuance of ADSs	Distribution of securities distributed to holders of deposited securities (including rights) that are distributed by the depositary to ADS holders
US$0.05 (or less) per ADS per calendar year	Depositary services
Registration or transfer fees	Transfer and registration of shares on our share register to or from the name of the depositary or its agent when you deposit or withdraw shares
Expenses of the depositary	Cable (including SWIFT) and facsimile transmissions (when expressly provided in the deposit agreement) Converting foreign currency to U.S. dollars
Taxes and other governmental charges the depositary or the custodian has to pay on any ADSs or shares underlying ADSs, such as stock transfer taxes, stamp duty or withholding taxes	As necessary
Any charges incurred by the depositary or its agents for servicing the deposited securities	As necessary

The depositary collects its fees for delivery and surrender of ADSs directly from investors depositing shares or surrendering ADSs for the purpose of withdrawal or from intermediaries acting for them. The depositary collects fees for making distributions to investors by deducting those fees from the amounts distributed or by selling a portion of distributable property to pay the fees. The depositary may collect its annual fee for depositary services by deduction from cash distributions or by directly billing investors or by charging the book-entry system accounts of participants acting for them. The depositary may collect any of its fees by deduction from any cash distribution payable (or by selling a portion of securities or other property distributable) to ADS holders that are obligated to pay those fees. The depositary may generally refuse to provide fee-attracting services until its fees for those services are paid.

From time to time, the depositary may make payments to us to reimburse us for costs and expenses generally arising out of establishment and maintenance of the ADS program, waive fees and expenses for services provided to us by the depositary or share revenue from the fees collected from ADS holders. In

performing its duties under the deposit agreement, the depositary may use brokers, dealers, foreign currency dealers or other service providers that are owned by or affiliated with the depositary and that may earn or share fees, spreads or commissions.

The depositary may convert currency itself or through any of its affiliates, or the custodian or we may convert currency and pay U.S. dollars to the depositary. Where the depositary converts currency itself or through any of its affiliates, the depositary acts as principal for its own account and not as agent, advisor, broker or fiduciary on behalf of any other person and earns revenue, including, without limitation, transaction spreads, that it will retain for its own account. The revenue is based on, among other things, the difference between the exchange rate assigned to the currency conversion made under the deposit agreement and the rate that the depositary or its affiliate receives when buying or selling foreign currency for its own account. The depositary makes no representation that the exchange rate used or obtained by it or its affiliate in any currency conversion under the deposit agreement will be the most favorable rate that could be obtained at the time or that the method by which that rate will be determined will be the most favorable to ADS holders, subject to the depositary's obligation to act without negligence or bad faith. The methodology used to determine exchange rates used in currency conversions made by the depositary is available upon request. Where the custodian converts currency, the custodian has no obligation to obtain the most favorable rate that could be obtained at the time or to ensure that the method by which that rate will be determined will be the most favorable to ADS holders, and the depositary makes no representation that the rate is the most favorable rate and will not be liable for any direct or indirect losses associated with the rate. In certain instances, the depositary may receive dividends or other distributions from the United States in U.S. dollars that represent the proceeds of a conversion of foreign currency or translation from foreign currency at a rate that was obtained or determined by us and, in such cases, the depositary will not engage in, or be responsible for, any foreign currency transactions and neither it nor we make any representation that the rate obtained or determined by us is the most favorable rate and neither it nor we will be liable for any direct or indirect losses associated with the rate.

Payment of Taxes

You will be responsible for any taxes or other governmental charges payable on your ADSs or on the deposited securities represented by any of your ADSs. The depositary may refuse to register any transfer of your ADSs or allow you to withdraw the deposited securities represented by your ADSs until those taxes or other charges are paid. It may apply payments owed to you or sell deposited securities represented by your ADSs to pay any taxes owed and you will remain liable for any deficiency. If the depositary sells deposited securities, it will, if appropriate, reduce the number of ADSs to reflect the sale and pay to ADS holders any proceeds, or send to ADS holders any property, remaining after it has paid the taxes. Your obligation to pay taxes and indemnify us and the depository against any tax claims will survive the transfer or surrender of your ADSs, the withdrawal of the deposited ordinary shares as well as the termination of the deposit agreement.

Tender and Exchange Offers; Redemption, Replacement or Cancellation of Deposited Securities

The depositary will not tender deposited securities in any voluntary tender or exchange offer unless instructed to do so by an ADS holder surrendering ADSs and subject to any conditions or procedures the depositary may establish.

If deposited securities are redeemed for cash in a transaction that is mandatory for the depositary as a holder of deposited securities, the depositary will call for surrender of a corresponding number of ADSs and distribute the net redemption money to the holders of called ADSs upon surrender of those ADSs.

If there is any change in the deposited securities such as a sub-division, combination or other reclassification, or any merger, consolidation, recapitalization or reorganization affecting the issuer of deposited securities in which the depositary receives new securities in exchange for or in lieu of the old deposited securities, the depositary will hold those replacement securities as deposited securities under the deposit agreement. However, if the depositary decides it would not be lawful and practical to hold the replacement

securities because those securities could not be distributed to ADS holders or for any other reason, the depositary may instead sell the replacement securities and distribute the net proceeds upon surrender of the ADSs.

If there is a replacement of the deposited securities and the depositary will continue to hold the replacement securities, the depositary may distribute new ADSs representing the new deposited securities or ask you to surrender your outstanding ADRs in exchange for new ADRs identifying the new deposited securities.

If there are no deposited securities underlying ADSs, including if the deposited securities are cancelled, or if the deposited securities underlying ADSs have become apparently worthless, the depositary may call for surrender of those ADSs or cancel those ADSs upon notice to the ADS holders.

Amendment and Termination

How may the deposit agreement be amended?

We may agree with the depositary to amend the deposit agreement and the ADRs without your consent for any reason. If an amendment adds or increases fees or charges, except for taxes and other governmental charges or expenses of the depositary for registration fees, facsimile costs, delivery charges or similar items, or prejudices a substantial right of ADS holders, it will not become effective for outstanding ADSs until 30 days after the depositary notifies ADS holders of the amendment. *At the time an amendment becomes effective, you are considered, by continuing to hold your ADSs, to agree to the amendment and to be bound by the ADRs and the deposit agreement as amended.*

How may the deposit agreement be terminated?

The depositary will initiate termination of the deposit agreement if we instruct it to do so. The depositary may initiate termination of the deposit agreement if

- 60 days have passed since the depositary told us it wants to resign but a successor depositary has not been appointed and accepted its appointment;
- we delist the ADSs from an exchange in the United States on which they were listed and do not list the ADSs on another exchange in the United States or make arrangements for trading of ADSs on the U.S. over-the-counter market;
- we delist our shares from an exchange outside the United States on which they were listed and do not list the shares on another exchange outside the United States;
- the depositary has reason to believe the ADSs have become, or will become, ineligible for registration on Form F-6 under the Securities Act;
- we appear to be insolvent or enter insolvency proceedings;
- all or substantially all the value of the deposited securities has been distributed either in cash or in the form of securities;
- there are no deposited securities underlying the ADSs or the underlying deposited securities have become apparently worthless; or
- there has been a replacement of deposited securities.

If the deposit agreement will terminate, the depositary will notify ADS holders at least 90 days before the termination date. At any time after the termination date, the depositary may sell the deposited securities. After that, the depositary will hold the money it received on the sale, as well as any other cash it is holding under the deposit agreement, unsegregated and without liability for interest, for the pro rata benefit of the ADS holders that have not surrendered their ADSs. Normally, the depositary will sell as soon as practicable after the termination date.

After the termination date and before the depositary sells, ADS holders can still surrender their ADSs and receive delivery of deposited securities, except that the depositary may refuse to accept a surrender for the

purpose of withdrawing deposited securities or reverse previously accepted surrenders of that kind that have not settled if it would interfere with the selling process. The depositary may refuse to accept a surrender for the purpose of withdrawing sale proceeds until all the deposited securities have been sold. The depositary will continue to collect distributions on deposited securities, but, after the termination date, the depositary is not required to register any transfer of ADSs or distribute any dividends or other distributions on deposited securities to the ADSs holder (until they surrender their ADSs) or give any notices or perform any other duties under the deposit agreement except as described in this paragraph.

Limitations on Obligations and Liability

Limits on our Obligations and the Obligations of the Depositary; Limits on Liability to Holders of ADSs

The deposit agreement expressly limits our obligations and the obligations of the depositary. It also limits our liability and the liability of the depositary. We and the depositary:

- are only obligated to take the actions specifically set forth in the deposit agreement without negligence or bad faith, and the depositary will not be a fiduciary or have any fiduciary duty to holders of ADSs;
- are not liable if we are or it is prevented or delayed by law or by events or circumstances beyond our or its ability to prevent or counteract with reasonable care or effort from performing our or its obligations under the deposit agreement;
- are not liable if we or it exercises discretion permitted under the deposit agreement;
- are not liable for the inability of any holder of ADSs to benefit from any distribution on deposited securities that is not made available to holders of ADSs under the terms of the deposit agreement, or for any special, consequential or punitive damages for any breach of the terms of the deposit agreement;
- have no obligation to become involved in a lawsuit or other proceeding related to the ADSs or the deposit agreement on your behalf or on behalf of any other person;
- may rely upon any documents we believe or it believes in good faith to be genuine and to have been signed or presented by the proper person;
- are not liable for the acts or omissions of any securities depository, clearing agency or settlement system; and
- the depositary has no duty to make any determination or provide any information as to our tax status, or any liability for any tax consequences that may be incurred by ADS holders as a result of owning or holding ADSs or be liable for the inability or failure of an ADS holder to obtain the benefit of a foreign tax credit, reduced rate of withholding or refund of amounts withheld in respect of tax or any other tax benefit.

In the deposit agreement, we and the depositary agree to indemnify each other under certain circumstances.

Requirements for Depositary Actions

Before the depositary will deliver or register a transfer of ADSs, make a distribution on ADSs, or permit withdrawal of shares, the depositary may require:

- payment of stock transfer or other taxes or other governmental charges and transfer or registration fees charged by third parties for the transfer of any shares or other deposited securities;
- satisfactory proof of the identity and genuineness of any signature or other information it deems necessary; and
- compliance with regulations it may establish, from time to time, consistent with the deposit agreement, including presentation of transfer documents.

The depositary may refuse to deliver ADSs or register transfers of ADSs when the transfer books of the depositary or our transfer books are closed or at any time if the depositary or we think it advisable to do so.

Your Right to Receive the Shares Underlying your ADSs

ADS holders have the right to cancel their ADSs and withdraw the underlying shares at any time except:

- when temporary delays arise because: (i) the depositary has closed its transfer books or we have closed our transfer books; (ii) the transfer of shares is blocked to permit voting at a shareholders' meeting; or (iii) we are paying a dividend on our shares;
- when you owe money to pay fees, taxes and similar charges; or
- when it is necessary to prohibit withdrawals in order to comply with any laws or governmental regulations that apply to ADSs or to the withdrawal of shares or other deposited securities.

This right of withdrawal may not be limited by any other provision of the deposit agreement.

Direct Registration System

In the deposit agreement, all parties to the deposit agreement acknowledge that the Direct Registration System, also referred to as DRS, and Profile Modification System, also referred to as Profile, will apply to the ADSs. DRS is a system administered by DTC that facilitates interchange between registered holding of uncertificated ADSs and holding of security entitlements in ADSs through DTC and a DTC participant. Profile is a feature of DRS that allows a DTC participant, claiming to act on behalf of a registered holder of uncertificated ADSs, to direct the depositary to register a transfer of those ADSs to DTC or its nominee and to deliver those ADSs to the DTC account of that DTC participant without receipt by the depositary of prior authorization from the ADS holder to register that transfer.

In connection with and in accordance with the arrangements and procedures relating to DRS/Profile, the parties to the deposit agreement understand that the depositary will not determine whether the DTC participant that is claiming to be acting on behalf of an ADS holder in requesting registration of transfer and delivery as described in the paragraph above has the actual authority to act on behalf of the ADS holder (notwithstanding any requirements under the Uniform Commercial Code). In the deposit agreement, the parties agree that the depositary's reliance on and compliance with instructions received by the depositary through the DRS/Profile system and in accordance with the deposit agreement will not constitute negligence or bad faith on the part of the depositary.

Shareholder Communications; Inspection of Register of Holders of ADSs

The depositary will make available for your inspection at its office all communications that it receives from us as a holder of deposited securities that we make generally available to holders of deposited securities. The depositary will send you copies of those communications or otherwise make those communications available to you if we ask it to. You have a right to inspect the register of holders of ADSs, but not for the purpose of contacting those holders about a matter unrelated to our business or the ADSs.

Each holder of ADSs may be required from time to time to provide certain information, including proof of taxpayer status, residence and beneficial ownership (as applicable), from time to time and in a timely manner as we, the depositary or the custodian may deem necessary or proper to fulfill obligations under applicable law.

Jury Trial Waiver

The deposit agreement provides that, to the extent permitted by law, ADS holders waive the right to a jury trial of any claim they may have against us or the depositary arising out of or relating to our shares, the ADSs or the deposit agreement, including any claim under the U.S. federal securities laws. If we or the depositary opposed a jury trial demand based on the waiver, the court would determine whether the waiver was enforceable in the facts and circumstances of that case in accordance with applicable case law. You will not, by agreeing to the terms of the deposit agreement, be deemed to have waived our or the depositary's compliance with U.S. federal securities laws or the rules and regulations promulgated thereunder.

DESCRIPTION OF PRE-FUNDED WARRANTS

The following is a brief summary of certain terms and conditions of the pre-funded warrants being offered in this offering. The following description is subject in all respects to the provisions contained in the pre-funded warrants.

Form

The pre-funded warrants will be issued as individual warrant agreements to the purchasers. The form of pre-funded warrant has been filed as an exhibit to the registration statement of which this prospectus forms a part.

Term

The pre-funded warrants will not expire until they are fully exercised.

Exercisability

The pre-funded warrants are exercisable for ADSs at any time (subject to limited exceptions as described in the pre-funded warrants) until they are fully exercised. The pre-funded warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us and the Depositary a duly executed exercise notice. The pre-funded warrants may be exercised on a "cashless" basis. No fractional ADSs will be issued in connection with the exercise of a pre-funded warrant.

Exercise Limitations

We may not effect the exercise of any pre-funded warrant, and a holder will not be entitled to exercise any portion of any pre-funded warrant that, upon giving effect to such exercise, would cause: (i) the aggregate number of ordinary shares (including ordinary shares underlying ADSs) beneficially owned by such holder (together with its affiliates) to exceed 9.99% of the number of ordinary shares (including ordinary shares underlying ADSs) outstanding immediately after giving effect to the exercise; or (ii) the combined voting power of our securities beneficially owned by such holder (together with its affiliates) to exceed 9.99% of the combined voting power of all of our securities outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. However, any holder of a pre-funded warrant may increase such percentage not in excess of 19.99% upon at least 61 days' prior written notice from the holder to us.

Exercise Price

The exercise price of ADSs purchasable upon the exercise of the pre-funded warrants is US$0.00001 per share. The exercise price of the pre-funded warrants and the number of ADSs issuable upon exercise of the pre-funded warrants is subject to appropriate adjustment in the event of certain dividends and distributions, share splits, share combinations, reclassifications or similar events affecting our ordinary shares, as well as upon any distribution of assets, including cash, shares or other property, to our shareholders, subject to the terms and conditions of the deposit agreement.

Transferability

Subject to applicable laws, the pre-funded warrants may not be offered for sale, sold, transferred or assigned without our consent.

Exchange Listing

We do not intend to list the pre-funded warrants on the Nasdaq Global Select Market, any other national securities exchange or any other nationally recognized trading system.

Fundamental Transactions

Upon the consummation of a fundamental transaction (as described in the pre-funded warrants, and generally including any reorganization, recapitalization or reclassification of our ordinary shares, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding ordinary shares (including ordinary shares underlying ADSs), or any person or group becoming the beneficial owner of 50% of the voting power of our outstanding ordinary shares (including ordinary shares underlying ADSs), including a takeover bid under the Corporations Act), any unexercised portion of each pre-funded warrant will be automatically net exercised in full immediately prior to the closing of such fundamental transaction, without giving effect to any election of exercise restrictions described above, following which each pre-funded warrant will immediately terminate.

Delivery of ADSs

To comply with applicable Australian law, in the event a pre-funded warrant is exercised while we reasonably believe we are in possession of material non-public information about our company and operations, the terms of the pre-funded allow us to delay the delivery of the ADSs underlying the exercised warrant until such time that we have publicly disclosed such information.

No Rights as a Shareholder

Except by virtue of such holder's ownership of any ADSs, the holder of a pre-funded warrant does not have the rights or privileges of a holder of ADSs or our ordinary shares, including any voting rights, until such holder exercises the pre-funded warrant.

SHARES AND AMERICAN DEPOSITARY SHARES ELIGIBLE FOR FUTURE SALE

Our ordinary shares have been trading on the ASX since 1985, and certain ADSs have been traded on the over-the-counter market in the United States since June 2011 through our existing sponsored Level I ADR facility with The Bank of New York Mellon, as depositary. While the ADSs have been approved for listing on Nasdaq, we cannot assure you that an active trading market for the ADSs will develop.

Upon completion of this offering, we will have 8,572,521 ADSs outstanding (including 9,221 ADSs that were outstanding prior to this offering) representing 68,580,168 ordinary shares, or approximately 20.3% of our ordinary shares in issue and outstanding, and assuming no exercise of any pre-funded warrants offered and sold in this offering. In addition, we will have 269,084,001 ordinary shares not represented by ADSs in issue and outstanding. If the underwriters exercise their option to purchase 1,425,000 additional ADSs in full, we will have 9,997,521 ADSs outstanding, representing 79,980,168 ordinary shares, or approximately 22.9% of our ordinary shares in issue and outstanding. All of the ADSs sold in this offering will be freely tradable without restrictions or further registration under the Securities Act, except for any ADSs sold to our "affiliates," as that term is defined under Rule 144 under the Securities Act. The ordinary shares held by existing shareholders are "restricted securities," as that term is defined in Rule 144 under the Securities Act. Restricted securities may be sold in the United States only if registered with the SEC or if their resale qualifies for exemption from registration described below under Rule 144 or Rule 701 promulgated under the Securities Act.

Future sales of ADSs in the U.S. public market after this offering, and the availability of ADSs for future sale, could adversely affect the market price of the ADSs prevailing from time to time. As described below, a significant number of currently outstanding ordinary shares will not be available for sale shortly after this offering due to contractual restrictions on transfers of ordinary shares and ADSs. However, sales of substantial amounts of ADSs or ordinary shares, or the perception that these sales could occur, could adversely affect prevailing market prices for the ADSs and could impair our future ability to raise equity capital.

Rule 144

In general, a person who has beneficially owned restricted ordinary shares for at least six months would be entitled to sell their securities pursuant to Rule 144 under the Securities Act provided that (1) such person is not deemed to have been one of our affiliates at the time of, or at any time during the 90 days preceding, a sale and (2) we have been subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale. Persons who have beneficially owned restricted ordinary shares for at least six months, but who are our affiliates at the time of, or at any time during the 90 days preceding a sale, would be subject to additional restrictions, by which such person would be entitled to sell within any three-month period only a number of securities that does not exceed the greater of either of the following:

- 1.0% of the number of ordinary shares (including ordinary shares in the form of ADSs) then outstanding, which will equal approximately 3,376,642 ordinary shares immediately after the closing of this offering; and
- the average weekly trading volume of our ordinary shares (including ordinary shares in the form of ADSs) during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale;

provided, in each case, that we have been subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale. Such sales both by affiliates and by non-affiliates must also comply with the manner of sale, current public information and notice provisions of Rule 144. Non-affiliate resales of restricted shares under Rule 144 also are subject to the availability of current public information about us until a period of one year has elapsed since the securities were acquired from the issuer or an affiliate of the issuer.

Rule 701

Rule 701 under the Securities Act permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the holding period requirement. Most of our employees, senior management or directors who purchased shares under a written compensatory plan or contract

may be entitled to rely on the resale provisions of Rule 701, but all holders of Rule 701 shares are required to wait until 90 days after the date of this prospectus before selling their shares subject also to Australian law.

The SEC has indicated that Rule 701 will apply to typical options granted by an issuer before it becomes subject to the reporting requirements of the Exchange Act, along with the shares acquired upon exercise of such options, including exercises after an issuer becomes subject to the reporting requirements of the Exchange Act.

Lock-up Agreements

We and our officers and directors have agreed that, without the prior written consent of Citigroup Global Markets Inc. and SVB Leerink LLC, or, collectively, the Representatives, on behalf of the underwriters, we and they will not, during the period ending 90 days after the date of this prospectus (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any ordinary shares, ADSs or any securities convertible into or exercisable or exchangeable for our ordinary shares or ADSs or (ii) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the ordinary shares or ADSs. In addition, we have agreed that, without the prior written consent of the Representatives on behalf of the underwriters, we will not, during the restricted period, file any registration statement with the SEC relating to the offering of any ordinary shares or ADSs or any securities convertible into or exercisable or exchangeable for ordinary shares or ADSs. The restrictions described in this paragraph are subject to certain exceptions. See “Underwriting.”

The Representatives, in their sole discretion, may release the ordinary shares, ADSs and other securities subject to the lock-up agreements described above in whole or in part at any time.

We do not currently expect any release of ordinary shares or ADSs subject to lock-up agreements prior to the expiration of the applicable lock-up periods. Upon the expiration of the applicable lock-up periods, substantially all of the ordinary shares and ADSs subject to such lock-up restrictions will become eligible for sale, subject to the limitations described above.

MATERIAL UNITED STATES FEDERAL INCOME AND AUSTRALIAN TAX CONSIDERATIONS

The following summary of the material Australian and U.S. federal income tax consequences of an investment in the ADSs or ordinary shares is based upon laws and relevant interpretations thereof in effect as of the date of this prospectus, all of which are subject to change, possibly with retroactive effect. This summary does not deal with all possible tax consequences relating to an investment in the ADSs or ordinary shares, such as the tax consequences under U.S. state, local and other tax laws other than U.S. federal income tax laws and certain Australian tax laws.

Material United States Federal Income Tax Considerations

The following describes material United States federal income tax considerations relating to the purchase, ownership and disposition of our ordinary shares or ADSs and the purchase, ownership and disposition of pre-funded warrants to purchase our ADSs pursuant to this offering, in each case, by a U.S. holder (as defined below). The ordinary shares, ADSs, and the pre-funded warrants are collectively referred to in this section as our "securities." This summary addresses these tax considerations only for U.S. holders that are initial purchasers of our securities pursuant to this offering and that will hold such securities as capital assets (generally, property held for investment). This summary does not address all U.S. federal income tax matters that may be relevant to a particular U.S. holder. This summary does not address tax considerations applicable to a holder of our securities that may be subject to special tax rules including, without limitation, the following:

- banks, financial institutions or insurance companies;
- brokers, dealers or traders in securities, currencies, commodities, or notional principal contracts;
- tax-exempt entities or organizations, including an "individual retirement account" or "Roth IRA" as defined in Section 408 or 408A of the Code (as defined below), respectively;
- real estate investment trusts, regulated investment companies or grantor trusts;
- persons that hold our securities as part of a "hedging," "integrated," "wash sale" or "conversion" transaction or as a position in a "straddle" for U.S. federal income tax purposes;
- S corporations, partnerships, or other entities or arrangements classified as partnerships for U.S. federal income tax purposes;
- certain former citizens or long-term residents of the United States;
- persons that received our securities as compensation;
- persons subject to Section 451(b) of the Code;
- persons acquiring our securities in connection with a trade or business conducted outside of the United States, including a permanent establishment or a fixed base in Australia;
- holders that own directly, indirectly, or through attribution 10% or more of the voting power or value of our securities; and
- holders that have a "functional currency" other than the U.S. dollar.

Holders of our securities who fall within one of the categories above are advised to consult their tax advisor regarding the specific tax consequences which may apply to their particular situation.

For the purposes of this description, a "U.S. holder" is a beneficial owner of our securities that is (or is treated as), for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity taxable as a corporation, created or organized in or under the laws of the United States, any state therein or the District of Columbia;

- an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust, if a court within the United States is able to exercise primary supervision over its administration and one or more U.S. persons have the authority to control all of the substantial decisions of such trust, or if such trust has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

If a partnership (or any other entity treated as a partnership for U.S. federal income tax purposes) holds our securities, the tax consequences relating to an investment in our securities will depend in part upon the status of the partner and the activities of the partnership. Such a partner or partnership should consult its tax advisor regarding the specific tax considerations of acquiring, owning and disposing of our securities in its particular circumstances.

Persons considering an investment in our securities should consult their own tax advisors as to the particular tax consequences applicable to them relating to the acquisition, ownership and disposition of our securities, including the applicability of U.S. federal, state and local tax laws, Australian tax laws and other non-U.S. tax laws.

This description does not address the U.S. federal estate, gift, or alternative minimum tax considerations, or any U.S. state, local, or non-U.S. tax considerations of the acquisition, ownership and disposition of our securities.

This description is based on the U.S. Internal Revenue Code of 1986, as amended, or the Code, existing, proposed and temporary U.S. Treasury Regulations promulgated thereunder and administrative and judicial interpretations thereof, in each case as in effect and available on the date hereof. All the foregoing is subject to change, which change could apply retroactively, and to differing interpretations, all of which could affect the tax considerations described below. There can be no assurances that the U.S. Internal Revenue Service, or the IRS, will not take a position concerning the tax consequences of the acquisition, ownership and disposition of our securities or that such a position would not be sustained by a court. We have not obtained, nor do we intend to obtain, a ruling with respect to the U.S. federal income tax considerations in the purchase, ownership or disposition of our securities. Accordingly, holders should consult their own tax advisors concerning the U.S. federal, state, local and non-U.S. tax consequences of acquiring, owning and disposing of our securities in their particular circumstances.

In general, and taking into account the earlier assumptions, for U.S. federal income tax purposes, a U.S. holder holding ADSs will be treated as the owner of the ordinary shares represented by the ADSs. Exchanges of ordinary shares for ADSs, and ADSs for ordinary shares, generally will not be subject to U.S. federal income tax.

Treatment of Pre-Funded Warrants

Although it is not entirely free from doubt, we believe a pre-funded warrant should be treated as an ADS for U.S. federal income tax purposes and a holder of pre-funded warrants should generally be taxed in the same manner as a holder of our ordinary shares or ADSs, as described below (except as otherwise noted below). However, our characterization is not binding on the IRS and the IRS may treat the pre-funded warrants as warrants to acquire our ordinary shares or ADSs. If so, the tax consequences, including the amount and character of your gain, with respect to an investment in our pre-funded warrants could change. Accordingly, each holder should consult his, her or its own tax advisor regarding the risks associated with the acquisition of pre-funded warrants pursuant to this offering (including potential alternative characterizations). The balance of this discussion generally assumes that the characterization described above is respected for U.S. federal income tax purposes unless otherwise noted.

United States Federal Income Tax Consequences If We Are Not a PFIC. The description of the U.S. federal income tax consequences of the receipt of distributions and the sale or other taxable exchange of our

securities, described in the following two sections "—Distributions" and "—Sale, Exchange or Other Taxable Disposition," apply only if we are not a PFIC in the relevant year and our stock is not subject to the rules described above under "—Passive Foreign Investment Company Considerations."

Distributions. As described above under the heading "—Dividend Policy," we do not expect to make any distributions in respect of our securities. Subject to the discussion under "—Passive Foreign Investment Company Considerations," below, the gross amount of any distribution (including any amounts withheld in respect of foreign tax) actually or constructively received by a U.S. holder with respect to our securities will generally be taxable to the U.S. holder as a dividend to the extent of the U.S. holder's pro rata share of our current or accumulated earnings and profits as determined under U.S. federal income tax principles. Distributions in excess of earnings and profits will generally be non-taxable to the U.S. holder to the extent of, and will be applied against and reduce, the U.S. holder's adjusted tax basis in our securities. Distributions in excess of earnings and profits and such adjusted tax basis will generally be taxable to the U.S. holder as either long-term or short-term capital gain depending upon whether the U.S. holder has held our securities for more than one year as of the time such distribution is received. However, since we do not calculate our earnings and profits under U.S. federal income tax principles, it is expected that any distribution will be reported as a dividend, even if that distribution would otherwise be treated as a non-taxable return of capital or as capital gain under the rules described above. Non-corporate U.S. holders may qualify for the preferential rates of taxation with respect to dividends on our securities applicable to long-term capital gains (i.e., gains from the sale of capital assets held for more than one year) and qualified dividend income (as discussed below) if we are a "qualified foreign corporation" and certain other requirements (discussed below) are met. A non-U.S. corporation (other than a corporation that is classified as a PFIC for the taxable year in which the dividend is paid or the preceding taxable year) generally will be considered to be a qualified foreign corporation (a) if it is eligible for the benefits of a comprehensive tax treaty with the United States which the Secretary of Treasury of the United States determines is satisfactory for purposes of this provision and which includes an exchange of information provision, or (b) with respect to any dividend it pays on ADSs which are readily tradable on an established securities market in the United States. The ADSs have been approved for listing on Nasdaq, which is an established securities market in the United States, and we expect the ADSs to be readily tradable on Nasdaq. There can be no assurance that the ADSs will be considered readily tradable on an established securities market in the United States in later years. Furthermore, it is uncertain whether the pre-funded warrants will be considered readily tradable on an established securities market in the United States. In addition, the Company, which is incorporated under the laws of Australia, believes that it qualifies as a resident of Australia for purposes of, and is eligible for the benefits of, the Convention between the Government of the United States of America and the Government of Australia for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with Respect to Taxes on Income, signed on August 6, 1982, as amended and currently in force, or the U.S.-Australia Tax Treaty, although there can be no assurance in this regard. Further, the IRS has determined that the U.S.-Australia Tax Treaty is satisfactory for purposes of the qualified dividend rules and that it includes an exchange-of-information program. Therefore, subject to the discussion under "—Passive Foreign Investment Company Considerations," below, such dividends will generally be "qualified dividend income" in the hands of individual U.S. holders, provided that a holding period requirement (more than 60 days of ownership, without protection from the risk of loss, during the 121-day period beginning 60 days before the ex-dividend date) and certain other requirements are met. The dividends will not be eligible for the dividends-received deduction generally allowed to corporate U.S. holders.

A U.S. holder generally may claim the amount of any Australian withholding tax as either a deduction from gross income or a credit against its U.S. federal income tax liability. The foreign tax credit is subject to numerous complex limitations that must be determined and applied on an individual basis. Generally, the credit cannot exceed the proportionate share of a U.S. holder's U.S. federal income tax liability that such U.S. holder's taxable income from foreign sources bears to such U.S. holder's worldwide taxable income. In applying this limitation, a U.S. holder's various items of income and deduction must be classified, under complex rules, as either "foreign source" or "U.S. source." This limitation is calculated separately with respect to specific categories of income. The amount of a distribution with respect to the ADSs that is treated as a "dividend" may be lower for U.S.

federal income tax purposes than it is for Australian income tax purposes, potentially resulting in a reduced foreign tax credit for the U.S. holder. In addition, the creditability of foreign taxes could be affected by actions taken by intermediaries in the chain of ownership between the holders of our securities and our company if, as a result of such actions, the holders of our securities are not properly treated as beneficial owners of the underlying ordinary shares. Each U.S. holder should consult its own tax advisors regarding the foreign tax credit rules.

In general, the amount of a distribution paid to a U.S. holder in a foreign currency will be the U.S. dollar value of the foreign currency calculated by reference to the spot exchange rate on the day the depositary receives the distribution, in the case of the ADSs, or on the day the distribution is received by the U.S. holder, in the case of ordinary shares, regardless of whether the foreign currency is converted into U.S. dollars at that time. Any foreign currency gain or loss a U.S. holder realizes on a subsequent conversion of foreign currency into U.S. dollars will be U.S. source ordinary income or loss. If dividends received in a foreign currency are converted into U.S. dollars on the day they are received, a U.S. holder should not be required to recognize foreign currency gain or loss in respect of the dividend.

Certain Adjustments to the Pre-Funded Warrants

The terms of each pre-funded warrant provide for an adjustment to the number of ADSs for which the pre-funded warrant may be exercised or to the exercise price of the pre-funded warrant in certain events, and a distribution upon exercise that corresponds to distributions, if any, made on the ADSs after issuance of the pre-funded warrant and prior to exercise. Such adjustments may be treated as a constructive distribution to a U.S. holder of the pre-funded warrants depending on the circumstances of such adjustment if, and to the extent that, such adjustment has the effect of increasing such U.S. holder's proportionate interest in our "earnings and profits" or assets, depending on the circumstances of such adjustment. Any such constructive distribution may be taxable whether or not there is an actual distribution of cash or other property. U.S. holders should consult their tax advisors regarding the proper treatment of any adjustments to the pre-funded warrants and the interaction of any adjustments and the PFIC rules.

Sale, Exchange or Other Taxable Disposition. A U.S. holder will generally recognize gain or loss for U.S. federal income tax purposes upon the sale, exchange or other taxable disposition of our securities in an amount equal to the difference between the U.S. dollar value of the amount realized from such sale or exchange and the U.S. holder's adjusted tax basis in those securities, determined in U.S. dollars. Subject to the discussion under "—Passive Foreign Investment Company Considerations" below, this gain or loss will generally be a capital gain or loss. The adjusted tax basis in our securities generally will be equal to the cost of such securities. Capital gain from the sale, exchange or other taxable disposition of our securities by a non-corporate U.S. holder is generally eligible for a preferential rate of taxation applicable to capital gains, if the non-corporate U.S. holder's holding period determined at the time of such sale, exchange or other taxable disposition for such securities exceeds one year (i.e., such gain is long-term taxable gain). The deductibility of capital losses for U.S. federal income tax purposes is subject to limitations. Any such gain or loss that a U.S. holder recognizes generally will be treated as U.S. source gain or loss for foreign tax credit limitation purposes.

For a cash basis taxpayer, units of foreign currency paid or received are translated into U.S. dollars at the spot rate on the settlement date of the purchase or sale. In that case, no foreign currency exchange gain or loss will result from currency fluctuations between the trade date and the settlement date of such a purchase or sale.

An accrual basis taxpayer, however, may elect the same treatment required of cash basis taxpayers with respect to purchases and sales of our ordinary shares or ADSs that are traded on an established securities market, provided the election is applied consistently from year to year. Our pre-funded warrants are not expected to be treated as traded on an established securities market. Such election may not be changed without the consent of the IRS. For an accrual basis taxpayer who does not make such election, units of foreign currency paid or received are translated into U.S. dollars at the spot rate on the trade date of the purchase or sale. Such an accrual basis taxpayer may recognize exchange gain or loss based on currency fluctuations between the trade date and

the settlement date. Any foreign currency gain or loss a U.S. holder realizes will be U.S. source ordinary income or loss.

Exercise or Lapse of a Pre-Funded Warrant

Subject to the PFIC rules described above and except as discussed below with respect to the cashless exercise of a pre-funded warrant, a U.S. holder generally will not recognize gain or loss on the exercise of a pre-funded warrant and related receipt of an ADS, unless cash is received in lieu of the issuance of a fractional ADS. However, under a proposed Treasury Regulation (which is proposed to have retroactive effect), a U.S. holder would recognize gain if the pre-funded warrant was treated as stock of a PFIC with respect to a U.S. holder at the time of the exercise of the pre-funded warrant and the stock received upon the exercise was not treated as stock of a PFIC for the taxable year in which the exercise occurs.

A U.S. holder's initial tax basis in the ADS received on the exercise of a pre-funded warrant should be equal to the sum of (i) the U.S. holder's tax basis in pre-funded warrant plus (ii) the exercise price paid by the U.S. holder on the exercise of the pre-funded warrant. Although it is not entirely clear, a U.S. holder's holding period for ADSs received on exercise of a pre-funded warrant will likely include the period during which the U.S. holder held the pre-funded warrant.

The U.S. federal income tax treatment of a cashless exercise of pre-funded warrants into ADSs is unclear, and the tax consequences of a cashless exercise could differ from the consequences upon the exercise of a pre-funded warrant described in the preceding paragraph.

Due to the absence of authority on the U.S. federal income tax treatment of a cashless exercise, there can be no assurance as to the tax treatment that would be adopted by the IRS or a court of law. Accordingly, U.S. holders should consult their own tax advisors regarding the U.S. federal income tax consequences of a cashless exercise of pre-funded warrants.

Medicare Tax. Certain U.S. holders that are individuals, estates or trusts are subject to a 3.8% tax on all or a portion of their "net investment income," which may include all or a portion of their dividend income and net gains from the disposition of our securities. Each U.S. holder that is an individual, estate or trust is urged to consult its tax advisors regarding the applicability of the Medicare tax to its income and gains in respect of its investment in our securities.

Passive Foreign Investment Company Considerations. If we are classified as a PFIC in any taxable year, a U.S. holder will be subject to special rules generally intended to reduce or eliminate any benefits from the deferral of U.S. federal income tax that a U.S. holder could derive from investing in a non-U.S. company that does not distribute all of its earnings on a current basis.

We will be classified as a PFIC for U.S. federal income tax purposes in any taxable year in which, after applying certain look-through rules with respect to the income and assets of our subsidiaries, either: (1) at least 75% of the gross income is "passive income" or (2) at least 50% of the average quarterly value of our total gross assets (which would generally be measured by fair market value of our assets, and for which purpose the total value of our assets may be determined in part by the market value of the ADSs and our ordinary shares, which are subject to change) is attributable to assets that produce "passive income" or are held for the production of "passive income."

Passive income for this purpose generally includes dividends, interest, royalties, rents, gains from commodities and securities transactions, the excess of gains over losses from the disposition of assets which produce passive income, and includes amounts derived by reason of the temporary investment of funds raised in offerings of our securities. If a non-U.S. corporation owns directly or indirectly at least 25% by value of the stock of another corporation or the partnership interests in a partnership, the non-U.S. corporation is treated for

purposes of the PFIC tests as owning its proportionate share of the assets of the other corporation or partnership and as receiving directly its proportionate share of the other corporation's or partnership's income. The determination of whether we are a PFIC is a fact-intensive determination made on an annual basis and the applicable law is subject to varying interpretation. If we are classified as a PFIC in any taxable year during which a U.S. holder owns our securities, such U.S. holder will be subject to special tax rules discussed below and could suffer adverse tax consequences.

The market value of our assets may be determined in large part by reference to the market price of the ADSs and our ordinary shares, which is likely to fluctuate after this offering. Therefore, fluctuations in the market price of our securities may result in our being a PFIC for any taxable year. In addition, the composition of our income and assets will be affected by how, and how quickly, we use the cash proceeds from this offering in our business. Whether we are a PFIC for any taxable year will depend on the nature and composition of our income, assets, activities and market capitalization in each year, and because this is a factual determination made annually after the end of each taxable year, there can be no assurance that we will not be considered a PFIC in any taxable year. We believe that we were not characterized as a PFIC in our taxable year ended June 30, 2019. Based on the nature and composition of our income, assets, activities and market capitalization for our taxable year ended June 30, 2020, we believe that we would not be classified as a PFIC for our taxable year ended June 30, 2020; however, there can be no assurance that we will not be considered a PFIC in any past, current or future taxable year. As a result, our PFIC status may change from year to year. Our status as a PFIC will depend on the composition of our income (including whether we receive certain grants or subsidies and whether such amounts will constitute gross income for purposes of the PFIC income test) and the composition and value of our assets, which may be determined in large part by reference to the market value of the ADSs and our ordinary shares, which may be volatile, from time to time. Our status may also depend, in part, on how quickly we utilize the cash proceeds from this offering in our business. Our U.S. counsel expresses no opinion regarding our conclusions or our expectations regarding our PFIC status.

If we are classified as a PFIC in any year with respect to which a U.S. holder owns our securities, we will continue to be treated as a PFIC with respect to such U.S. holder in all succeeding years during which the U.S. holder owns the securities, regardless of whether we continue to meet the tests described above unless we cease to be a PFIC and the U.S. holder has made a "deemed sale" election under the PFIC rules or is eligible to make and makes a mark-to-market election (as described below), with respect to all taxable years during such U.S. holder's holding period in which we are a PFIC. If the "deemed sale" election is made, a U.S. holder will be deemed to have sold the securities the U.S. holder holds at their fair market value as of the date of such deemed sale and any gain from such deemed sale would be subject to the rules described below. After the deemed sale election, so long as we do not become a PFIC in a subsequent taxable year, the U.S. holder's securities with respect to which such election was made will not be treated as shares in a PFIC and the U.S. holder will not be subject to the rules described below with respect to any "excess distribution" the U.S. holder receives from us or any gain from an actual sale or other disposition of the securities. U.S. holders should consult their tax advisors as to the possibility and consequences of making a deemed sale election if such election becomes available.

If we are a PFIC, and you are a U.S. holder that does not make one of the elections described above (and below in further detail), a special tax regime will apply to both (a) any "excess distribution" by us to you (generally, your ratable portion of distributions in any year, other than the taxable year in which your holding period in the shares or ADSs begins, which are greater than 125% of the average annual distribution received by you in the shorter of the three preceding years or the portion of your holding period for our securities that preceded the year of the distribution) and (b) any gain realized on the sale or other disposition of our securities. Under this regime, any excess distribution and realized gain will be treated as ordinary income and will be subject to tax as if (a) the excess distribution or gain had been realized ratably over your holding period, (b) the amount deemed realized in each year had been subject to tax in each year of that holding period at the highest marginal rate for such year (other than income allocated to the current period or any taxable period before we became a PFIC, which would be subject to tax at the U.S. holder's regular ordinary income rate for the current year and would not be subject to the interest charge discussed below) and (c) the interest charge generally

applicable to underpayments of tax had been imposed on the taxes deemed to have been payable in those years. In addition, dividend distributions made to you will not qualify for the lower rates of taxation applicable to qualified dividends discussed above under "Distributions."

Subject, to the proposed Treasury Regulations described below with respect to options, warrants, or other rights to acquire stock of a PFIC, certain elections may alleviate some of the adverse consequences of PFIC status and would result in an alternative treatment of our ordinary shares or ADSs. U.S. holders should note that the pre-funded warrants are not likely to be treated as regularly traded on a qualified exchange and thus it is unlikely that a mark-to-market election can be made with respect to the pre-funded warrants.

If a U.S. holder makes a mark-to-market election, with respect to our ordinary shares or ADSs, the U.S. holder generally will recognize as ordinary income any excess of the fair market value of our ordinary shares or ADSs at the end of each taxable year over their adjusted tax basis, and will recognize an ordinary loss in respect of any excess of the adjusted tax basis of our ordinary shares or ADSs over their fair market value at the end of the taxable year (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). If a U.S. holder makes the election, the U.S. holder's tax basis in our ordinary shares or ADSs will be adjusted to reflect these income or loss amounts. Any gain recognized on the sale or other disposition of our ordinary shares or ADSs in a year in which we are a PFIC will be treated as ordinary income and any loss will be treated as an ordinary loss (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). The mark-to-market election is available only if we are a PFIC and our ordinary shares or ADSs are "regularly traded" on a "qualified exchange." Our ordinary shares or ADSs will be treated as "regularly traded" in any calendar year in which more than a de minimis quantity of our ordinary shares or ADSs are traded on a qualified exchange on at least 15 days during each calendar quarter (subject to the rule that trades that have as one of their principal purposes the meeting of the trading requirement are disregarded). Nasdaq is a qualified exchange for this purpose and, consequently, if the ADSs are regularly traded, the mark-to-market election will be available to a U.S. holder. It should be noted that it is intended that only the ADSs and not our ordinary shares will be listed on Nasdaq. Consequently, our ordinary shares may not be marketable if the ASX (where our ordinary shares are currently listed) does not meet the applicable requirements. U.S. holders should consult their tax advisors regarding the availability of the mark-to-market election for ordinary shares that are not represented by ADSs.

However, a mark-to-market election generally cannot be made for equity interests in any lower-tier PFICs that we own, unless shares of such lower-tier PFIC are themselves "marketable." As a result, even if a U.S. holder validly makes a mark-to-market election with respect to our ordinary shares or ADSs, the U.S. holder may continue to be subject to the PFIC rules (described above) with respect to its indirect interest in any of our investments that are treated as an equity interest in a PFIC for U.S. federal income tax purposes. U.S. holders should consult their tax advisors as to the availability and desirability of a mark-to-market election, as well as the impact of such election on interests in any lower-tier PFICs.

We do not currently intend to provide the information necessary for U.S. holders to make qualified electing fund elections if we were treated as a PFIC for any taxable year. U.S. holders should consult their tax advisors to determine whether any of the other elections described above would be available and if so, what the consequences of the alternative treatments would be in their particular circumstances.

If we are determined to be a PFIC, the general tax treatment for U.S. holders described in this section would apply to indirect distributions and gains deemed to be realized by U.S. holders in respect of any of our subsidiaries that also may be determined to be PFICs. U.S. holders should consult their tax advisors regarding the application of the PFIC rules to our subsidiaries.

Under proposed Treasury Regulations, if a U.S. holder has an option, warrant, or other right to acquire stock of a PFIC, such option, warrant or right is considered to be PFIC stock also subject to the default rules discussed above. Under proposed Treasury Regulations, if a U.S. holder holds an option, warrant or other right to acquire

stock of a PFIC, the holding period with respect to shares of stock of the PFIC acquired upon exercise of such option, warrant or other right will include the period that the option, warrant or other right was held. pre-funded warrants. Because of the complexity and uncertainty of the treatment of pre-funded warrants under the PFIC rules, each U.S. holder should consult his own tax advisor regarding the application of the PFIC rules to the ADSs acquired upon an exercise of pre-funded warrants.

If a U.S. holder owns our securities during any taxable year in which we are a PFIC, the U.S. holder generally will be required to file an IRS Form 8621 (Information Return by a Shareholder of a Passive Foreign Investment Company or Qualified Electing Fund) with respect to the company, generally with the U.S. holder's federal income tax return for that year. If our company were a PFIC for a given taxable year, then you should consult your tax advisor concerning your annual filing requirements.

The U.S. federal income tax rules relating to PFICs are complex. Prospective U.S. investors are urged to consult their own tax advisors with respect to the acquisition, ownership and disposition of our ordinary shares or ADSs, the consequences to them of an investment in a PFIC, any elections available with respect to our securities and the IRS information reporting obligations with respect to the acquisition, ownership and disposition of our securities.

Backup Withholding and Information Reporting. U.S. holders generally will be subject to information reporting requirements with respect to dividends on our securities and on the proceeds from the sale, exchange or disposition of our securities that are paid within the United States or through U.S.-related financial intermediaries, unless the U.S. holder is an "exempt recipient." In addition, U.S. holders may be subject to backup withholding on such payments, unless the U.S. holder provides a taxpayer identification number and a duly executed IRS Form W-9 or otherwise establishes an exemption. Backup withholding is not an additional tax, and the amount of any backup withholding will be allowed as a credit against a U.S. holder's U.S. federal income tax liability and may entitle such holder to a refund, provided that the required information is timely furnished to the IRS.

Certain Reporting Requirements With Respect to Payments of Offer Price. U.S. holders paying more than $100,000 for our securities generally may be required to file IRS Form 926 reporting the payment of the offer price for our securities to us. Substantial penalties may be imposed upon a U.S. holder that fails to comply. Each U.S. holder should consult its own tax advisor as to the possible obligation to file IRS Form 926.

Foreign Asset Reporting. Certain individual U.S. holders are required to report information relating to an interest in our securities, subject to certain exceptions (including an exception for shares held in accounts maintained by U.S. financial institutions) by filing IRS Form 8938 (Statement of Specified Foreign Financial Assets) with their federal income tax return. U.S. holders are urged to consult their tax advisors regarding their information reporting obligations, if any, with respect to their ownership and disposition of our securities.

THE DISCUSSION ABOVE IS A SUMMARY OF THE U.S. FEDERAL INCOME TAX CONSEQUENCES OF AN INVESTMENT IN OUR SECURITIES AND IS BASED UPON LAWS AND RELEVANT INTERPRETATIONS THEREOF IN EFFECT AS OF THE DATE OF THIS PROSPECTUS, ALL OF WHICH ARE SUBJECT TO CHANGE, POSSIBLY WITH RETROACTIVE EFFECT. EACH PROSPECTIVE INVESTOR IS URGED TO CONSULT ITS OWN TAX ADVISOR ABOUT THE TAX CONSEQUENCES TO IT OF AN INVESTMENT IN OUR SECURITIES IN LIGHT OF THE INVESTOR'S OWN CIRCUMSTANCES.

Material Australian Tax Considerations

In this section, we discuss the material Australian income tax, stamp duty and goods and services tax considerations related to the acquisition, ownership and disposal by the absolute beneficial owners of the ADSs or ordinary shares represented by ADSs. It is based upon existing Australian tax law as of the date of this

registration statement, which is subject to change, possibly retrospectively. This discussion does not address all aspects of Australian tax law which may be important to particular investors in light of their individual investment circumstances, such as ADSs or shares held by investors subject to special tax rules (for example, financial institutions, insurance companies or tax exempt organizations). In addition, this summary does not discuss any non-Australian or state tax considerations, other than stamp duty and goods and services tax.

Prospective investors are urged to consult their tax advisors regarding the Australian and non-Australian income and other tax considerations of the acquisition, ownership and disposition of the ADSs or shares. This summary is based upon the premise that the holder of an ADS is not an Australian tax resident and is not carrying on business in Australia through a permanent establishment (referred to as a "Non-Australian Holder" in this summary). This summary is also based on the assumption that a Non-Australian Holder is "absolutely entitled" to the ordinary shares represented by an ADS (see "—Nature of ADSs for Australian Taxation Purposes" below).

Nature of ADSs for Australian Taxation Purposes

Non-Australian Holders of ADSs should obtain specialist Australian tax advice regarding their rights and obligations under the deposit agreement with the depositary, including whether the deposit arrangement constitutes a "bare trust" resulting in the holders of an ADS being "absolutely entitled" to the underlying shares represented by the ADS for Australian taxation purposes. Apart from certain aspects of the Australian tax legislation (for example, the Australian capital gains tax and withholding tax provisions, which are discussed below), there is no express legislative basis for disregarding "bare trusts" for Australian tax purposes generally.

This summary proceeds on the assumption that the deposit arrangement constitutes a bare trust, which results in holders of ADSs being "absolutely entitled" to the underlying shares. On this basis, holders of ADSs can be treated as the owners of the underlying ordinary shares for Australian capital gains tax purposes. Dividends paid on the underlying ordinary shares will also be treated as dividends derived by the holders of ADSs as the persons presently entitled to those dividends.

Taxation of Dividends

Australia operates a dividend imputation system under which dividends may be declared to be "franked" to the extent they are paid out of company profits that have been subject to income tax. Fully franked dividends are not subject to dividend withholding tax. To the extent that they are unfranked, dividends payable to Non-Australian Holders will be subject to dividend withholding tax except to the extent they are declared to be "conduit foreign income", or CFI. Dividend withholding tax will be imposed at 30%, unless a shareholder is a resident of a country with which Australia has a double taxation treaty and qualifies for the benefits of the treaty. Under the provisions of the current Double Taxation Convention between Australia and the United States, the Australian tax withheld on unfranked dividends that are not declared to be CFI paid by us to which a resident of the United States is beneficially entitled is limited to 15%.

Under the Double Taxation Convention between Australia and the United States, if a U.S. resident company that is a Non-Australian Holder directly owns a 10% or more voting interests, the Australian tax withheld on unfranked dividends that are not declared to be CFI paid by us to which the company is beneficially entitled is limited to 5%.

Character of ADSs or Shares for Australian Taxation Purposes

The Australian tax treatment of a sale or disposal of the ADSs or underlying shares will depend on whether they are held on revenue or capital account. ADSs may be held on revenue rather than capital account, for example, where they are held by share traders or any profit arises from a profit-making undertaking or scheme entered into by the holder. Non-Australian Holders of ADSs should obtain specialist Australian tax advice regarding the characterization of any gain or loss on a sale or disposal of the ADSs or underlying shares as revenue or capital in nature.

Tax on Sales or other Dispositions of Shares or ADSs—Capital Gains Tax

Non-Australian Holders who are treated as the owners of the underlying shares on the basis that they are absolutely entitled to those shares will not be subject to Australian capital gains tax on the gain made on a sale or other disposal of ordinary shares, provided the shares are not "taxable Australian property." Taxable Australian property includes "indirect Australian real property interests," which are interests in a company where:

- the Non-Australian Holders, together with associates, hold 10% or more of our issued shares, at the time of disposal or for a 12 month period during the two years prior to disposal; and
- more than 50% of our assets held directly or indirectly, determined by reference to market value, consists of Australian real property (which includes land and leasehold interests) or Australian mining, quarrying or prospecting rights at the time of disposal.

Australian capital gains tax applies to net capital gains at a taxpayer's marginal tax rates. Net capital gains are calculated after reduction for capital losses, which may only be offset against capital gains.

If a Non-Australian Holder of ADSs was not absolutely entitled to the underlying shares, and the ADSs were held on capital account, the same principles would apply in determining whether a gain on the sale or disposal of the ADSs would be subject to Australian capital gains tax. That is, a Non-Australian Holder should not be subject to Australian capital gains tax provided the ADSs are not taxable Australian property.

The 50% capital gains tax discount is not available to Non-Australian Holders on gains from assets acquired after May 8, 2012 where they were non-Australian residents during the entire holding period. Companies are not entitled to a capital gains tax discount.

Broadly, where there is a disposal of "taxable Australian property," which includes indirect Australian real property interests, the purchaser will be required to withhold and remit to the Australian Taxation Office, or the ATO, 12.5% of the proceeds from the sale. A transaction is excluded from the withholding requirements in certain circumstances, including where the transaction is an on-market transaction conducted on an approved stock exchange, a securities lending arrangement, or the transaction is conducted using a broker operated crossing system. There may also be an exception to the requirement to withhold where a Non-Australian Holder provides a declaration that their ordinary shares are not "indirect Australian real property interests". The Non-Australian Holder may be entitled to receive a tax credit for the tax withheld by the purchaser which they may claim in their Australian income tax return.

Tax on Sales or other Dispositions of ADSs—Revenue Account

Non-Australian Holders who hold their ADSs on revenue account may have the gains made on the sale or other disposal of the ADSs included in their assessable income under the ordinary income provisions of the income tax law, if the gains are sourced in Australia. In the case of gains which are ordinary income, there are no express provisions which treat holders of ADSs as the owners of the underlying shares where they are absolutely entitled to those shares under a bare trust.

Non-Australian Holders assessable under these ordinary income provisions in respect of gains made on ADSs held on revenue account would be assessed for such gains at the Australian tax rates for non-Australian residents, which start at a marginal rate of 32.5% for individuals and would be required to file an Australian tax return. Some relief from Australian income tax may be available to a Non-Australian Holder who is resident of a country with which Australia has a double taxation treaty, qualifies for the benefits of the treaty and does not, for example, derive the gain in carrying on business through a permanent establishment in Australia.

To the extent an amount would be included in a Non-Australian Holder's assessable income under both the capital gains tax provisions and the ordinary income provisions, the capital gain amount may be reduced, so that the holder may not be subject to double Australian tax on any part of the gain.

The statements under "—Tax on Sales or Other Dispositions of Shares—Capital Gains Tax" regarding a purchaser being required to withhold 12.5% tax on the acquisition of certain taxable Australian property are also relevant where the disposal of the ADSs by a Non-Australian Holder is likely to generate gains on revenue account, rather than a capital gain.

Dual Residency

If a holder of ADSs is a resident of both Australia and the United States under those countries' domestic taxation laws, that holder may be subject to tax as an Australian resident. If, however, the holder is determined to be a U.S. resident for the purposes of the Double Taxation Convention between the United States and Australia and qualifies for the benefit of that treaty, the Australian tax may be subject to limitation by the Double Taxation Convention. Holders should obtain specialist taxation advice in these circumstances.

Stamp Duty

No Australian stamp duty is payable by Australian residents or non-Australian residents on the issue, transfer and/or surrender of the ADSs or ordinary shares, provided that the securities issued, transferred and/or surrendered do not represent 90% or more of our issued shares.

Australian Death Duty

Australia does not have estate or death duties. As a general rule, no capital gains tax liability is realized upon the inheritance of a deceased person's shares. The disposal of inherited shares by beneficiaries may, however, give rise to a capital gains tax liability if the gain falls within the scope of Australia's jurisdiction to tax.

Goods and Services Tax

No Australian goods and services tax will be payable on the supply of the ADSs or ordinary shares.

THE DISCUSSION ABOVE IS A SUMMARY OF THE AUSTRALIAN TAX CONSEQUENCES OF AN INVESTMENT IN OUR ORDINARY SHARES OR ADSs AND IS BASED UPON LAWS AND RELEVANT INTERPRETATIONS THEREOF IN EFFECT AS OF THE DATE OF THIS PROSPECTUS, ALL OF WHICH ARE SUBJECT TO CHANGE, POSSIBLY WITH RETROACTIVE EFFECT. EACH PROSPECTIVE INVESTOR IS URGED TO CONSULT ITS OWN TAX ADVISOR ABOUT THE TAX CONSEQUENCES TO IT OF AN INVESTMENT IN OUR ORDINARY SHARES OR ADSs IN LIGHT OF THE INVESTOR'S OWN CIRCUMSTANCES.

ENFORCEMENT OF CIVIL LIABILITIES

We are a public limited company incorporated under the laws of Australia. Certain of our directors are non-residents of the United States and substantially all of their assets are located outside the United States. As a result, it may not be possible or practicable for you to:

- effect service of process within the United States upon our non-U.S. resident directors or on us;
- enforce in U.S. courts judgments obtained against our non-U.S. resident directors or us in the United States courts in any action, including actions under the civil liability provisions of U.S. securities laws;
- enforce in U.S. courts judgments obtained against our non-U.S. resident directors or us in courts of jurisdictions outside the United States in any action, including actions under the civil liability provisions of U.S. securities laws; or
- bring an original action in an Australian court to enforce liabilities against our non-U.S. resident directors or us based solely upon U.S. securities laws.

You may also have difficulties enforcing in courts outside the United States judgments that are obtained in U.S. courts against any of our non-U.S. resident directors or us, including actions under the civil liability provisions of the U.S. securities laws.

With that noted, there are no treaties between Australia and the United States that would affect the recognition or enforcement of foreign judgments in Australia. We also note that investors may be able to bring an original action in an Australian court against us to enforce liabilities based in part upon U.S. federal securities laws. The disclosure in this section is not based on the opinion of counsel.

We have appointed Corporation Service Company as our agent to receive service of process with respect to any action brought against us under the federal securities laws of the United States.

UNDERWRITING

Citigroup Global Markets Inc. and SVB Leerink LLC are acting as book-running managers of this offering and as representatives of the underwriters named below. Subject to the terms and conditions stated in the underwriting agreement dated the date of this prospectus, the underwriters named below have severally agreed to purchase, and we have agreed to sell to them, the number of ADSs or pre-funded warrants to purchase ADSs indicated below:

Underwriter	Number of ADSs	Number of Pre-funded Warrants
Citigroup Global Markets Inc.	3,767,852	412,148
SVB Leerink LLC	3,082,788	337,212
Oppenheimer & Co. Inc.	856,330	93,670
Truist Securities, Inc.	856,330	93,670
Total	8,563,300	936,700

The underwriting agreement provides that the obligations of the underwriters to purchase the ADSs or pre-funded warrants to purchase ADSs included in this offering are subject to approval of legal matters by counsel and to other conditions. The underwriters are obligated to purchase all of the ADSs (other than those covered by the over-allotment option described below) or pre-funded warrants to purchase ADSs if they purchase any.

ADSs or pre-funded warrants to purchase ADSs sold by the underwriters to the public will initially be offered at the applicable initial public offering price set forth on the cover of this prospectus. Any ADSs or pre-funded warrants to purchase ADSs sold by the underwriters to securities dealers may be sold at a discount from the initial public offering price not to exceed US$0.5670 per ADS or pre-funded warrant. After the initial public offering of the ADSs and pre-funded warrants to purchase ADSs, if all the ADSs or pre-funded warrants to purchase ADSs are not sold at the applicable initial public offering price, the underwriters may change the offering price and the other selling terms. The representatives have advised us that the underwriters do not intend to make sales to discretionary accounts.

The address of Citigroup Global Markets Inc. is 390 Greenwich Street, New York, New York 10013, the address of SVB Leerink LLC is One Federal Street, 37th Floor, Boston, Massachusetts 02110, the address of Oppenheimer & Co. Inc. is 85 Broad Street, 26th Floor, New York, New York 10004, and the address of Truist Securities, Inc. is 3333 Peachtree Road NE, 9th floor, Atlanta, Georgia 30326.

If the underwriters sell more ADSs than the total number set forth in the table above, we have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to 1,425,000 additional ADSs at the initial public offering price less the underwriting discount. The underwriters may exercise the option solely for the purpose of covering over-allotments, if any, in connection with this offering. To the extent the option is exercised, each underwriter must purchase a number of additional ADSs approximately proportionate to that underwriter's initial purchase commitment set forth in the table above. Any ADSs issued or sold under the option will be issued and sold on the same terms and conditions as the other ADSs that are the subject of this offering.

We and our officers and directors have agreed that, subject to specified limited exceptions, for a period of 90 days from the date of this prospectus, we and they will not, without the prior written consent of Citigroup Global Markets Inc. and SVB Leerink LLC, offer, sell, contract to sell, pledge or otherwise dispose of, including the filing of a registration statement in respect of, or hedge any ordinary shares or ADSs or any securities convertible into, or exercisable or exchangeable for, our ordinary shares or ADSs, collectively referred to as lock-up securities. Citigroup Global Markets Inc. and SVB Leerink LLC in their sole discretion may release any of the securities subject to these lock-up agreements at any time, which, in the case of officers and directors, shall be with notice.

The lock-up restrictions relating to our officers and directors described in the immediately preceding paragraph are subject to specified exceptions, including the following:

a. transfers of lock-up securities (i) as a bona fide gift or gifts, (ii) by will, other testamentary document or intestacy or (iii) to any immediate family member of the lock-up party or to any trust or other legal entity for the benefit of the lock-up party or immediate family of the lock-up party, or if the lock-up party is a trust, to a trustor or beneficiary of the trust or to the estate of a beneficiary of such trust,

b. transfers of lock-up securities to a partnership, limited liability company or other entity of which lock-up party and the lock-up party's immediate family are the legal and beneficial owner of all of the outstanding equity securities or similar interests;

c. transfers of lock-up securities to a corporation, member, partner, partnership, limited liability company, trust or other entity that is an affiliate of the lock-up party;

d. transfers of lock-up securities to any investment fund or other entity controlled or managed by the lock-up party or its affiliates (including where the lock-up party is a partnership, to a successor partnership or fund, or any other funds managed by such partnership);

e. transfers of lock-up securities to a nominee or custodian of a person or entity to whom a disposition or transfer would be permissible above;

f. transfers of lock-up securities by operation of law, pursuant to a qualified domestic order, divorce settlement, divorce decree or separation agreement or other final court order;

g. transfers of lock-up securities to us upon death, disability, termination of employment or cessation of services;

h. transfers of lock-up securities acquired in open market transactions after the closing of this offering;

i. transfers of ordinary shares or ADSs to us in connection with the vesting, settlement, or exercise of options and other equity awards to purchase ordinary shares or ADSs (including, in each case, by way of "net" or "cashless" exercise), including for the payment of exercise price and tax withholdings or remittance payments due as a result of the vesting, settlement, or exercise of such equity awards;

j. transfers of lock-up securities pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction (including a takeover bid under Chapter 6 of the Corporations Act 2001 (Cth) and a scheme of arrangement implemented under Part 5.1 of the scheme of arrangement under the Corporations Act 2001 (Cth)) that is approved by our board of directors and made to all holders of our share capital involving a change of control;

k. the receipt from us of shares of common stock in connection with the exercise of options or other rights granted under an equity incentive plan or other equity award plan or program or pursuant to an individual award agreement between us and the lock-up party; or

l. the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act or to a similar effect permitted under the rules and regulations of the Australian Securities Exchange for the transfer of shares of common stock, provided that such plan does not provide for the transfer of common stock,

provided that:

- in the case of any transfer or distribution pursuant to clauses (a) through (f) above, each donee, trustee, distributee or transferee shall sign and deliver a lock-up agreement;
- in the case of any transfer or distribution pursuant to clause (h) above, no filing under the Exchange Act or other public announcement would be required or be voluntarily made;

- in the case of any transfer or distribution pursuant to clauses (a) through (k), any filing under the Exchange Act or other public report or announcement would clearly indicate the nature and conditions of the transfer or distribution; and
- in the case of any transfer or distribution pursuant to clauses (a) through (e) above, such transfer or distribution would not involve a disposition for value.

Prior to this offering, there has been no public market for the ADSs and pre-funded warrants to purchase ADSs in the United States. Our ordinary shares have been trading on the Australian Securities Exchange, or the ASX, since April 1985 under the symbol "OPT." The initial public offering price for the ADSs and pre-funded warrants to purchase ADSs were determined by negotiations between us and the representatives and were based, in part, on the prevailing price of our ordinary shares on the ASX. Among the factors considered in determining the initial public offering prices were our stage of development, our current financial condition, our future prospects, our markets, the economic conditions in and future prospects for the industry in which we compete, our management, and currently prevailing general conditions in the equity securities markets, including current market valuations of publicly traded companies considered comparable to our company. We cannot assure you, however, that the price at which the ADSs will sell in the public market after this offering will not be lower than the initial public offering price or that an active trading market in our shares of ADSs will develop and continue after this offering.

The ADSs have been approved for listing on the Nasdaq Global Select Market under the symbol "OPT." We do not intend to list the pre-funded warrants on any securities exchange or nationally recognized trading system.

The following table shows the per ADS, per pre-funded warrant and total underwriting discounts and commissions that we are to pay to the underwriters and proceeds to us, before estimated offering expenses, in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the underwriters' over-allotment option:

			Total	
	Per ADS	Per Pre-funded Warrant	No exercise	Full exercise
Public offering price	$13.50000	$13.49999	$128,249,991	$147,487,491
Underwriting discounts and commissions paid by us	$ 0.94500	$ 0.94500	$ 8,977,499	$ 10,324,124
Proceeds to us, before expenses	$12.55500	$12.55499	$119,272,491	$137,163,366

We estimate that expenses payable by us in connection with this offering, exclusive of underwriting discounts, will be approximately $2.9 million. We have also agreed to reimburse the underwriters for expenses in an amount up to $30,000 relating to the clearance of this offering with the Financial Industry Regulatory Authority, Inc.

In connection with this offering, the underwriters may purchase and sell ADSs in the open market. Purchases and sales in the open market may include short sales, purchases to cover short positions, which may include purchases pursuant to the underwriters' over-allotment option, and other transactions that would stabilize, maintain or otherwise affect the price of the ADSs.

- Short sales involve secondary market sales by the underwriters of a greater number of ADSs than they are required to purchase in this offering:
  - "Covered" short sales are sales of ADSs in an amount up to the number of ADSs represented by the underwriters' over-allotment option.
  - "Naked" short sales are sales of ADSs in an amount in excess of the number of ADSs represented by the underwriters' over-allotment option.

- The underwriters can close out a short position by purchasing additional ADSs, either pursuant to the underwriters' over-allotment option or in the open market.
    - To close a naked short position, the underwriters must purchase ADSs in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the ADSs in the open market after pricing that could adversely affect investors who purchase in this offering.
    - To close a covered short position, the underwriters must purchase ADSs in the open market or exercise their over-allotment option. In determining the source of ADSs to close the covered short position, the underwriters will consider, among other things, the price of ADSs available for purchase in the open market as compared to the price at which they may purchase ADSs through their over-allotment option.
- As an additional means of facilitating this offering, the underwriters may bid for, and purchase, ADSs on the Nasdaq Global Select Market, as long as such bids do not exceed a specified maximum, to stabilize the price of the ADSs.

Purchases to cover short positions and stabilizing purchases, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the shares. They may also cause the price of the ADSs to be higher than the price that would otherwise prevail in the open market in the absence of these transactions. The underwriters may conduct these transactions on the Nasdaq Global Select Market, in the over-the-counter market or otherwise. The underwriters are not required to engage in any of these transactions and may discontinue them at any time.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make because of any of those liabilities.

A prospectus in electronic format may be made available on websites maintained by one or more of the underwriters or their respective affiliates. The representatives may agree with us to allocate a number of ADSs to underwriters for sale to their online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' or their respective affiliates' websites and any information contained in any other website maintained by any of the underwriters or their respective affiliates is not part of this prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors in this offering.

Other Relationships

The underwriters are full-service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, principal investment, hedging, financing and brokerage activities. The underwriters and their respective affiliates may, from time to time, engage in transactions with and perform services for us in the ordinary course of their business for which they may receive customary fees and reimbursement of expenses. In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (which may include bank loans or credit default swaps) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

Notice to Prospective Investors in the European Economic Area

In relation to each member state of the European Economic Area that has implemented the Prospectus Directive (each, a relevant member state), with effect from and including the date on which the Prospectus Directive is implemented in that relevant member state (the relevant implementation date), an offer of ADSs described in this prospectus may not be made to the public in that relevant member state other than:

- to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the relevant Dealer or Dealers nominated by us for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive;

provided that no such offer of ADSs shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

For purposes of this provision, the expression an "offer of securities to the public" in any relevant member state means the communication in any form and by any means of sufficient information on the terms of the offer and the ADSs to be offered so as to enable an investor to decide to purchase or subscribe for any ADSs, as the expression may be varied in that member state by any measure implementing the Prospectus Directive in that member state, the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive) and includes any relevant implementing measure in the relevant member state, and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

The sellers of the ADSs have not authorized and do not authorize the making of any offer of ADSs through any financial intermediary on their behalf, other than offers made by the underwriters with a view to the final placement of the ADSs as contemplated in this prospectus. Accordingly, no purchaser of the ADSs, other than the underwriters, is authorized to make any further offer of the ADSs on behalf of the sellers or the underwriters.

Notice to Prospective Investors in the United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (1) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, or the Order, or (2) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (each such person being referred to as a relevant person).

This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

Notice to Prospective Investors in Australia

No prospectus or other disclosure document (as defined in the Corporations Act 2001 (Cth) of Australia, or Corporations Act) in relation to the ADSs has been or will be lodged with the Australian Securities & Investments Commission, or ASIC. This document has not been lodged with ASIC and is only directed to certain categories of exempt persons. Accordingly, if you receive this document in Australia:

- you confirm and warrant that you are either:
    - a "sophisticated investor" under Section 708(8)(a) or (b) of the Corporations Act;

- a "sophisticated investor" under Section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to us which complies with the requirements of Section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;
- a person associated with the company under Section 708(12) of the Corporations Act; or
- a "professional investor" within the meaning of Section 708(11)(a) or (b) of the Corporations Act, and to the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act any offer made to you under this document is void and incapable of acceptance; and

- you warrant and agree that you will not offer any of the ADSs for resale in Australia within 12 months of that ADSs being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under Section 708 of the Corporations Act.

Notice to Prospective Investors in Canada

The securities may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the securities must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to Section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Notice to Prospective Investors in France

Neither this prospectus nor any other offering material relating to the ADSs described in this prospectus has been submitted to the clearance procedures of the *Autorité des Marchés Financiers* or of the competent authority of another member state of the European Economic Area and notified to the *Autorité des Marchés Financiers*. The ADSs have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France.

Neither this prospectus nor any other offering material relating to the ADSs has been or will be:

- released, issued, distributed or caused to be released, issued or distributed to the public in France; or
- used in connection with any offer for subscription or sale of the ADSs to the public in France.

Such offers, sales and distributions will be made in France only:

- to qualified investors (*investisseurs qualifiés*) and/or to a restricted circle of investors (*cercle restreint d'investisseurs*), in each case investing for their own account, all as defined in and in accordance with articles L.411-2, D.411-1, D.411-2, D.734-1, D.744-1, D.754-1 and D.764-1 of the French Code monétaire et financier;

- to investment services providers authorized to engage in portfolio management on behalf of third parties; or
- in a transaction that, in accordance with article L.411-2-II-1° -or-2° -or 3° of the French Code *monétaire et financier* and article 211-2 of the General Regulations (*Règlement Général*) of the *Autorité des Marchés Financiers*, does not constitute a public offer (*appel public à l'épargne*).

The ADSs may be resold directly or indirectly, only in compliance with articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French Code *monétaire et financier*.

Notice to Prospective Investors in Hong Kong

The ADSs may not be offered or sold in Hong Kong by means of any document other than (1) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), or (2) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (3) in other circumstances which do not result in the document being a "prospectus" within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong) and no advertisement, invitation or document relating to the ADSs may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to ADSs which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Notice to Prospective Investors in the State of Israel

In the State of Israel, this prospectus shall not be regarded as an offer to the public to purchase shares of ADSs under the Israeli Securities Law, 5728 - 1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728 - 1968, including, inter alia, if: (1) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions, or the Addressed Investors; or (2) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728 - 1968, subject to certain conditions, or Qualified Investors. The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. We have not and will not take any action that would require us to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728 - 1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for the ADSs to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728—1968. In particular, we may request that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (1) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728 - 1968; (2) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728 - 1968 regarding Qualified Investors is applicable to it; (3) that it will abide by all provisions set forth in the Israeli Securities Law, 5728 - 1968 and the regulations promulgated thereunder in connection with this offering; (4) that the shares of ADSs that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728 -1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728 -1968; and (5) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor's name, address and passport number or Israeli identification number.

Notice to Prospective Investors in Japan

The ADSs offered in this prospectus have not been and will not be registered under the Financial Instruments and Exchange Law of Japan. The ADSs have not been offered or sold and will not be offered or sold, directly or indirectly, in Japan or to or for the account of any resident of Japan (including any corporation or other entity organized under the laws of Japan), except (1) pursuant to an exemption from the registration requirements of the Financial Instruments and Exchange Law and (2) in compliance with any other applicable requirements of Japanese law.

Notice to Prospective Investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the ADSs may not be circulated or distributed, nor may the ADSs be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (1) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (2) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA or (3) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to compliance with conditions set forth in the SFA.

Where the ADSs are subscribed or purchased under Section 275 of the SFA by a relevant party which is:

- a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, shares, debentures and units of ADSs and debentures of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the ADSs pursuant to an offer made under Section 275 of the SFA except:
    - to an institutional investor (for corporations, under Section 274 of the SFA) or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of ADSs and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than $200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions specified in Section 275 of the SFA;
    - where no consideration is or will be given for the transfer; or
    - where the transfer is by operation of law.

EXPENSES RELATING TO THE OFFERING

The following table sets forth the costs and expenses, other than underwriting discounts and commissions, payable in connection with this offering. All amounts are estimated except the SEC registration fee, the Financial Industry Regulatory Authority, Inc., or FINRA, filing fee and the Nasdaq initial listing fee. Except as otherwise noted, all the expenses below will be paid by us.

Expense	Amount
SEC registration fee	US$ 16,091
FINRA filing fee	22,624
Nasdaq initial listing fee	150,000
Legal fees and expenses	1,700,000
Accounting fees and expenses	500,000
Printing expenses	300,000
Miscellaneous fees and expenses	211,285
Total	US$2,900,000

LEGAL MATTERS

The validity of the ordinary shares represented by the ADSs and certain other matters of Australian law will be passed upon for us by Gilbert + Tobin. Certain matters as to U.S. federal law and New York state law and the validity of the pre-funded warrants offered hereby will be passed upon for us by Cooley LLP, New York, New York and Cooley LLP, Singapore. Legal counsel to the underwriters in connection with this offering are Goodwin Procter LLP, Boston, Massachusetts, with respect to U.S. federal law, and Herbert Smith Freehills, Melbourne, Australia, with respect to Australian law.

EXPERTS

The financial statements included in this prospectus have been audited by Deloitte Touche Tohmatsu, an independent registered public accounting firm, as stated in their report appearing herein. Such financial statements are included in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

The offices of Deloitte Touche Tohmatsu are located at Tower 2, Brookfield Place, 123 St. Georges Terrace, Perth, WA 6000, Australia.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a Registration Statement on Form F-1 under the Securities Act with respect to the ADSs and pre-funded warrants offered in this prospectus. A related registration statement on Form F-6 (File No. 333-249327) has been filed with the SEC to register the ADSs. This prospectus, which forms a part of the Registration Statement, does not contain all of the information included in the Registration Statement. Certain information is omitted and you should refer to the Registration Statement and its exhibits for that information. With respect to references made in this prospectus to any contract or other document of Opthea, such references are not necessarily complete and you should refer to the exhibits attached to the Registration Statement for copies of the actual contract or document.

Upon the closing of this offering, we will become subject to periodic reporting and other informational requirements of the Exchange Act as applicable to foreign private issuers. Accordingly, we will be required to file reports, including annual reports on Form 20-F, periodic reports and other information, with the SEC.

We are allowed four months after the end of our fiscal year to file our annual report with the SEC, and we are not required to disclose certain detailed information regarding executive compensation that is required from U.S. domestic issuers. Also, as a foreign private issuer, we are exempt from the rules of the Exchange Act prescribing the furnishing of proxy statements to shareholders, and the members of our board of directors, our senior management and our principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act.

As a foreign private issuer, we are also exempt from the requirements of Regulation FD (Fair Disclosure) which, generally, are meant to ensure that select groups of investors are not privy to specific information about an issuer before other investors. We are, however, still subject to the anti-fraud and anti-manipulation rules of the SEC, such as Rule 10b-5. Since many of the disclosure obligations required of us as a foreign private issuer are different than those required of U.S. domestic reporting companies, our shareholders, potential shareholders and the investing public in general should not expect to receive information about us in the same amount, or at the same time, as information is received from, or provided by, other U.S. domestic reporting companies. We are only liable for violations of the rules and regulations of the SEC that apply to us as a foreign private issuer.

The SEC maintains a website at www.sec.gov that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC. You also can inspect our registration statement, as well as any other information we file with or furnish to the SEC, on this website. This reference to the SEC's website is an inactive textual reference only and is not a hyperlink.

We expect to make our annual reports and other information filed with or furnished to the SEC available, free of charge, through our website at www.opthea.com as soon as reasonably practicable after those reports and other information are filed with or furnished to the SEC. The information contained on, or that can be accessed through, our website is not part of, and is not incorporated into, this prospectus.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of Opthea Limited

Opinion on the Financial Statements

We have audited the accompanying consolidated statements of financial position of Opthea Limited and subsidiary (the "Company") as of June 30, 2020 and 2019, the related consolidated statements of profit or loss and other comprehensive income, changes in equity, and cash flows for each of the two years in the period ended June 30, 2020 and the related notes (collectively referred to as the "financial statements").

In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of June 30, 2020 and 2019, and the results of its operations and its cash flows for each of the two years in the period ended June 30, 2020, in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audit, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audit provides a reasonable basis for our opinion.

/s/ Deloitte Touche Tohmatsu

DELOITTE TOUCHE TOHMATSU

Perth, Australia

1 September 2020

We have served as the Company's auditor since 2012.

CONSOLIDATED STATEMENT OF PROFIT OR LOSS AND OTHER COMPREHENSIVE INCOME
FOR THE YEARS ENDED JUNE 30, 2019 AND 2020

	Note	2019 A$	2020 A$
Revenue	7	159,064	87,075
Other income	8	836,821	783,830
Research and development expenses	9	(31,347,891)	(17,954,073)
Patent expenses		(161,148)	(429,229)
Intellectual property costs		(112,795)	(114,046)
Administrative expenses	10	(5,174,755)	(7,001,507)
Occupancy expenses	10	(108,904)	(33,846)
Net foreign exchange gain / (loss)		362,574	(400,608)
Loss before income tax		(35,547,034)	(25,062,404)
Income tax benefit	11	14,636,973	8,533,123
Loss for the year	21	(20,910,061)	(16,529,281)
Other Comprehensive income			
Items that will not be reclassified subsequently to profit or loss:			
Fair value gains on investments in financial assets		259,864	58,840
Other comprehensive income for the period, net of tax		259,864	58,840
Total comprehensive loss for the year		(20,650,197)	(16,470,441)
Loss for the year is attributable to:			
Owners of the Company	21	(20,910,061)	(16,529,281)
		(20,910,061)	(16,529,281)
Total comprehensive loss for the year is attributable to:			
Owners of the Company		(20,650,197)	(16,470,441)
		(20,650,197)	(16,470,441)
Loss per share attributable to Owners of the Company—basic and diluted (in cents)	12	(8.98)	(6.34)

The above consolidated statement of profit or loss and other comprehensive income should be read in conjunction with the accompanying notes.

CONSOLIDATED STATEMENT OF FINANCIAL POSITION AS AT JUNE 30, 2019 AND 2020

	Note	2019 A$	2020 A$
ASSETS			
Current Assets			
Cash and cash equivalents	13	21,534,919	62,020,382
Current tax receivable	11	14,636,973	8,533,123
Receivables	14	295,786	284,391
Prepayments		424,603	478,632
Total Current Assets		36,892,281	71,316,528
Non-current Assets			
Investments in financial assets	15	714,118	289,980
Plant and equipment		54,063	37,180
Right-of-use asset	16	—	243,510
Total Non-Current Assets		768,181	570,670
TOTAL ASSETS		37,660,462	71,887,198
LIABILITIES			
Current Liabilities			
Payables	17	5,951,942	5,895,034
Lease liabilities	16	—	145,043
Other financial liabilities		25,592	237,820
Provisions	18	538,547	640,934
Total Current Liabilities		6,516,081	6,918,831
Non-Current Liabilities			
Lease liabilities	16	—	120,033
Provisions	19	24,844	40,197
Total Non-Current Liabilities		24,844	160,230
TOTAL LIABILITIES		6,540,925	7,079,061
EQUITY			
Contributed equity	20	113,021,993	162,102,553
Accumulated losses	21	(86,060,060)	(102,589,341)
Reserves	21	4,157,604	5,294,925
TOTAL EQUITY		31,119,537	64,808,137
TOTAL LIABILITIES AND EQUITY		37,660,462	71,887,198

The above consolidated statement of financial position should be read in conjunction with the accompanying notes.

CONSOLIDATED STATEMENT OF CHANGES IN EQUITY
FOR THE YEARS ENDED JUNE 30, 2019 AND 2020

	Note	Contributed equity A$	Options reserve A$	Share-based payments reserve A$	Fair value of investments reserve A$	Accumulated losses A$	Total equity A$
As July 1, 2018		98,403,149	1,989,067	2,452,838	477,391	(65,149,999)	38,172,446
Fair value gains on investments in financial assets(1)	21	—	—	—	259,864	—	259,864
Loss for the year(1)		—	—	—	—	(20,910,061)	(20,910,061)
Total comprehensive income and expense for the period		—	—	—	259,864	(20,910,061)	(20,650,197)
Recognition of share-based payment	21	—	—	967,511	—	—	967,511
Transfer from option reserve on exercise of options	20	1,989,067	(1,989,067)	—	—	—	—
Issue of ordinary shares on exercise of options	20	12,629,777	—	—	—	—	12,629,777
As June 30, 2019		113,021,993	–	3,420,349	737,255	(86,060,060)	31,119,537
Fair value gains on investments in financial assets(1)	21	—	—	—	58,840	—	58,840
Loss for the year(1)		—	—	—	—	(16,529,281)	(16,529,281)
Total comprehensive income and expense for the period		—	—	—	58,840	(16,529,281)	(16,470,441)
Recognition of share-based payment	21	—	—	1,078,481	—	—	1,078,481
Issue of ordinary shares on exercise of options	20	420,000	—	—	—	—	420,000
Issue of ordinary shares	20	48,660,560	—	—	—	—	48,660,560
As June 30, 2020		162,102,553	—	4,498,830	796,095	(102,589,341)	64,808,137

(1) Amounts are after tax.

The above consolidated statement of changes in equity should be read in conjunction with the accompanying notes.

CONSOLIDATED STATEMENT OF CASH FLOWS
FOR THE YEARS ENDED JUNE 30, 2019 AND 2020

	Note	2019 A$	2020 A$
CASH FLOWS FROM OPERATING ACTIVITIES			
Interest received		817,314	742,014
Royalty and license income received		170,750	138,916
Grant income received		77,745	62,500
Payment of lease interest		—	(7,680)
Payments to suppliers and employees and for research and development and intellectual property costs (inclusive of Goods and Service Tax)		(37,268,212)	(24,354,991)
Research and development tax incentive scheme credit received		12,017,247	14,636,973
Net cash flows used in operating activities	24	(24,185,156)	(8,782,268)
CASH FLOWS FROM INVESTING ACTIVITIES			
Cash received on disposal of financial assets		339,046	482,978
Purchase of plant and equipment		(18,070)	(7,238)
Net cash flows provided by investing activities		320,976	475,740
CASH FLOWS FROM FINANCING ACTIVITIES			
Payment of lease liabilities		—	(100,189)
Net proceeds on issue of ordinary shares	20	—	48,660,560
Cash received for ordinary shares issued on exercise of options	20	12,629,777	420,000
Net cash flows provided by financing activities		12,629,777	48,980,371
Net (decrease)/increase in cash and cash equivalents		(11,234,403)	40,673,843
Cash and cash equivalents at beginning of year		32,510,230	21,534,919
Effects of exchange rate changes on cash held in foreign currencies		259,092	(188,380)
Cash and cash equivalents at the end of the year	13	21,534,919	62,020,382

The above consolidated statement of cash flows should be read in conjunction with the accompanying notes.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS
FOR THE YEARS ENDED JUNE 30, 2019 AND 2020

1. Reporting entity

The significant accounting policies adopted in preparing the consolidated financial statements of Opthea Limited ("Opthea" or the "Company") and its subsidiary (the "Consolidated Entity" or "Group") for the years ended June 30, 2019 and 2020, are stated to assist in a general understanding of the consolidated financial statements.

Opthea is a company limited by shares, incorporated and domiciled in Australia and has its registered office on Suite 403, Level 4, 650 Chapel Street, South Yarra, Victoria. The Company's ordinary shares are listed on the Australian Securities Exchange (the "ASX") under the symbol "OPT."

The Group's principal activity is the research and development of OPT-302 for the treatment of retinal diseases.

The financial statements for the year ended June 30, 2020 were authorized for issue by the directors on September 1, 2020.

2. Basis of accounting

These financial statements are general purpose financial statements which have been prepared in accordance with International Financial Reporting Standards ("IFRS") as issued by the International Accounting Standards Board (the "IASB").

The financial statements comprise the consolidated financial statements of the Group. For the purposes of preparing the consolidated financial statements, the Company is a for-profit entity.

3. Summary of accounting policies

The consolidated financial statements have been prepared using the significant accounting policies and measurement bases summarized below.

Basis of measurement

The consolidated financial statements have been prepared on a historical cost basis, except for investments classified as financial assets, which have been measured at fair value. All amounts are presented in Australian dollars.

Basis of consolidation

The consolidated financial statements incorporate the financial statements of the Company and its subsidiary. Control is achieved when the Company:

- has power over the investee;
- is exposed, or has rights, to variable returns from its involvement with the investee; and
- has the ability to use its power to affect its returns.

Consolidation of a subsidiary begins when the Company obtains control over the subsidiary and ceases when the Company loses control of the subsidiary.

All intragroup assets and liabilities, equity, income, expenses and cash flows relating to transactions between members of the Group are eliminated in full on consolidation.

Foreign currency translation

Functional and presentation currency

Both the functional and presentation currency of the Group is Australian dollars (A$).

Transactions and balances

Transactions in foreign currencies are initially recorded in the functional currency by applying the exchange rates ruling at the date of the transaction. Monetary assets and liabilities denominated in foreign currencies are retranslated at the rate of exchange ruling at the reporting date.

Non-monetary items that are measured in terms of historical cost in a foreign currency are translated using the exchange rate as at the date of the initial transaction. Non-monetary items measured at fair value in a foreign currency are translated using the exchange rates at the date when the fair value was determined.

Financial assets and liabilities

Recognition and derecognition of financial assets

Purchases and sales of financial assets that require delivery of assets within the time frame generally established by regulation or convention in the market place are recognized on the trade date, i.e., the date that the Group commits to purchase the asset. Financial assets are derecognized when the right to receive cash flows from the financial assets has expired or when the entity transfers substantially all the risks and rewards of the financial assets. If the entity neither retains nor transfers substantially all of the risks and rewards, it derecognizes the asset if it has transferred control of the assets.

When financial assets are recognized initially, they are measured at fair value, plus directly attributable transaction costs.

Cash and cash equivalents

Cash and cash equivalents in the statement of financial position comprise cash at bank and in hand and short-term deposits with an original maturity of three months or less that are readily convertible to known amounts of cash and which are subject to an insignificant risk of changes in value.

For the purposes of the statement of cash flows, cash and cash equivalents consist of cash and cash equivalents as defined above.

Other receivables

Other receivables generally comprise bank interest receivable, other receivables from external parties and Goods and Services Tax (“GST”) credits receivable and are recognized and carried at original invoice amount less an allowance for any uncollectible amounts. The amounts are usually received within 30 to 60 days of recognition.

The Group measures the loss allowance for receivables at an amount equal to lifetime expected credit losses (“ECL”). The ECL on receivables are estimated under the simplified approach as permitted under IFRS 9 “Financial Instruments.” This uses a provision matrix by reference to past experience of the debtor and an analysis of the debtor’s current financial position, adjusted for factors that are specific to the debtors and general economic conditions of the industry in which the debtors operate.

The Group writes off a receivable when there is information indicating that the debtor is in severe financial difficulty and there is no realistic prospect of recovery.

Investments

Investments in financial assets comprise of the Group's non-current investments in listed companies.

On initial recognition, the Group may make an irrevocable election (on an instrument-by-instrument basis) to designate investments in equity instruments as fair value through other comprehensive income ("FVTOCI"). Designation at FVTOCI is not permitted if the equity instrument is held for trading.

Investments in equity instruments at FVTOCI are initially measured at fair value plus transaction costs. Subsequently, they are measured at fair value with gains or losses arising from changes in the fair value recognized in other comprehensive income and accumulated in the fair value of investments reserve. The fair values of investments in financial assets that are actively traded in organized financial markets is determined by reference to quoted market bid prices at the close of business on the reporting date. The cumulative gain or loss is not reclassified to profit or loss on disposal of the equity instruments.

Dividends on these investments in equity instruments are recognized in profit or loss in accordance with IFRS.

Finance income

Almost all of the Group's finance income is earned on short-term bank deposits, and as such, finance income is recognized when the Group's right to receive the payment is established.

Payables

Payables are carried at amortized cost and due to their short-term nature, they are not discounted. They represent liabilities for goods and services provided to the Group prior to the end of the financial year that are unpaid and arise when the Group becomes obliged to make future payments in respect of the purchase of these goods and services.

The amounts are unsecured and are usually paid within 30 days of recognition.

Other financial liabilities

Other financial liabilities in the statement of financial position represent the year end marked-to-market value of forward rate foreign exchange contracts to purchase US dollars ("Contracts"). These Contracts are used to settle US dollar denominated payables and expire within one year.

The foreign exchange loss on recognition of the Contracts is included in "net foreign exchange gain/(loss)" in the Consolidated Statement of Profit or Loss and Other Comprehensive Income.

Plant and equipment

Plant and equipment is stated at historical cost less accumulated depreciation and any accumulated impairment losses. Depreciation on plant and equipment is calculated on a straight-line basis over their useful economic lives as follows:

- Equipment and furniture—3 to 10 years
- Leasehold improvements—8 years or the term of the lease if shorter

The assets' residual values, useful lives and amortization methods are reviewed, and adjusted if appropriate, at each financial year end.

An item of plant and equipment is derecognized upon disposal or when no further economic benefits are expected from its use or disposal.

Leases

The Group has applied IFRS 16 "Leases" using the cumulative catch-up approach and therefore comparative information has not been restated and is presented under International Accounting Standard ("IAS") 17 "Leases". The details of accounting policies under both IAS 17 and IFRS 16 are presented separately below.

Policies applicable from July 1, 2019

The Group assesses at contract inception whether a contract is, or contains, a lease. A contract is, or contains, a lease if the contract conveys the right to control the use of an identified asset for a period of time in exchange for consideration.

The Group applies a single recognition and measurement approach for all leases, except for short-term leases and leases of low-value assets. The Group recognizes lease liabilities to make lease payments and right-of-use assets representing the right to use the underlying assets.

Right-of-use assets

Right-of-use assets are recognized at the commencement date of the lease (that is the date the underlying asset is available for use). Right-of-use assets are measured at cost, less any accumulated depreciation and any impairment losses, and adjusted for any remeasurement of lease liabilities. The cost of right-of-use assets includes the amount of lease liabilities recognized, initial direct costs incurred, and lease payments made at or before the commencement date less any lease incentives received. Right-of-use assets are depreciated on a straight-line basis over the shorter of the lease terms and the estimated useful lives of the assets.

Lease liabilities

Lease liabilities are recognized at the commencement date of the lease at the present value of lease payments to be made over the lease term. The lease payments include fixed payments (including in-substance fixed payments) less any lease incentives receivable.

In calculating the present value of lease payments, the Group uses its incremental borrowing rate at the lease commencement date because the interest rate implicit in the lease is not readily determinable. The incremental borrowing rate is determined using market yields on bonds with similar terms to maturity. After the commencement date, the amount of lease liabilities is increased to reflect the accretion of interest and reduced for the lease payments made. In addition, the carrying amount of lease liabilities is remeasured if there is a modification, a change in the lease term, a change in lease payments (e.g., a change to future lease payments resulting from a change in an index or rate).

Leases of low-value assets

For short-term leases (lease term of 12 months or less) and leases of low-value assets (such as photo copiers and telephones), the Group has opted to recognize a lease expense on a straight-line basis as permitted by IFRS 16. This expense is presented within "administrative expenses" in the Consolidated Statement for Profit or Loss and Other Comprehensive Income.

Policies applicable prior to July 1, 2019

The determination of whether an arrangement is or contains a lease is based on the substance of the arrangement and requires an assessment of whether the fulfilment of the arrangement is dependent on the use of a specific asset or assets and the arrangement conveys a right to use the asset, even if that right is not explicitly specified in an arrangement.

Leases are classified as finance leases whenever the terms of the lease transfer substantially all the risks and rewards of ownership to the lessee. All other leases are classified as operating leases.

Operating lease payments are recognized as an expense in profit or loss on a straight-line basis over the lease term. Operating lease incentives are recognized in the statement of comprehensive income as an integral part of the total lease expense.

The Group held no finance leases during the 2019 or 2020 financial years.

Research and development costs

Research costs are expensed as incurred. An intangible asset arising from the development expenditure on an internal project will only be recognized when the Group can demonstrate the technical feasibility of completing the intangible asset so that it will be available for use or sale, its intention to complete and its ability to use or sell the asset, how the asset will generate future economic benefits, the availability of resources to complete the development and the ability to measure reliably the expenditure attributable to the intangible asset during its development.

As of June 30, 2019 and 2020, the Group is in the research phase and has not capitalized any development costs to date.

Provisions and employee benefits

Wages, salaries, annual leave and sick leave

Liabilities for wages and salaries, including non-monetary benefits and annual leave expected to be settled within 12 months of the reporting date, are recognized in current provisions in respect of employees' services up to the reporting date. They are measured at the amounts expected to be paid when the liabilities are settled. Expenses for non-accumulating sick leave are recognized when the leave is taken and are measured at the rate paid or payable.

Long service leave

The liability for long service leave is recognized in the provision for employee benefits and measured as the present value of expected future payments to be made in respect of services provided by employees up to the reporting date. Consideration is given to expected future wage and salary levels, experience of employee departures, and periods of service. Expected future payments are discounted using market yields at the reporting date on bonds with terms to maturity that match, as closely as possible, the estimated future cash outflows.

Share-based payment transactions

The Group provides benefits to directors and employees (including key management personnel) of the Group in the form of share-based payments, whereby employees render services in exchange for shares or rights over shares (equity-settled transactions).

The cost of these equity-settled transactions with employees is measured by reference to the fair value at the date at which they are granted. Binomial models are used to value the options issued.

The cost of the equity-settled transactions is recognized, together with a corresponding increase in equity, over the period in which the performance conditions are fulfilled (the vesting period), ending on the date on which the relevant employees become fully entitled to the award (the vesting date).

The charge to profit or loss for the period is the cumulative amount less the amounts already charged in previous periods. There is a corresponding credit to equity.

Until an award has vested, any amounts recorded are contingent and will be adjusted if more or fewer awards vest than were originally anticipated to do so.

Contributed equity

Ordinary shares are classified as equity. Incremental costs directly attributable to the issue of new shares or options are shown in equity as a deduction, net of tax, from the proceeds.

Revenue recognition

License revenue in connection with licensing of the Group's intellectual property (including patents) to customers is recognized as a right to use the Group's intellectual property as it exists at the point in time in which the license is granted. This is because the contracts for the license of intellectual property are distinct and do not require, nor does the customer reasonably expect, that the Group will undertake further activities that significantly affect the intellectual property to which the customer has the rights. Although the Group is entitled to sales-based royalties from the eventual sales of goods and services to third parties using the intellectual property licensed, these royalty arrangements do not in themselves indicate that the customer would reasonably expect the Group to undertake such activities, and no such activities are undertaken or contracted in practice. Accordingly, the promise to provide rights to the Group's intellectual property is accounted for as a performance obligation satisfied at a point in time.

The following consideration is received in exchange for licenses of intellectual property:

- *Up-front license fees*—these are fixed amounts and are recognized at the point in time when the Group transfers the intellectual property to the customer.
- *Sales-based royalties*—these are variable consideration amounts promised in exchange for the license of intellectual property and are recognized when the sales to third parties occur given the performance obligation to transfer the intellectual property to the customer is already satisfied.

During the years ended June 30, 2019 and 2020, the Group's only revenue related to sales-based royalties.

Income tax

Current tax

Current tax assets and liabilities for the current and prior periods are measured at the amount expected to be recovered from or paid to the taxation authorities based on the current period's taxable income.

The tax rates and tax laws used to compute the amount are those that are enacted or substantively enacted by the reporting date.

Research and development tax incentive

The Research and Development ("R&D") Tax Incentive Scheme is an Australian Federal Government program under which eligible companies with annual aggregated revenue of less than A$20 million can receive cash amounts equal to 43.5% of eligible research and development expenditures from the Australian Taxation Office ("ATO"). The R&D Tax Incentive Scheme incentive relates to eligible expenditure incurred in Australia and, under certain circumstances, overseas on the development of the Group's lead candidate, OPT-302. The R&D tax incentive is applied annually to eligible expenditure incurred during the Group's financial year following annual application to AusIndustry, an Australian governmental agency, and subsequent filing of its Income Tax Return with the ATO after the financial year end.

The Group estimates the amount of R&D tax incentive after the completion of the financial year based on eligible Australia and overseas expenditures incurred during that year.

The Group has presented incentives in respect of the R&D Tax Incentive Scheme within income tax benefit in the Statement of Profit or Loss and Other Comprehensive Income by analogizing with IAS 12 "Income Taxes".

Deferred tax

Deferred income tax is provided on all temporary differences at the reporting date between the tax bases of assets and liabilities and their carrying amounts for financial reporting purposes.

Deferred income tax liabilities are recognized for all taxable temporary differences except when the deferred income tax liability arises from the initial recognition of goodwill or of an asset or liability in a transaction that is not a business combination and that, at the time of the transaction, affects neither the accounting profit nor taxable profit or loss.

Deferred income tax assets are recognized for all deductible temporary differences, carry forward of unused tax assets (or credits) and unused tax losses, to the extent that it is probable that taxable profit will be available against which the deductible temporary differences, and the carry forward of unused tax credits and unused tax losses can be utilized, except when the deferred income tax asset relating to the deductible temporary differences arises from the initial recognition of an asset or liability in a transaction that is not a business combination and, at the time of the transaction, affects neither the accounting profit or taxable profit or loss.

The carrying amount of deferred income tax assets is reviewed at each reporting date and reduced to the extent that it is no longer probable that sufficient taxable profit will be available to allow all or part of the deferred income tax asset to be utilized.

Unrecognized deferred income tax assets are reassessed at each reporting date and are recognized to the extent that it has become probable that future taxable profit will allow the deferred tax asset to be recovered.

Deferred income tax assets and liabilities are measured at the tax rates that are expected to apply to the year when the asset is realized or the liability is settled, based on tax rates (and tax laws) that have been enacted or substantively enacted at balance date.

Income taxes relating to items recognized directly in equity are recognized directly in equity and not in profit or loss.

Tax consolidation legislation

Tax consolidation is a system adopted by the ATO that treats a group of entities as a single entity for tax purposes. Opthea Limited and its 100% owned subsidiary formed a tax consolidated group effective July 1, 2003. The head entity, Opthea Limited, and its controlled entity, Vegenics Pty Ltd, are current members of the tax consolidated group and account for their own current and deferred tax amounts. Members of the tax consolidated group have adopted the "separate taxpayer within group" method to allocate the current and deferred tax amounts to each entity within the Group. This method requires adjustments for transactions and events occurring within the tax consolidated group that do not give rise to a tax consequence for the Group or that have a different tax consequence at the level of the Group.

Other taxes

Revenues, expenses, assets and liabilities are recognized net of the amount of GST except:

- when the GST incurred on a purchase of goods and services is not recoverable from the taxation authority, in which case the GST is recognized as part of the cost of acquisition of the asset or as part of the expense item as applicable; and
- receivables and payables are stated with the amount of GST included.

The net amount of GST recoverable from, or payable to the taxation authority is included as part of receivables or payables in the statement of financial position.

Cash flows are included in the statement of cash flows on a gross basis and the GST component of cash flows arising from investing and financing activities, which is recoverable from, or payable to, the taxation authority is classified as part of operating cash flows.

Commitments and contingencies are disclosed net of the amount of GST recoverable from, or payable to, the taxation authority.

Reclassification

Certain amounts previously reported in the consolidated financial statements have been reclassified to conform to current year presentation. Such reclassifications did not affect net loss, shareholders' equity or cash flows.

Immaterial error correction

During the year ended June 30, 2020, the Group corrected a prior period immaterial error to the consolidated statement of changes in equity for the year ended June 30, 2019. Specifically, the Group corrected the subtotaled consolidated total comprehensive income and expense for the period included in the Consolidated Statement of Changes in Equity for the year ended June 30, 2019, which had previously included opening amounts for those categories in the subtotals as well. The update of the subtotals had no impact on shareholders' equity, net loss, total other comprehensive losses included in the Consolidated Statement of Profit or Loss and Other Comprehensive Income or Consolidated Statement of Cash Flows for the periods ended June 30, 2019 as well as June 30, 2020.

4. Critical accounting judgments and key sources of estimation uncertainty

In applying the Group's accounting policies, management continually evaluates judgments, estimates and assumptions based on experience and other factors, including expectations of future events that may have an

impact on the Group. All judgments, estimates and assumptions made are believed to be reasonable based on the most current set of circumstances available to management. Actual results may differ from the judgments, estimates and assumptions.

Significant judgments, estimates and assumptions made by management in the preparation of these financial statements are outlined below:

4.1 Critical judgments in applying accounting policies Research and development costs

The majority of Opthea's expenditure is incurred as a result of clinical trials for OPT-302. During the years ended June 30, 2019 and 2020, Opthea progressed Phase 2b wet age-related macular degeneration ("wet AMD") and Phase 1b/2a diabetic macular edema ("DME") trials. A key measure of the Company's performance is the level of expenditure incurred on the research of OPT-302.

Judgment is required in relation to:

- the classification of expenses in the income statement between research and development costs and operating expenses; and
- whether costs relate to R&D, and consequently if they meet the capitalization criteria under International Accounting Standards 38 "Intangible Assets."

The directors have determined that the Group is still in a research phase and accordingly, no development costs have been capitalized as of June 30, 2019 and 2020.

Taxation

Research and development tax incentive

The R&D Tax Incentive Scheme is an Australian Federal Government program under which eligible companies can receive cash refunds of 43.5% of eligible R&D expenditure. Judgments are required as to the R&D tax incentive refundable offset eligibility in respect of:

- the Group's ability to make claims and its continued compliance under the scheme;
- R&D and other supporting costs previously approved by Australian tax authorities;
- estimated amounts, timing and geographical location of future costs related to the projects for which applications have been approved to date; and
- assessment of whether expenditure on projects for which approval has been given by Australian tax authorities relate to Australian or overseas expenditure.

For the years ended June 30, 2019 and 2020, the Group has recognized an R&D tax incentive receivable of A$14.6 million and A$8.5 million respectively within the Consolidated Statement of Financial Position, with a corresponding amount recognized within income tax benefit within the Consolidated Statement of Profit or Loss and Other Comprehensive Income. The R&D tax incentive receivable as at June 30, 2020 is based on the legislation as currently enacted as at June 30, 2020. Any proposed changes to the legislation may have a retrospective impact if the legislation is passed in its currently proposed form.

Investment tax credits such as the R&D tax incentive are outside of the scope of IAS 12 "Income Taxes" and IAS 20 "Accounting for Government Grants and Disclosure of Government Assistance." Based on the guidance in IAS 8 "Accounting Policies, Changes in Accounting Estimates and Errors," companies need to make an accounting policy choice on how to present these incentives, which in practice is done by either analogizing with IAS 12 or with IAS 20. In the Group's opinion, the R&D tax incentive should be presented by analogizing

to IAS 12 because the nature of the incentive is considered to be more closely aligned to income taxes, based on the following considerations:

- The R&D tax incentive is considered an income tax offset which will be offset against the Group's tax obligation if and when the Group returns to a net tax payable position. In addition, whilst the Group is currently eligible to receive cash payments under the scheme since its consolidated revenue is currently below A$20 million, if and when the Group generates revenue in excess of A$20 million the R&D tax incentive will become non-refundable and can only be offset against any future income tax payable by the Group.
- The ATO, which is the tax authority in Australia, manages the annual claims process as the R&D tax incentive is included in the Group's annual income tax return.
- The ATO is also responsible for making the R&D tax incentive cash payment if a company is eligible for a cash refund under the program, oversees compliance with the requirements of the R&D tax incentive scheme and performs pre-issuance reviews.

Income tax

The Group's accounting policy for taxation requires judgments as to the differences between tax and accounting treatments of income and costs recognized in the Consolidated Statement of Profit or Loss and Other Comprehensive Income. Judgment is also required in assessing whether deferred tax assets and liabilities are recognized in the statement of financial position and if accumulated income tax losses can be used to offset potential future tax profits.

4.2 Key sources of estimation uncertainty

Share-based payment transactions

The Group measures the cost of equity-settled transactions with employees by reference to the fair value of the equity instruments at the date at which they are granted. Fair values are determined internally using Binomial models. The related assumptions are detailed in note 28. The accounting estimates and assumptions relating to equity-settled share-based payments have no impact on the carrying amounts of assets and liabilities in future reporting periods but may impact expenses and equity. Should one or more of the assumptions and estimates used in estimating the fair value of share-based payments change, this could have a material impact on the amounts recognized in equity and employee-related expenses.

5. Application of new and revised Accounting Standards

Amendments to Accounting Standards that are mandatorily effective for the current year

The Group has adopted all of the new and revised Standards and Interpretations issued by the IASB that are relevant to its operations and effective for the current year.

New and revised Standards and amendments thereof and Interpretations effective for the current year that are relevant to the Group include:

- IFRS 16 "Leases";
- Annual Improvements to IFRS Standards 2015–2017 Cycle Amendments to IFRS 3 "Business Combinations", IFRS 11 "Joint Arrangements", IAS 12 "Income Taxes" and IAS 23 "Borrowing Costs"; and
- International Financial Reporting Interpretations Committee ("IFRIC") 23 "Uncertainty over Income Tax Treatments".

IFRS 16 Leases

In the current year, the Group has adopted IFRS 16, which is effective for annual periods that begin on or after January 1, 2019.

IFRS 16 introduces new or amended requirements with respect to lease accounting. It introduces significant changes to lessee accounting by removing the distinction between operating and finance lease and requiring the recognition of a right-of-use asset and a lease liability at commencement for all leases, except for short-term leases and leases of low value assets. Details of these new requirements are described in note 3.

The date of initial application of IFRS 16 for the Group is July 1, 2019. The Group has applied IFRS 16 using the cumulative catch-up approach which:

- requires the Group to recognize the cumulative effect of initially applying IFRS 16 as an adjustment to the opening balance of retained earnings at the date of initial application; and
- does not permit restatement of comparatives, which continue to be presented under IAS 17 and IFRIC 4 "Determining whether an Arrangement Contains a Lease".

The Group has made use of the practical expedient available on transition to IFRS 16 not to reassess whether a contract is or contains a lease. Accordingly, the definition of a lease in accordance with IAS 17 and IFRIC 4 will continue to be applied to those leases entered or changed before 1 July 2019.

The change in definition of a lease mainly relates to the concept of control. IFRS 16 determines whether a contract contains a lease based on whether the customer has the right to control the use of an identified asset for a period of time in exchange for consideration. This is in contrast to the focus on "risks and rewards" in IAS 17 and IFRIC 4.

Impact on lease accounting

Former operating leases

IFRS 16 changes how the Group accounts for leases previously classified as operating leases under IAS 17, which operating lease payments were recognized as an expense in profit or loss on a straight line basis over the lease term.

Applying IFRS 16, for all leases (except as noted below), the Group:

- Recognizes right-of-use assets and lease liabilities in the consolidated statement of financial position, initially measured at the present value of the future lease payments;
- Recognizes depreciation of right-of-use assets and interest on lease liabilities in profit or loss; and
- Separates the total amount of cash paid into a principal portion (presented within financing activities) and interest (presented within operating activities) in the consolidated statement of cash flows.

Lease incentives (e.g. rent-free period) are recognized as part of the measurement of the right-of-use assets and lease liabilities whereas under IAS 17 they resulted in the recognition of a lease incentive, amortized as a reduction of rental expenses generally on a straight-line basis. Under IFRS 16, right-of-use assets are tested for impairment in accordance with IAS 36 Impairment of Assets.

For short-term leases (lease term of 12 months or less) and leases of low-value assets (such as photo copier and telephones), the Group has opted to recognize a lease expense on a straight-line basis as permitted by IFRS 16. This expense is presented within 'administrative expenses' in profit or loss.

Financial impact of the initial application of IFRS 16

The Group's previous lease for Opthea's headquarters expired on July 14, 2019: the adoption of IFRS 16 did not have a material impact on the Group's results on the date of transition. Following the renewal of the leased office premises on July 15, 2019, the Group recognized a right-of-use asset of A$365,264 and a corresponding lease liability of A$365,264 in respect of this lease during the year ended June 30, 2020. The impact on profit or loss in the year ended June 30, 2020 was to decrease occupancy expenses by A$110,800; increase depreciation by A$121,754; and increase finance interest expense by A$7,680.

Under IAS 17, all lease payments on operating leases are presented as part of cash flows from operating activities. During the year ended June 30, 2020, the impact of the changes under IFRS 16 reduced the cash used in operating activities by A$100,189 and increased net cash generated from financing activities by the same amount.

Other pronouncements adopted for the first time in the year ended June 30, 2020

In the year ended June 30, 2020, the Group applied a number of amendments to International Financial Reporting Standards and Interpretations issued by the IASB that are effective for an annual period that begins on or after January 1, 2019. Their adoption has not had any material impact on the disclosures or on the amounts reported in these financial statements.

New and revised International Financial Reporting Standards and Interpretations on issue but not yet effective

At the date of authorization of the financial statements, the Group has not applied the following new and revised International Financial Reporting Standards, Interpretations and amendments that have been issued but are not yet effective:

Standard amendment	Effective for annual reporting periods beginning on or after
Amendments to IAS—Sale or Contribution of Assets between an Investor and its Associate or Joint Venture (IFRS 10 and IAS 28) Amendments to IFRS and IAS—Effective Date of Amendments to IFRS 10 and IAS 28 Amendments to IFRS and IAS—Effective Date of Amendments to IFRS 10 and IAS 28 and Editorial Corrections	January 1, 2022
IFRS 17 "Insurance Contracts"	January 1, 2023
Amendments to IFRS 3 "Business Combinations—Definition of a Business"	January 1, 2020
Amendments to IFRS 17, and amendments to the basis for conclusions on IAS 1, IAS 8 and Conceptual Framework—Definition of Material	January 1, 2020

The new and revised International Financial Reporting Standards, Interpretations and amendments listed above are not expected to have a material impact on the amounts recognized or disclosures included in the Group's financial statements.

6. Segment information

The Group operates in one industry and one geographical area, those being the biotechnology and healthcare industry and Australia, respectively.

The Group is focused primarily on developing a novel therapy for the treatment of highly prevalent and progressive retinal diseases.

The chief executive officer regularly reviews entity wide information that is compliant with IFRS. There is only one segment for segment reporting purposes, and the information reviewed by the chief executive officer for the purpose of resources allocation and performance assessment is the same as the information presented in the consolidated financial statements.

The Group's only revenue stream in the current financial year is royalty income generated from licenses granted in respect of the Group's intellectual property that are unrelated to the Group's core business and the development of OPT-302 and that are not under development. These licenses are primarily used by third-party licensees for research purposes. All of the royalty income of A$159,064 and A$87,075 for the years ended June 30, 2019 and 2020, respectively, was generated from customers based outside Australia. The Group does not have any major customers. All property, plant and equipment is located in Australia.

7. Revenue

	2019 A$	2020 A$
Sales based royalties	159,064	87,075
Total revenue	159,064	87,075

8. Other income

	2019 A$	2020 A$
Finance income	755,776	721,330
Grant income	77,745	62,500
Other	3,300	—
Total other income	836,821	783,830

9. Research and development expenses

	2019 A$	2020 A$
Research project costs(1)	31,347,891	17,954,073
Total research and development expenses	31,347,891	17,954,073

(1) The research project costs relate to the research programs for the treatment of retinal diseases by OPT-302.

10. Expenses

	2019 A$	2020 A$
(A) ADMINISTRATIVE EXPENSES		
Employee benefits expenses:		
Salaries and fees	2,020,795	2,124,792
Cash bonuses	414,423	288,811
Superannuation/pensions	217,592	210,383
Share-based payments expense	967,511	1,078,481
Total employee benefits expense	3,620,321	3,702,467
Other expenses:		
Insurance	377,181	500,953
Investor relations costs	411,181	379,255
Audit and accounting	138,156	330,318
Travel expenses	84,103	66,420
Payroll tax	87,247	201,172
Legal fees	22,464	555,622
Advisory fees	—	620,745
Other expenses	401,009	498,680
Total other expenses	1,521,341	3,153,165
Depreciation of:		
Equipment and furniture	19,898	21,754
Leasehold improvements	13,195	513
Right-of-use asset	—	121,754
Total depreciation expense	33,093	144,021
Loss on disposal of non-current assets	—	1,854
Total Administrative Expenses	5,174,755	7,001,507
(B) OCCUPANCY EXPENSES		
Operating lease rentals	78,883	—
Short term and low value lease expenses	—	2,239
Lease incidental costs	30,021	31,607
Total Occupancy Expenses	108,904	33,846

11. Income tax

	2019 A$	2020 A$
(a) Income tax benefit		
The major components of income tax benefit are:		
Statement of Profit or Loss and Other Comprehensive Income		
CURRENT TAX		
Current income tax incentive	14,636,973	8,533,123
	14,636,973	8,533,123
DEFERRED TAX		
In respect of the current year	—	—
Total income tax benefit recognized in the Statement of Profit or Loss and Other Comprehensive Income	14,636,973	8,533,123

	June 30, 2019 A$	June 30, 2020 A$
(b) Current tax receivable		
Research and Development Tax Incentive receivable	14,636,973	8,533,123

(c) Numerical reconciliation between aggregate income tax benefit recognized in the statement of Profit or Loss and Other Comprehensive Income and benefit calculated per the statutory income tax rate

A reconciliation between income tax benefit and the product of accounting loss before income tax multiplied by the Group's applicable income tax rate is as follows:

	2019 A$	2020 A$
Accounting loss before tax	(35,547,034)	(25,062,404)
At the Company's statutory income tax rate of 27.5%	9,775,434	6,892,161
R&D tax incentive on eligible expenses	14,636,973	8,533,123
Non-deductible R&D expenditure	(9,261,833)	(5,394,503)
Other non-deductible expenses—share-based payment expense	(266,066)	(296,582)
Amount of temporary differences and carried forward tax losses not recognized	(247,535)	(1,201,076)
Income tax benefit reported in the Statement of Profit or Loss and Other Comprehensive income	14,636,973	8,533,123

	2019 A$	2020 A$
(d) Recognized deferred tax assets and liabilities in statement of financial position		
Deferred income tax relates to the following:		
DEFERRED TAX LIABILITIES:		
Interest and royalty income receivable (future assessable income)	(56,114)	(103,135)
	(56,114)	(103,135)
DEFERRED TAX ASSETS RELATED TO TEMPORARY DIFFERENCES:		
Accrued expenses and other liabilities	151,821	441,162
Employee provisions	154,933	187,311
Other miscellaneous items	276,942	546,964
	583,696	1,175,437
Less: temporary differences not recognized	(527,582)	(1,072,302)
Net deferred tax recognized in the statement of financial position	—	—

(e) Unrecognized temporary differences

Temporary differences with respect to deferred tax assets associated with intellectual property and other miscellaneous items which have a low probability of realization are unrecognized. These amounted to A$1,072,302 as of June 30, 2020 (2019: A$527,582).

(f) Carry forward unrecognized tax losses

The Group had income tax losses of A$17,287,687 as at June 30, 2020 (2019: A$15,819,190) and capital losses of A$877,704 at June 30, 2020 (2019: A$877,704) for which no deferred tax asset is recognized on the statement of financial position as they are currently not considered probable of realization. These tax losses are available indefinitely for offset against future assessable income subject to continuing to meet relevant statutory tests.

(g) Franking credit balance

Franking credits are a type of tax credit in Australia that is available to the Group's shareholders to reduce double taxation on any dividends paid by the Group. The franking credit balance at the end of the financial year at 30% is A$330,630 (2019: A$330,630), which represents the amount of franking credits available for the subsequent financial year. Franking credits are not recognized in the Consolidated Statement of Financial Position.

12. Earnings per share

	2019 A$	2020 A$
The following reflects the income used in the basic and diluted earnings per share computations:		
(A) EARNINGS USED IN CALCULATING EARNINGS PER SHARE		
Net loss attributable to Owners of the Company	(20,910,061)	(16,529,281)
(B) WEIGHTED AVERAGE NUMBER OF SHARES		
Weighted average number of ordinary shares on issue for basic earnings per share	232,795,371	260,795,745
Dilutive share options	—	—
Weighted average number of ordinary shares adjusted for the effect of dilution	232,795,371	260,795,745
Loss per share (basic and diluted, in cents)	8.98	6.34

Diluted earnings per share is calculated as net loss divided by the weighted average number of ordinary shares and dilutive potential ordinary shares. Options granted under the Long Term Incentive ("LTIP") and Non-Executive Director Share and Option ("NED Plan") plans would generally be included in the calculation due to the conditions of the issuance being satisfied.

As the Group is in a loss position, the options are anti-dilutive and, accordingly, the basic loss per share is the same as the diluted loss per share.

A total number of 18,044,000 options outstanding as of June 30, 2020 (2019: 18,919,000) were anti-dilutive and were therefore excluded from the weighted average number of ordinary shares for the purpose of diluted earnings per share. These options related to the following option plans:

	June 30, 2019	June 30, 2020
NED Plan	6,000,000	6,000,000
LTIP	12,919,000	12,044,000
	18,919,000	18,044,000

All 18,044,000 outstanding options as of June 30, 2020 were exercisable as of that date (2019: 9,905,000).

13. Current assets—cash and cash equivalents

	June 30, 2019 A$	June 30, 2020 A$
Cash at bank and in hand	1,034,919	3,020,382
Short-term deposits	20,500,000	59,000,000
Total cash and cash equivalents	21,534,919	62,020,382

Cash at bank earns interest at floating rates based on daily bank deposit rates. The carrying amounts of cash and cash equivalents represent fair value.

Short term-deposits are with two major Australian banks and are made for varying periods of between 30 and 90 days, depending on the immediate cash requirements of the Group, and earn interest at a fixed rate for the respective short-term deposit periods. At year end, the average rate was 1.01% (2019: 2.36%).

14. Current assets—other receivables

	June 30, 2019 A$	June 30, 2020 A$
Interest receivable	102,162	81,478
GST receivable(1)	91,736	152,866
Royalties receivable(1)	101,888	50,047
Total current receivables	295,786	284,391

(1) The GST and Royalties receivables are non-interest bearing. There were no receivables with a material expected credit loss recorded during the financial year (2019: nil).

15. Non-current assets—Investments in financial assets

	June 30, 2019 A$	June 30, 2020 A$
Listed Australian shares—at fair value(1)	714,118	289,980

Listed investments	Ownership Interest %	Fair value at June 30 (2) A$	Disposal in the financial year (3) A$	Fair value gain/(loss) recognized in OCI (4) A$	Opening fair value A$
June 30, 2019					
Non-current investments:					
Antisense Therapeutics Ltd	1.24%	233,579	(339,047)	317,860	254,766
Optiscan Imaging Limited	1.76%	480,539	—	(57,996)	538,535
Total listed investments		714,118	(339,047)	259,864	793,301
June 30, 2020					
Non-current investments:					
Antisense Therapeutics Ltd	—	—	(482,978)	249,399	233,579
Optiscan Imaging Limited	1.73%	289,980	—	(190,559)	480,539
Total listed investments		289,980	(482,978)	58,840	714,118

(1) These financial assets are investments in equity instruments and are not held for trading; they are held for medium to long-term strategic purposes. Accordingly, the Group has elected to designate these investments in equity instruments as at FVTOCI as recognizing short-term fluctuations in these investments' fair value in profit or loss would not be consistent with the Group's strategy of holding these investments for long-term purposes and realizing their performance potential in the long run.

(2) The fair value represents the share (bid) price at year end and does not include any capital gains tax or selling costs that may be applicable on the disposal of these investments. These non-current investments in listed shares consist of investments in ordinary shares, and therefore have no fixed maturity date or coupon rate.

(3) During the year ended June 30, 2019, 49% of the Group's investment in Antisense Therapeutics Ltd. was sold for net proceeds of A$339,047. As a result, A$214,046 of the previously unrealized net fair value gains recorded in the fair value of investments reserve was realized at this date. Subsequently, during the year ended June 30, 2020, the Group disposed of its remaining 51% investment for net proceeds of A$482,978. As a result, A$249,399 of the previously unrealized net fair value gains recorded in the fair value of investments reserve was realized at this date. In accordance with the Group's accounting policy, the realized gain remains within the fair value of investments reserve. The Group disposed of the investment in line with its Treasury and Investments Policy.

(4) A fair value increase of A$58,840 (2019: A$259,864) in the carrying value of investments has been made through other comprehensive income in the year due to a net increase in their market value in the year.

16. Leases

Right-of-use asset

The Group has a three-year lease contract for its head office premises in Melbourne, Australia which commenced on July 15, 2019. The agreement does not contain any extension options. The carrying amount of the lease at June 30, 2020 is as follows:

	2020 A$
Right-of-Use Asset cost	
Opening balance as at July 1	—
Additions	365,264
	365,264
Right-of-Use Asset Depreciation	
Opening balance as at July 1	—
Depreciation of right-of-use asset	(121,754)
	(121,754)
Net carrying amount as at June 30	243,510

Lease liabilities

Lease liabilities are as indicated below:

At the commencement date of the lease of its office premises, the Group recognizes lease liabilities measured at the present value of lease payments to be made over the lease term ending on July 14, 2022, using an incremental borrowing rate of 3%.

	2020 A$
Carrying amount at July 1	—
New lease	365,264
Payments	(100,189)
Carrying amount at June 30	265,076
Maturity analysis:	
Year 1	152,723
Year 2	127,713
	280,436
Less: unearned interest	(15,360)
	265,076
Analyzed into:	
Current portion	145,043
Non-current portion	120,033
	265,076
The amounts recognized in profit or loss in relation to leases is as follows:	
Depreciation expense on right-of-use asset	121,754
Interest on lease liabilities	7,680
Expense relating to leases of low value assets	9,669
	139,103

The Group did not have any short-term leases during the year ended June 30, 2020.

17. Current liabilities—payables and accrued expenses

	June 30, 2019 A$	June 30, 2020 A$
Accounts payable (unsecured)(1)	5,895,925	5,838,115
Payroll related tax liability	56,017	56,919
Total current payables	5,951,942	5,895,034

(1) Accounts payable are non-interest bearing and are normally settled on 30-day terms.

18. Current liabilities—provisions

	June 30, 2019 A$	June 30, 2020 A$
Annual leave	320,132	403,479
Long service leave	218,415	237,455
Total current provisions	538,547	640,934

19. Non-current liabilities—provisions

	June 30, 2019 A$	June 30, 2020 A$
Long service leave	24,844	40,197

20. Contributed equity

	June 30, 2019 A$	June 30, 2020 A$
(a) Ordinary shares		
Issued and fully paid as of June 30, 2019 and 2020	113,021,993	162,102,553
Movement in ordinary shares:		
Opening balance	98,403,149	113,021,993
Issue of shares on exercise of options	12,629,777	420,000
Issue of shares	—	48,660,560
Transfer from option reserve	1,989,067	—
Total issued and fully paid ordinary shares	113,021,993	162,102,553

Ordinary shares on issue:	No. of Shares	No. of Shares
	2019	2020
Opening balance	202,637,888	249,414,839
Issue of shares	46,776,951	19,742,930
	249,414,839	269,157,769

Fully paid ordinary shares carry one vote per share and carry the right to dividends.

Issued capital at June 30, 2020 amounted to A$162,102,553 (269,157,769 fully paid ordinary shares) net of share issue costs and tax. During the year ended June 30, 2020, the Company issued 18,867,930 ordinary shares in a private placement to institutional investors and 875,000 on the exercise of options for A$49,080,560. At June 30, 2020, the Company had no options outstanding, other than options granted to directors and employees and described in note 28, as all options had been exercised or expired by November 25, 2018. The fair value of the options at their issue date of A$1,989,067, originally recognized in the options reserve (note 21) was transferred to contributed equity during the year ended June 30, 2019.

(b) Options granted to directors and employees

The Company has two share based-payment schemes, the Long Term Incentive Plan and Non-Executive Director Share and Option Plan. Options to subscribe for the Company's shares have been granted under these plans to certain employees and directors. The Company granted 8,844,000 options over ordinary shares under these plans during the year ended June 30, 2019 (note 28). These options had a weighted average fair value at their grant date of A$0.22 per option. During the year ended June 30, 2020, 875,000 options granted under the LTIP were exercised for A$420,000. No options were granted during the year ended June 30, 2020.

(c) Capital management

The Group is not subject to any externally imposed capital requirements. When managing share capital, management's objective is to ensure the entity continues as a going concern as well as to provide benefits to shareholders and for other stakeholders. In order to maintain or achieve an appropriate capital structure, the Company may issue new shares or reduce its share capital, subject to the provisions of the Company's constitution. The Group only commits to significant R&D expenditure when this is fully funded either by existing funds or further equity raises.

21. Accumulated Losses and Reserves

	June 30, 2019 A$	June 30, 2020 A$
(a) Movements in accumulated losses were as follows:		
Balance at July 1	(65,149,999)	(86,060,060)
Net loss for the period	(20,910,061)	(16,529,281)
Balance at June 30	(86,060,060)	(102,589,341)
(b) Reserves		
Fair value of investments reserve (i)	737,255	796,095
Share-based payments reserve (ii)	3,420,349	4,498,830
Option reserve (iii)	—	—
Total reserves	4,157,604	5,294,925
(i) Movement in fair value of investments reserve:		
Opening balance	477,391	737,255
Fair value gains on investments in financial assets	259,864	58,840
Closing balance	737,255	796,095
(ii) Movement in share-based payments reserve:		
Opening balance	2,452,838	3,420,349
Share based payments expense	967,511	1,078,481
Closing balance	3,420,349	4,498,830
(iii) Movement in option reserve:		
Opening balance	1,989,067	—
Transferred to contributed equity	(1,989,067)	—
Closing balance	—	—

(c) Nature and purpose of reserves

Fair value of investments reserve

This reserve records fair value changes on listed investments.

Share-based payment reserve

This reserve is used to record the value of equity benefits provided to executives and employees as part of their remuneration.

Option reserve

On November 25, 2014, the Company issued options to purchase 49,726,672 ordinary shares with an exercise price of A$0.27 expiring on November 25, 2018. The fair value of the options at their issue date of A$1,989,067 was recognized in the option reserve. The same amount, A$1,989,067, was transferred to contributed equity on November 25, 2018 following the exercise and expiry of all quoted options. The balance on the option reserve at June 30, 2020 was nil (2019: nil).

22. Financial risk management objectives and policies

The Group's principal financial assets comprise cash, receivables, short-term deposits and investments in listed shares.

The Group manages its exposure to key financial risks, including interest rate and currency risk in accordance with the Group's financial risk management practices. The objective is to support the delivery of the Group's financial targets while protecting future financial security.

The Group's other various financial assets and liabilities, such as receivables and payables, arise directly from its operations. The main risks arising from the Group's financial assets and liabilities are interest rate risk, foreign currency risk, equity securities price risk and liquidity risk.

The Group uses different methods to measure and manage different types of risks to which it is exposed. These include monitoring levels of exposure to interest rate and foreign exchange risk and assessments of market forecasts for interest rates and foreign exchange rates. Liquidity risk is monitored through future rolling cash flow forecasts.

The board reviews and agrees policies for managing each of these risks as summarized below.

Risk exposures and responses

The Group has investigated the main financial risk areas which could impact its financial assets and determined the impact on post tax (losses) or profits for a range of sensitivities. These can be seen in the post-tax (loss)/profit impact for each risk area.

For each risk area, the equity impact relates solely to reserve movements and excludes movements in accumulated losses as the impact of these can be seen within the post-tax (loss)/profit impact.

(i) Interest rate risk

The Group's exposure to market interest rates relates primarily to the short-term deposits. The deposits are held with two of Australia's largest banks.

The objective of managing interest rate risk is to minimize the Group's exposure to fluctuations in interest rates that might impact its interest income and cash flow. To manage interest rate risk, the Group invests the majority of its cash in short-term deposits for varying periods of between 30 days and 90 days, depending on the short and long-term cash requirements of the Group which is determined based on the Group's cash flow forecast. This consideration also takes into account the costs associated with recalling a term deposit should early access to cash and cash equivalents be required. Cash is not locked into long-term deposits at fixed rates so as to mitigate the risk of earning interest below the current floating rate.

The Group does not have any borrowings at June 30, 2019 or June 30, 2020. The following sensitivity analysis (an annual effect) is based on the interest rate risk exposures at June 30, 2019 and 2020.

At June 30, 2020, if interest rates moved, with all variables held constant, post tax (loss)/profit and equity would have been affected as illustrated in the following table:

	Post tax (loss)/profit impact		Cost of investment	
	2019 A$	**2020 A$**	**2019 A$**	**2020 A$**
Judgments of reasonably possible movements				
+ 0.50% (50 basis points)	71,903	206,700	—	—
– 0.50% (50 basis points)	(71,903)	(206,700)	—	—

The post-tax figures include an offset for unrecognized tax losses (bringing the tax effect to nil) for the years ended June 30, 2019 and 2020.

Significant assumptions used in the interest rate sensitivity analysis include:

- The reasonably possible movement of 0.5% was calculated by taking the interest rates as at balance date, moving these by plus and minus 0.5% and then re-calculating the interest on term deposits with the 'new-interest-rate'.
- The net exposure at balance date is representative of what the Group was and is expecting to be exposed to in the next twelve months from balance date.

(ii) Price risk

The Group's investment in listed shares is exposed to equity securities price risk and as such their fair values are exposed to fluctuations as a result of changes in market prices.

Equity price risk is the risk that the fair value of equities will decrease as a result of share price movements. The Group's equity investments are publicly traded on the Australian Securities Exchange (ASX) and are designated and accounted for as investments in financial assets.

The investments in listed shares are not held for short-term trading. Their values are reviewed regularly by management and the board. The strategy for realizing any part of these investments is determined based on the liquidity of the respective stocks, potential off-market acquirers and likely developments in their values based on publicly available information.

At June 30, 2019 and 2020, had the share price moved with all other variables held constant, post tax (loss)/ profit and equity would have been affected as illustrated in the table below:

	Impact of loss after tax	Impact on equity after tax	Impact of loss after tax	Impact on equity after tax
	2019 A$	2019 A$	2020 A$	2020 A$
Judgments of reasonably possible movements				
Change in variables 10% increase in listed share price	49,988	49,988	20,299	20,299
10% decrease in listed share price	(49,988)	(49,988)	(20,299)	(20,299)

(iii) Foreign currency risk

As a result of services provided by non-related entities in the United States, Canada, United Kingdom and Europe, part of the Group's financial assets and liabilities are affected by movements in the exchange rate.

The Group does not enter into any hedging transactions.

At the reporting date, the Group has the following exposure to foreign currencies:

	As of June 30, 2019			
2019	USD A$	EUR A$	GBP A$	CAD A$
Financial assets				
Cash	551,719	—	—	—
Receivables	101,888	—	—	—
Financial liabilities				
Payables	(5,135,089)	—	(51,269)	(4,351)
Net exposure	(4,481,482)	—	(51,269)	(4,351)

	As of June 30, 2020			
2020	USD A$	EUR A$	GBP A$	CAD A$
Financial assets				
Cash	61,680	—	—	—
Receivables	37,547	—	—	—
Financial liabilities				
Payables	(4,878,718)	(14,887)	(34,144)	—
Other financial liabilities	(237,820)	—	—	—
Net exposure	(5,017,313)	(14,887)	(34,144)	—

The following sensitivity is based on the foreign currency risk exposures in existence at June 30, 2019 and 2020.

As of June 30, 2019 and 2020, had the Australian dollar moved with all other variables held constant, post tax (loss) profit and equity would have been affected as illustrated in the table below:

	Post tax (loss)/profit impact		Cost of investment	
	June 30, 2019 A$	June 30, 2020 A$	June 30, 2019 A$	June 30, 2020 A$
Judgments of reasonably possible movements				
AUD/USD +10%	285,185	319,284	—	—
AUD/USD –10%	(348,560)	(390,235)	—	—

There was minimal or insignificant exposure to the GBP, EUR and CAD during the years ended June 30, 2019 and 2020.

Significant assumptions used in the foreign currency exposure sensitivity analysis include:

The reasonably possible movement of 10% was calculated by taking the currency spot rates as at balance date, moving these up and down by 10% and then re-converting the currencies into AUD with the new spot rate. This methodology reflects the translation methodology undertaken by the Group.

The net exposure at balance date is representative of what the Group was and is expecting to be exposed to in the next 12 months from the balance date.

Management believes the balance date risk exposures are representative of the risk exposure inherent in the financial instruments.

(iv) Credit risk

Credit risk is associated with those financial assets of the Group which comprise cash and cash equivalents, receivables and listed investments. The Group's exposure to credit risk arises from default of the counterparty, with a maximum exposure equal to the carrying amount of these investments. Credit risk is considered minimal as the Group transacts with reputable recognized Australian banks.

(v) Liquidity risk

Liquidity risk arises from the financial liabilities of the Group and the Group's subsequent ability to meet their obligations to repay their financial liabilities as and when they fall due. The Group has minimal liquidity risk because of the high balances of cash and cash equivalents; however, the Group manages liquidity risk by maintaining reserves and by monitoring forecast and actual cash flows and by matching the maturity profiles of financial assets and liabilities. The financial liabilities of the Group relate to trade payables that are all expected to be paid within 12 months.

The Group's objective is to maintain an appropriate cash asset balance to fund its operations.

(vi) Fair value

The Group has investments in listed equities which are calculated using the quoted prices in an active market and are considered level 1 fair value measurements. The Group does not have any derivative investments where the fair value is estimated using inputs other than quoted prices that are observable for the asset or

liability, either directly (as prices) or indirectly (i.e. derived from prices). The Group also does not hold any financial instruments where fair value measurement uses observable inputs that require significant adjustments based on observable inputs to estimate its value.

Details of the fair value of the investment in financial assets are disclosed in note 15 of the financial statements.

The fair value of financial assets and financial liabilities in the consolidated statement of financial position at June 30, 2019 and 2020 is the same as their carrying amounts.

The methods for estimating fair value are also outlined in the relevant notes to the financial statements.

23. Subsidiary

The consolidated financial statements include the financial statements of Opthea Limited and the subsidiary in the following table:

	Company % equity interest	
Name of company	2019%	2020%
Vegenics Pty Ltd (1)	100	100

(1) Opthea Limited is the ultimate parent entity. Vegenics Pty Ltd. is incorporated in Australia and has the same financial year as Opthea Limited.

Balances and transactions between the Company and its subsidiary, which is a related party of the Company, have been eliminated on consolidation and are not disclosed in this note.

24. Cash flow statement reconciliation

(a) Reconciliation to cash at the end of the year

	June 30, 2019 A$	June 30, 2020 A$
Cash at bank and in hand (note 13)	21,534,919	62,020,382
	21,534,919	62,020,382
(b) Reconciliation of net loss after tax to net cash flows from operations		
Net loss for the year	(20,910,061)	(16,529,281)
Adjustments for:		
Income tax benefit recognized in profit or loss	(14,636,973)	(8,533,123)
Depreciation of non-current assets	33,093	22,267
Net loss on disposal of non-current assets	—	1,854
Depreciation of right-of-use assets	—	121,754
Share-based payments	967,511	1,078,481
Net exchange differences	(259,092)	400,608
	(13,895,461)	(6,908,159)
Changes in working capital:		
Payables	(1,427,978)	(56,907)
Receivables	97,946	11,395
Prepayments	(132,346)	(54,029)
Provisions	65,497	117,740
Net cash used in operating activities	(36,202,403)	(23,419,241)
R&D tax incentive received	12,017,247	14,636,973
Net cash generated by operating activities	(24,185,156)	(8,782,268)
(c) Reconciliation of borrowings arising from financing activities		
Balance at July 1	—	—
Non-cash additions(1)	—	365,265
Payment of lease liabilities	—	(100,189)
Balance at June 30	—	265,076

(1) Non-cash addition represents the new lease on the Company's office premises in Melbourne, Australia that commenced on July 15, 2019.

25. Commitments

Lease commitments—Group as lessee

Lease commitments are in respect of low value leases which have not been recognized in the Statement of Financial Position. These leases are expensed on a straight-line basis over the term of the lease.

	June 30, 2019 A$	June 30, 2020 A$
Within one year	7,029	6,540
After one year but not more than five years	—	16,895
	7,029	23,435

Research projects and license commitments

The Group has entered into R&D contracts and intellectual property license agreements with various third parties in respect of services for the Phase 2a DME clinical trial and the clinical grade manufacture of OPT-302. Expenditure commitments relating to these and intellectual property license agreements are payable as follows:

	June 30, 2019 A$	June 30, 2020 A$
Within one year	7,776,947	11,139,196
After one year but not more than five years	85,446	427,248
After more than five years	128,169	109,061
	7,990,562	11,675,505

26. Contingencies

The Group is party to research license/collaboration agreements with three third parties with respect to which a commitment to pay is contingent on the achievement of research milestones. Assuming all milestones are achieved within the timeframes stipulated in the contracts, those which could become payable in less than one year total A$382,790 (2019: nil) and those which could become payable in more than one year total A$16,749,885 (2019: A$16,728,122).

Under these license/collaboration agreements, payments are to be made only if certain research and clinical development milestones are achieved and royalties may become payable on any eventual sales of products developed under these agreements.

The Group had a bank guarantee outstanding at June 30, 2020 in respect of a rental deposit for its office premises of A$57,281 (2019: A$43,841).

27. Key management personnel

(a) Compensation of Key Management Personnel

	June 30, 2019 A$	June 30, 2020 A$
Short-term employee benefits	1,002,359	1,011,460
Post-employment benefits	95,225	96,089
Share-based payments expense	752,306	619,325
Total compensation	1,849,890	1,726,874

(b) Other transactions and balances with director and key management personnel and their related parties

There were no other director and key management personnel related party transactions during the years ended June 30, 2019 and 2020.

28. Share-based payments

Recognized share-based payment expenses

The expense recognized for share-based payments during the year is shown in the table below:

	June 30, 2019 A$	June 30, 2020 A$
Expense arising from equity-settled share-based payment transactions:		
Director and employee services received	967,511	1,078,481

Non-executive director and employee share option plans

During the 2015 financial year, the Group introduced an ownership-based compensation scheme for non-executive directors, executives and senior employees, the Long Term Incentive Plan (LTIP) and Non-Executive Directors Share and Option Plan (NED Plan). In accordance with the terms of the plans, as approved by shareholders at the 2014 annual general meeting, eligible non-executive directors, executives and senior employees with the Group may be granted options to purchase ordinary shares.

Each director and employee option converts into one ordinary share of Opthea on exercise. No amounts are paid or payable by the recipient on receipt of the option. The options carry neither rights to dividends nor voting rights and are not transferable. Options may be exercised at any time from the date of vesting to the date of their expiration.

The number of options granted is subject to approval by the board and rewards executives and senior employees to the extent of the Group's and the individual's achievement judged against both qualitative and quantitative criteria as determined by the board on a case by case basis.

The vesting condition of options granted under the LTIP and NED Plan is continuous service.

Options/Rights series	Grant date	Grant date fair value A$	Exercise price A$	Expiry date	Vesting date
LTIP—director	March 7, 2016	0.19	0.48	March 7, 2021	June 30, 2016
LTIP—director FY2019	November 29, 2018	0.20	0.855	November 29, 2022	November 29, 2019
LTIP—employees	March 31, 2016	0.24	0.48	January 1, 2022	January 1, 2017
LTIP—employees FY2018	August 23, 2017	0.33	1.16	January 1, 2023	June 30, 2018
LTIP—employees FY2019	April 3, 2019	0.26	0.855	April 3, 2023	April 3, 2020
NED Plan	March 7, 2016	0.19	0.48	March 7, 2021	June 30, 2016
NED Plan FY2019	November 29, 2018	0.20	0.855	November 29, 2022	November 29, 2019

There has been no modification of the terms and conditions of the above share-based payment arrangements since the grant date.

Fair value of options granted

A binomial model has been used to determine the fair value of all options granted. Where relevant, the expected life used in the model has been adjusted based on management's best estimate for the effects of non-transferability, exercise restrictions (including the probability of meeting market conditions attached to the option), and behavioral considerations. Expected volatility is based on the historical share price volatility over the past four or five years.

	Grant date share price A$	Exercise price A$	Fair value per option A$	Expected volatility %	Option life years	Dividend yield %	Risk free interest rate %
LTIP—director	0.38	0.48	0.19	65	5	0	2.09
LTIP—director FY2019	0.57	0.855	0.20	58	4	0	2.04
LTIP—employees	0.70	0.48	0.24	65	5	0	2.09
LTIP—employees FY2018	0.43	1.16	0.32	66	5	0	2.09
LTIP—employees FY2019	0.67	0.855	0.26	57	4	0	2.04
NED Plan	0.38	0.48	0.19	65	5	0	2.09
NED Plan FY2019	0.57	0.855	0.20	58	4	0	2.04

Movements in options during the year

The following reconciles the options outstanding at the beginning and end of the year:

	June 30, 2019		June 30, 2020	
	Number of options	Weighted average exercise price A$	Number of options	Weighted average exercise price A$
Balance at beginning of year	10,075,000	0.46	18,919,000	0.67
Granted during the year:				
To employees and directors under the LTIP and NED Plan	8,844,000	0.855	—	—
Exercised during the year	—	—	(875,000)	0.48
Expired during the year	—	—	—	—
Balance at end of year	18,919,000	0.67	18,044,000	0.68
Exercisable at end of year	9,905,000	0.50	18,044,000	0.68

The options outstanding at June 30, 2020 had a weighted average exercise price of A$0.68 (2019: A$0.67) and a weighted average remaining contractual life of 626 days (2019: 716 days).

29. Events after the balance sheet date

On August 21, 2020, the Company announced it had completed End-of-Phase 2 meetings with the U.S. Food and Drug Administration and a Scientific Advice meeting with the European Medicines Agency to obtain guidance on the Company's Phase 3 clinical development plans. The outcome of the meetings support the progression of OPT-302 into Phase 3 and pre-commercial development. No other matters or circumstances have arisen since the end of the reporting period which significantly affected, or may significantly affect, the operations of the Group, the results of those operations, or the state of affairs of the Group in future financial years.

8,563,300 American Depositary Shares

Pre-Funded Warrants to Purchase 936,700 American Depositary Shares

Representing 76,000,000 Ordinary Shares

PROSPECTUS

October 16, 2020

Joint Book-Running Managers

Citigroup **SVB Leerink**

Lead Managers

Oppenheimer & Co. **Truist Securities**

Through and including November 10, 2020 (the 25th day after the date of this prospectus), all dealers effecting transactions in the ADSs, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.