Radius Health, Inc.
Form 10-K
February 28, 2019
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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
FORM 10-K

(Mark One)

ý ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2018

OR

o TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from to

Commission file number: 001-35726

Radius Health, Inc.
(Exact name of registrant as specified in its charter)

Delaware	80-0145732
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
950 Winter Street Waltham, Massachusetts (Address of principal executive offices)	02451 (Zip Code)

617-551-4000
(Registrant's telephone number, including area code)

Securities issued pursuant to Section 12(b) of the Act: Common Stock
Securities issued pursuant to Section 12(g) of the Act: None

Title of each class	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	The Nasdaq Global Market

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ý No o

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes o No ý

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ý No o

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ý No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ý

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ý Accelerated filer o Non-accelerated filer o Smaller reporting company o Emerging growth company o

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes o No ý

The aggregate market value of the registrant's common stock, $0.0001 par value per share ("Common Stock"), held by non-affiliates of the registrant, based on the last sale price of the Common Stock at the close of business on June 30, 2018 was $1.3 billion. For the purpose of the foregoing calculation only, all directors and executive officers of the registrant are assumed to be affiliates of the registrant.

Number of shares outstanding of the registrant's common stock, par value $0.0001 per share, as of February 25, 2019: 45,750,168

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement for its 2019 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

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For the Fiscal Year Ended December 31, 2018
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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This report, including in the sections titled “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Business,” contains, in addition to historical information, forward-looking statements. We may, in some cases, use words such as “project,” “believe,” “anticipate,” “plan,” “expect,” “estimate,” “intend,” “continue,” “should,” “would,” “could,” “potentially,” “will,” “may” or similar words and expressions that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements in this Annual Report on Form 10-K may include, among other things, statements about:

- our expectations regarding commercialization of TYMLOS® in the U.S., including our market access coverage expectations, and our ability to successfully commercialize TYMLOS in the U.S.;
- the therapeutic benefits and effectiveness of TYMLOS and our investigational product candidates and the potential indications and market opportunities therefor;
- our ability to obtain U.S. and foreign regulatory approval for our product candidates, and the timing thereof including the approval of abaloparatide-SC outside of the U.S.;
- our ability to compete with other companies that are or may be developing or selling products that are competitive with TYMLOS or our investigational product candidates;
- anticipated trends and challenges in the market in which TYMLOS will compete and in other potential markets in which we may compete;
- our expectations regarding the timing of our regulatory submissions;
- our expectations for our Phase 3 studies of elacestrant and abaloparatide-patch or other clinical trials, including projected costs, study designs or the timing for initiation, recruitment or completion;
- our plans with respect to collaborations and licenses related to the development, manufacture or sale of TYMLOS and our investigational product candidates, including our plans to enter into a global partnership for elacestrant;
- the progress of, timing of and amount of expenses associated with our research, development and commercialization activities;
- the safety profile and related adverse events of TYMLOS and our investigational product candidates;
- the ability of our investigational product candidates to meet existing or future regulatory standards;
- our expectations regarding federal, state and foreign regulatory requirements;
- the success of our clinical studies for our investigational product candidates;
- our expectations as to future financial performance, expense levels, future payment obligations and liquidity sources;
- our ability to attract, motivate, and retain key personnel; and
- other factors discussed elsewhere in this report.

The outcome of the events described in these forward-looking statements is subject to known and unknown risks, uncertainties and other important factors that could cause actual results to differ materially from the results anticipated by these forward-looking statements. These important factors include our financial performance, the uncertainties inherent in the early stages of commercializing any new pharmaceutical product or the initiation, execution and completion of clinical trials, uncertainties surrounding the timing of availability of data from our clinical trials, ongoing discussions with and actions by regulatory authorities, our ability to attract and retain customers, our development activities and those other factors we discuss in Item 1A of this Annual Report on Form 10-K under the caption “Risk Factors.” You should read these factors and the other cautionary statements made in this report as being applicable to all related forward-looking statements wherever they appear in this report. These risk factors are not exhaustive and other sections of this report may include additional factors which could adversely impact our business and financial performance.

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PART I

ITEM 1. BUSINESS.

Unless otherwise provided in this report, all references in this report to "we," "us," "Radius," "our company," "our," or the "Company" refer to Radius Health, Inc. and our subsidiaries.

Overview

We are a science-driven fully integrated biopharmaceutical company that is committed to developing and commercializing innovative endocrine therapeutics in the areas of osteoporosis and oncology. In April 2017, our first commercial product, TYMLOS (abaloparatide) injection, was approved by the U.S. Food and Drug Administration ("FDA") for the treatment of postmenopausal women with osteoporosis at high risk for fracture defined as history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy. In May 2017, we commenced U.S. commercial sales of TYMLOS and as of January 17, 2019, TYMLOS was available and covered for approximately 283 million U.S. insured lives, representing approximately 99% of U.S. commercial and 67% of Medicare insured lives. In May 2017, we announced positive top-line results from our completed 24-month ACTIVExtend clinical trial for TYMLOS, which met all of its primary and secondary endpoints. In July 2017, we entered into a license and development agreement with Teijin Limited ("Teijin") for abaloparatide for subcutaneous injection ("abaloparatide-SC") in Japan. Under this agreement, we received an upfront payment and are entitled to receive milestone payments upon the achievement of certain regulatory and sales milestones, and a fixed low double-digit royalty based on net sales of abaloparatide-SC in Japan during the royalty term. In addition, we have an option to negotiate for a co-promotion agreement with Teijin for abaloparatide-SC in Japan. In October 2018, the FDA approved a labelling supplement for TYMLOS in connection with the results from our ACTIVExtend trial to reflect that after 24 months of open-label alendronate therapy, the vertebral fracture risk reduction achieved with TYMLOS therapy was maintained. In March 2018, the Committee for Medicinal Products for Human Use ("CHMP") of the European Medicines Agency ("EMA") adopted a negative opinion on our European Marketing Authorisation Application ("MAA") for abaloparatide-SC. In July 2018, following a re-examination procedure, the CHMP maintained its negative opinion and on January 7, 2019, the European Commission adopted a decision refusing approval of the MAA on the basis of the negative opinion of the Committee. In March 2018, we initiated a clinical trial in men with osteoporosis which, if successful, will form the basis of a supplemental NDA seeking to expand the use of TYMLOS to treat men with osteoporosis at high risk for fracture. In July 2018, we initiated a bone histomorphometry study, which will enroll approximately 25 postmenopausal women with osteoporosis to evaluate the early effects of TYMLOS on tissue-based bone remodeling and structural indices.

We are developing an abaloparatide transdermal patch ("abaloparatide-patch"), for potential use in the treatment of postmenopausal women with osteoporosis. In January 2018, we met with the FDA and gained alignment with the agency on a single, pivotal bone mineral density ("BMD") non-inferiority bridging study to support an NDA submission. The FDA agreed that, depending on the study results, a randomized, open label, active-controlled, non-inferiority Phase 3 study of up to 500 patients with postmenopausal osteoporosis at high risk of fracture would be sufficient to gain approval for abaloparatide-patch. The FDA confirmed that the primary endpoint will be change in lumbar spine BMD at 12 months and that the non-inferiority margin must preserve 75% of the active control (abaloparatide-SC) based on the lower bound of the 95% confidence interval. We expect to initiate this pivotal study in mid-2019 and to complete it in 2020. In February 2018, we entered into a Scale-Up and Commercial Supply Agreement with 3M Company ("3M") pursuant to which 3M agreed to exclusively manufacture Phase 3 and global commercial supplies of abaloparatide-patch. In partnership with 3M, we selected Patheon N.V. (part of Thermo Fisher Scientific) to conduct the abaloparatide-patch coating process and packaging operations. We have made significant progress scaling up to support our planned Phase 3 study and potential commercial batches. In October 2018, we committed to fund 3M's purchase of capital equipment totaling approximately $9.6 million in preparation for manufacturing Phase 3 and potential commercial supplies of abaloparatide-patch. Milestone payments for the equipment commenced in the fourth quarter of 2018 and are expected to be paid in full in the third quarter of 2020.

We are also developing our investigational product candidate, elacestrant (RAD1901), a selective estrogen receptor degrader ("SERD"), for potential use in the treatment of hormone receptor-positive breast cancer. We initiated our Phase 3 EMERALD study of elacestrant in late November 2018 with a planned recruitment period of 18 to 21 months. The

Phase 3 study is a single, randomized, open label, active-controlled Phase 3 trial of elacestrant as a second or third-line monotherapy in approximately 460 patients with estrogen receptor-positive ("ER+") and human epidermal growth factor receptor 2-negative ("HER2-") advanced or metastatic breast cancer who have received prior treatment with one or two endocrine therapies, including a cyclin-dependent kinase ("CDK") 4/6 inhibitor. Patients in the study will be randomized to receive either elacestrant or the investigator's choice of an approved hormonal agent. The primary endpoint of the study will be progression-free survival ("PFS"), which we will analyze in the overall patient population and in patients with estrogen receptor 1 gene ("ESR1") mutations. Secondary endpoints will include evaluation of overall survival ("OS"), objective response rate ("ORR"),

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and duration of response (“DOR”). We believe that, depending on results, this single trial would support applications for marketing approvals for elacestrant as a second- and third-line monotherapy in the U.S., European Union (“EU”), and other markets. In November 2018, the FDA granted Fast Track designation for elacestrant for the population to be included in the Phase 3 study. We previously completed enrollment in our ongoing dose escalation Part A, and dose expansion Parts B and C, and in the 18F fluoroestradiol positron emission tomography (“FES-PET”) imaging Phase 1 studies of elacestrant in advanced or metastatic breast cancer. Enrollment in Part D of the Phase 1 dose-escalation and expansion study was discontinued as the data was no longer required to support the final design of our Phase 3 study. We plan to enter into a worldwide co-development and co-commercialization strategic collaboration with a global oncology partner to broaden development of elacestrant to potentially address earlier lines of treatment in combination with other anti-cancer agents.

We are developing our internally discovered investigational product candidate, RAD140, a non-steroidal selective androgen receptor modulator ("SARM") for potential use in the treatment of hormone receptor-positive breast cancer. In September 2017, we initiated a Phase 1 dose escalation study of RAD140 in patients with locally advanced or metastatic breast cancer. In November 2018, we provided an update on the study, noting that we had identified a provisional maximum tolerated dose and an additional cohort had been opened to further confirm tolerability, pharmacokinetics, and on-treatment pharmacodynamics effects of RAD140 at that dose.

Our Marketed Product and Investigational Product Candidates

The success of our business is primarily dependent upon our ability to commercialize TYMLOS in the U.S. and to develop and commercialize our current and future product candidates. The following table identifies our commercial product, TYMLOS, and the investigational product candidates in our current product portfolio, their potential indication and stage of development. We hold worldwide commercialization rights for all these product candidates, excluding abaloparatide-SC, for which we hold worldwide commercialization rights, except for Japan, where we have an option to negotiate a co-promotion agreement with Teijin.

Our Strategy

To achieve our goal of becoming a leading provider of innovative endocrine therapeutics in the areas of osteoporosis and oncology, we plan to:

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•Become a market leader for anabolic osteoporosis therapies. We commenced U.S. commercial sales of TYMLOS in May 2017 and we remain focused on growing our market share in anabolic appropriate patients. In October 2018, the FDA approved a labelling supplement for TYMLOS in connection with the results from our ACTIVExtend trial to reflect that after 24 months of open-label alendronate therapy, the vertebral fracture risk reduction achieved with TYMLOS therapy was maintained. We are conducting additional clinical research towards potential additional indications for TYMLOS, including a clinical trial in men with osteoporosis that we initiated in March 2018, and which, if successful, will form the basis of a supplemental NDA seeking to expand the use of TYMLOS to treat men with osteoporosis at high risk for fracture. In July 2018, we also initiated a bone histomorphometry study, which would enroll approximately 25 postmenopausal women with osteoporosis to evaluate the early effects of TYMLOS on tissue-based bone remodeling and structural indices.
•Selectively pursue partnerships or collaborations to commercialize abaloparatide-SC outside the U.S. In July 2017, we entered into a license and development agreement with Teijin for abaloparatide-SC in Japan. Under this agreement, we received an upfront payment and may receive up to an aggregate of $40.0 million upon the achievement of certain regulatory and sales milestones, and a fixed low double-digit royalty based on net sales of abaloparatide-SC in Japan during the royalty term. In addition, we have an option to negotiate for a co-promotion agreement with Teijin for abaloparatide-SC in Japan. We intend to enter into a collaboration for the commercialization of abaloparatide-SC outside of the United States and Japan.
•Expand abaloparatide's market potential through the continued development of abaloparatide-patch. We are developing our investigational abaloparatide-patch as a short-wear-time transdermal patch. In January 2018, we met with the FDA and gained alignment with the agency on a single, pivotal BMD non-inferiority bridging study to support an NDA submission. The FDA agreed that, depending on the study results, a randomized, open label, active-controlled, non-inferiority Phase 3 study of up to 500 patients with postmenopausal osteoporosis at high risk of fracture would be sufficient to gain approval for abaloparatide-patch. The FDA confirmed that the primary endpoint will be change in lumbar spine BMD at 12 months and that the non-inferiority margin must preserve 75% of the active control (abaloparatide-SC) based on the lower bound of the 95% confidence interval. We expect to initiate this pivotal study in mid-2019 and to complete it in 2020. In February 2018, we entered into a Scale-Up and Commercial Supply Agreement with 3M Company pursuant to which 3M agreed to exclusively manufacture Phase 3 and global commercial supplies of abaloparatide-patch. In partnership with 3M, we selected Patheon N.V. (part of Thermo Fisher Scientific) to conduct the abaloparatide-patch coating process and packaging operations. We have made significant progress scaling up to support our planned Phase 3 study and potential commercial batches.
•Become a leader in the field of hormone-receptor driven cancers. We are developing our investigational product candidate elacestrant as a potential treatment for hormone receptor-positive breast cancer as a single agent and in combination with other therapies. We initiated our Phase 3 EMERALD study of elacestrant in late November 2018 with a planned recruitment period of 18 to 21 months. The Phase 3 study is a single, randomized, open label, active-controlled Phase 3 trial of elacestrant as a second or third-line monotherapy in approximately 460 patients with ER+ and HER2- advanced or metastatic breast cancer who have received prior treatment with one or two endocrine therapies, including a CDK 4/6 inhibitor. Patients in the study will be randomized to receive either elacestrant or the investigator’s choice of an approved hormonal agent. The primary endpoint of the study will be PFS, which we will analyze in the overall patient population and in patients with ESR1 mutations. Secondary endpoints will include evaluation of OS, ORR, and DOR. We believe that, depending on results, this single trial would support applications for marketing approvals for elacestrant as a second- and third-line monotherapy in the U.S., EU, and other markets. We plan to enter into a worldwide co-development and co-commercialization strategic collaboration with a global oncology partner to broaden development of elacestrant to potentially address earlier lines of treatment in combination with other anti-cancer agents. We are advancing the development of RAD140 as a potential treatment for hormone receptor-positive breast cancer. In September 2017 we initiated a Phase 1 study of RAD140 in patients with locally advanced or metastatic breast cancer and in November 2018 we announced that we identified a provisional maximum tolerated dose and an additional cohort had been opened to further confirm tolerability, pharmacokinetics, and on-treatment pharmacodynamics effects of RAD140 at that dose.

•Continue to expand our product portfolio. We plan to leverage our drug development expertise to discover and develop additional investigational product candidates focused on osteoporosis, oncology and endocrine diseases and conditions. For example, we are leveraging our experience with elacestrant and RAD140 to develop a next generation hormonal agent for potential use in the treatment of hormone-driven cancers. We may also consider opportunistically expanding our product portfolio within these areas through in-licensing, acquisitions or partnerships.

Our Opportunity in Osteoporosis

Osteoporosis is a disease characterized by low bone mass and structural deterioration of bone tissue, which leads to greater fragility and an increase in fracture risk. All bones become more fragile and susceptible to fracture as the disease progresses. People tend to be unaware that their bones are getting weaker, and a person with osteoporosis can fracture a bone

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from even a minor fall. The debilitating effects of osteoporosis have substantial costs. Loss of mobility, admission to nursing homes and dependence on caregivers are all common consequences of osteoporosis. The prevalence of osteoporosis is growing and, per the National Osteoporosis Foundation ("NOF"), is significantly under-recognized and under-treated in the population. While the aging of the population is a primary driver of an increase in cases, osteoporosis is also increasing from the use of drugs that induce bone loss, such as chronic use of glucocorticoids and aromatase inhibitors that are increasingly used for breast cancer and hormone therapies used for prostate cancer.

The NOF has estimated that 10 million people in the United States, composed of eight million women and two million men, already have osteoporosis, and another approximately 44 million have low bone mass placing them at increased risk for osteoporosis. In addition, the NOF has estimated that osteoporosis is responsible for more than two million fractures in the United States each year resulting in an estimated $19 billion in costs annually. The NOF expects that the number of fractures in the United States due to osteoporosis will rise to three million by 2025, resulting in an estimated $23.5 billion in costs each year. Worldwide, osteoporosis affects an estimated 200 million women according to the International Osteoporosis Foundation ("IOF") and causes more than 8.9 million fractures annually, which is equivalent to an osteoporotic fracture occurring approximately every three seconds.

The IOF has estimated that 1.6 million hip fractures occur worldwide each year, and by 2050 this number could reach between 4.5 million and 6.3 million. The IOF estimates that in Europe alone, the annual cost of osteoporotic fractures could surpass €76 billion by 2050. The IOF, in its 2013 Asia-Pacific audit, estimated that osteoporosis affects 10% of the population in Japan over age 40; composed of 9.8 million women and 3 million men. By 2025, it is expected that 25% of Japan’s population will be over 70 years old with an average life expectancy of 87 years, and this is predicted to increase to 32% of Japan’s population in 2050 with an average life expectancy of 92 years. In 2050, it is also expected that over half of the Japanese population will be over 50 years old. The expected increase in the age of its population presents Japan with a significant need to focus on the health of its elderly, including osteoporosis.

In 2018, total sales of branded osteoporosis drugs approximated $7.4 billion, worldwide, of which more than $4.4 billion was attributable to injectable therapies. There are two main types of osteoporosis drugs currently available in the United States, anti-resorptive agents and anabolic agents. Anti-resorptive agents act to prevent further bone loss by inhibiting the breakdown of bone, whereas anabolic agents stimulate bone formation to build new bone.

We believe there is a large unmet need in the market for osteoporosis treatment because existing therapies have been reported to have shortcomings in efficacy, tolerability and convenience. For example, one current standard of care, bisphosphonates, which are anti-resorptive agents, have been associated with infrequent but serious adverse events, such as osteonecrosis of the jaw and atypical fractures, especially of long bones. These side effects, although uncommon, reportedly have created increasing concern with physicians and patients. We believe many physicians are seeking alternatives to bisphosphonates. Forteo/Forsteo® (teriparatide) marketed by Eli Lilly and Company ("Lilly") and Prolia® (denosumab) marketed by Amgen Inc. ("Amgen") are two alternatives to bisphosphonates that are approved for the treatment of osteoporosis. Prolia has also been associated with infrequent but serious adverse events, such as osteonecrosis of the jaw and atypical fractures. In 2018, Forteo/Forsteo had reported worldwide sales of approximately $1.6 billion, $0.8 billion in the United States and $0.8 billion outside of the United States, and Prolia had reported worldwide sales of approximately $2.3 billion, $1.5 billion in the United States and $0.8 billion outside of the United States.

We believe there is a significant opportunity for TYMLOS (abaloparatide), an anabolic agent which is approved in the U.S. for the treatment of postmenopausal women with osteoporosis at high risk for fracture defined as history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy. With the potential addition of new guidelines, expanding research, increased diagnosis effort, greater awareness of the long-term risk associated with osteoporotic fracture, and new, more effective therapies we believe osteoporosis treatment will expand and likewise our potential commercial opportunity. We also believe that there is a significant opportunity for abaloparatide outside the U.S., particularly in Japan, where we have a license and development agreement with Teijin for abaloparatide-SC under which we are entitled to receive payments up to an aggregate of $40.0 million upon the achievement of certain regulatory and sales milestones, a fixed low double-digit royalty based on net sales of abaloparatide-SC in Japan during the royalty term, and have an option to negotiate for a co-promotion agreement with Teijin for abaloparatide-SC in Japan.

Abaloparatide

In April 2017, the FDA approved TYMLOS for the treatment of postmenopausal women with osteoporosis at high risk for fracture defined as history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy. We are developing two formulations of abaloparatide: abaloparatide-SC and abaloparatide-patch.

Abaloparatide-SC

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TYMLOS was approved in the United States in April 2017 for the treatment of postmenopausal women with osteoporosis at high risk for fracture. The first commercial sales of TYMLOS in the United States occurred in May 2017 and as of January 17, 2019, TYMLOS was available and covered for approximately 283 million U.S. insured lives, representing approximately 99% of U.S. commercial and 67% of Medicare insured lives. We are commercializing TYMLOS in the United States through our commercial organization. We have built a distribution network for TYMLOS in the United States, comprised of well-established distributors and specialty pharmacies. Under our distribution model, both the distributors and specialty pharmacies take physical delivery of TYMLOS and the specialty pharmacies dispense TYMLOS directly to patients.

We hold worldwide commercialization rights to abaloparatide-SC, except for Japan, where we have an option to negotiate a co-promotion agreement with Teijin for abaloparatide-SC. We intend to enter into a collaboration for the commercialization of abaloparatide-SC outside of the United States and Japan. In March 2018, the CHMP of the EMA adopted a negative opinion on our European MAA for abaloparatide-SC. In July 2018, following a re-examination procedure, the CHMP maintained its negative opinion and on January 7, 2019, the European Commission adopted a decision refusing approval of the MAA on the basis of the negative opinion of the Committee.

In May 2017, we announced positive top-line results from the completed 24-month ACTIVExtend clinical trial of TYMLOS, which met all of its primary and secondary endpoints. In ACTIVExtend, patients who had completed 18 months of TYMLOS (abaloparatide) injections or placebo in the ACTIVE Phase 3 trial were transitioned to receive 24 additional months of open-label alendronate. For the subset of ACTIVE trial patients (n=1139) that enrolled in the ACTIVExtend trial, the previous TYMLOS-treated patients had a significant 84% relative risk reduction ($p<0.0001$) in the incidence of new vertebral fractures compared with patients who received placebo followed by alendronate. They also demonstrated a 39% risk reduction in nonvertebral fractures ($p=0.038$), a 34% risk reduction clinical fractures ($p=0.045$) and a 50% risk reduction in major osteoporotic fractures ($p=0.011$) compared with patients who received placebo followed by alendronate. At the 43-month timepoint, for all patients (n=1645) that enrolled in the ACTIVE trial, TYMLOS-treated patients had a statistically significant risk reduction in new vertebral fractures ($p<0.0001$), nonvertebral fractures ($p=0.038$), clinical fractures ($p=0.045$), and major osteoporotic fractures ($p<0.001$), compared with patients who received placebo followed by alendronate. While not a pre-specified endpoint, there was also a statistically significant risk reduction in hip fractures ($p=0.027$) at the 43-month time point in the TYMLOS-treated patients, compared with patients who received placebo followed by alendronate. The adverse events reported during the alendronate treatment period were similar between the previous TYMLOS-treated patients and the previous placebo group. The incidences of cardiovascular adverse events including serious adverse events were similar between groups. There have been no cases of osteonecrosis of the jaw or atypical femoral fracture in the entire TYMLOS development program. The results from the completed ACTIVExtend trial were presented at a major scientific meeting in September 2017.

In July 2017, we entered into a license and development agreement with Teijin for abaloparatide-SC in Japan. Pursuant to the agreement, we received an upfront payment and may receive additional milestone payments upon the achievement of certain regulatory and sales milestones, and a fixed low double-digit royalty based on net sales of abaloparatide-SC in Japan during the royalty term. In addition, we have an option to negotiate for a co-promotion agreement with Teijin for abaloparatide-SC in Japan. Teijin is conducting a Phase 3 clinical trial of abaloparatide in Japan for the treatment of postmenopausal osteoporosis.

In March 2018, we initiated a clinical trial in men with osteoporosis which, if successful, will form the basis of a supplemental NDA seeking to expand the use of TYMLOS to treat men with osteoporosis at high risk for fracture. The study is a randomized, double-blind, placebo-controlled trial that will enroll approximately 225 men with osteoporosis. The primary endpoint is change in lumbar spine BMD at 12 months compared with placebo. In previous clinical trials, TYMLOS has demonstrated increases in BMD in postmenopausal women. The study includes specialized high-resolution imaging to examine the effect of abaloparatide on bone structure, such as the hip, in a subset of the study participants.

In June 2018, the FDA approved a labeling supplement for TYMLOS to revise the needle length in the Instructions for Use from 8 mm to 5 mm. We believe health care providers, specialty pharmacies, and patients may prefer a shorter

needle size for injectable products like TYMLOS.

In July 2018, we initiated a bone histomorphometry study, which will enroll approximately 25 postmenopausal women with osteoporosis to evaluate the early effects of TYMLOS on tissue-based bone remodeling and structural indices.

In October 2018, the FDA approved a labelling supplement for TYMLOS to reflect that after 24 months of open-label alendronate therapy, the vertebral fracture risk reduction achieved with TYMLOS therapy was maintained.
Abaloparatide-patch

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We are also developing abaloparatide-patch, based on 3M's patented Microstructured Transdermal System technology, for potential use as a short wear-time transdermal patch. We hold worldwide commercialization rights to the abaloparatide-patch technology and we are developing abaloparatide-patch toward future global regulatory submissions to build upon the potential success of TYMLOS. Our development strategy for abaloparatide patch is to bridge to the established efficacy and safety of our approved abaloparatide-SC formulation.

We commenced a human replicative clinical evaluation of the optimized abaloparatide-patch in December 2015, with the goal of achieving comparability to abaloparatide-SC. In September 2016, we presented results from this evaluation of the first and second abaloparatide-patch prototypes, demonstrating that formulation technology can modify the pharmacokinetic profile of abaloparatide, including Tmax, half-life ("T1/2"), and area under the curve ("AUC"). In March 2018, we announced that through further optimization we had achieved comparability to the abaloparatide-SC profile with a third prototype (the "current abaloparatide-patch"). The current abaloparatide-patch optimized the drug-device combination through process improvements, a finalized formulation, selection of a dose (300 μg), and the introduction of a new clinical applicator, which were designed to improve the ease of use and patient experience. In the second half of 2018, we completed further evaluation confirming that a five minute application of the current abaloparatide-patch to the thigh resulted in a pharmacokinetic exposure highly similar (AUC >90%) to abaloparatide-SC.

In January 2018, we met with the FDA to align on a regulatory and development path for registration of abaloparatide-patch. We gained alignment with the agency on a single, pivotal BMD non-inferiority bridging study to support an NDA submission. The FDA agreed that, depending on the study results, a randomized, open label, active-controlled, non-inferiority Phase 3 study of up to 500 patients with postmenopausal osteoporosis at high risk of fracture would be sufficient to gain approval for abaloparatide-patch. The FDA confirmed that the primary endpoint will be change in lumbar spine BMD at 12 months and that the non-inferiority margin must preserve 75% of the active control (abaloparatide-SC) based on the lower bound of the 95% confidence interval. We expect to initiate this pivotal study in mid-2019 and to complete it in 2020.

In February 2018, we entered into a Scale-Up and Commercial Supply Agreement with 3M Company pursuant to which 3M agreed to exclusively manufacture Phase 3 and global commercial supplies of abaloparatide-patch. In partnership with 3M, we selected Patheon N.V. (part of Thermo Fisher Scientific) to conduct the abaloparatide-patch coating process and packaging operations. In October 2018, we committed to fund 3M's purchase of capital equipment totaling approximately $9.6 million in preparation for manufacturing Phase 3 and potential commercial supplies of abaloparatide-patch. Milestone payments for the equipment commenced in the fourth quarter of 2018 and are expected to be paid in full in the third quarter of 2020. We have made significant progress scaling up to support our planned Phase 3 study and potential commercial batches. We have also completed a significant portion of analytical method validations and are progressing on device design validation and verification activities to support the Phase 3 trial. We are working to finalize engineering equipment designs for commercial supplies and build out of the commercial manufacturing facilities has started and equipment installation at Patheon is planned to start in the first half of 2019.

Our Opportunity in Breast Cancer

According to the World Health Organization, breast cancer is the most common cancer in women and the global incidence is expected to increase in the coming years. The major cause of death from breast cancer is metastases, most commonly to the bone, liver, lung and brain. Approximately 30% of early-stage breast cancer patients develop metastatic disease, and of those patients 90% relapse during the course of their treatment. About 5% of breast cancer patients have distant metastases at the time of diagnosis. Patients with metastatic breast cancer have a five-year survival rate of only 25%, compared with a greater than 90% five-year survival rate for patients with only local disease at diagnosis. Importantly, even patients without metastases at diagnosis are at risk for developing metastases over time.

Approximately 70% of breast cancers express the ER and depend on estrogen signaling for growth and survival. The standard of care for ER+ advanced/metastatic breast cancer calls for endocrine therapy at all stages of treatment, with patients typically cycling through multiple anti-estrogen therapies, such as aromatase inhibitors ("AIs"), selective estrogen receptor modulators ("SERMs"), and selective estrogen receptor degraders ("SERDs").

These therapies inhibit the ER pathway either by inhibiting estrogen synthesis (AIs) or by directly inhibiting the estrogen receptor (SERMs and SERDs). While both SERMs and SERDs antagonize the estrogen receptor, SERDs

function to degrade the receptor. Although many patients initially respond to AIs and SERMs, a majority of patients will have progressive disease and the dependence on ER for tumor growth and sensitivity to other ER-targeting agents is often retained. On the basis of this continued dependence on ER, novel SERDs have gained widespread attention as a means of delivering more durable responses and increasing progression-free survival in this setting. Indeed, SERDs have demonstrated clinical efficacy in patients who have progressed on AIs or SERMs.

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Currently only one SERD, fulvestrant, an intramuscular injection, is approved for the treatment of ER-positive metastatic breast cancer. We believe a significant opportunity may exist for new oral therapies that can more effectively treat ER-positive breast cancer.

Elacestrant (RAD1901)

Elacestrant (RAD1901) is a SERD that we are evaluating for potential use as a once daily oral treatment for hormone-receptor positive breast cancer. We hold worldwide commercialization rights to elacestrant, which we licensed from Eisai Co. Ltd. ("Eisai"). Elacestrant is currently being investigated in women with ER-positive and HER2-negative breast cancer, the most common subtype of the disease. Studies completed to date indicate that the compound has the potential for use as a single agent or in combination with other therapies for the treatment of breast cancer.

We believe that, subject to successful development, regulatory review and approval, elacestrant could have the potential to offer the following advantages over other current standard of care treatments for ER-positive breast cancer:

•ability to degrade the estrogen receptor;
•favorable efficacy and tolerability profile;
•ability to effectively combine with other agents;
•treatment of hormone-resistant breast cancers; and
•once a day oral administration.

We have completed enrollment in our FES-PET imaging study and dose-escalation Part A and expansion study parts B and C Phase 1 breast cancer trials. These studies have identified a single oral dose of 400 mg per day for evaluation in subsequent monotherapy trials.

Phase 3 - EMERALD Study

We initiated our Phase 3 EMERALD study of elacestrant in late November 2018 with a planned recruitment period of 18 to 21 months. The Phase 3 Study is a single, randomized, open label, active-controlled Phase 3 trial of elacestrant as a second- or third-line monotherapy in approximately 460 patients with ER+ and HER2- advanced or metastatic breast cancer who have received prior treatment with one or two endocrine therapies, including a CDK 4/6 inhibitor. Patients in the study would be randomized to receive either elacestrant or the investigator’s choice of an approved hormonal agent. The primary endpoint of the study will be PFS, which we will analyze in the overall patient population and in patients with ESR1 mutations. Secondary endpoints will include evaluation of OS, ORR, and DOR. We believe that, depending on results, this single trial would support applications for marketing approvals for elacestrant as a second- and third-line monotherapy in the U.S., EU and other markets. In November 2018, the FDA granted Fast Track designation for elacestrant consistent with the population to be included in the Phase 3 study.

Phase 1 - Dose-Escalation and Expansion Study

In December 2014, we commenced a Phase 1, multicenter, open-label, multiple-part, dose-escalation study of elacestrant in postmenopausal women with ER-positive and HER2-negative advanced breast cancer in the United States to determine the recommended dose for a subsequent clinical trial and to make a preliminary evaluation of the potential anti-tumor effect of elacestrant. Part A of this Phase 1 study was designed to evaluate escalating doses of elacestrant. The Part B expansion cohort was initiated at 400-mg daily dosing in March 2016 to allow for an evaluation of additional safety, tolerability and preliminary efficacy. The patients enrolled in this study are heavily pretreated ER-positive, HER2-negative advanced breast cancer patients who have received a median of 3 prior lines of therapy including fulvestrant and CDK4/6 inhibitors, and about 50% of the patients had ESR1 mutations. We have completed enrollment in the ongoing dose-escalation Part A and expansion study parts B and C. In December 2017, we initiated enrollment of a Part D cohort in this study to provide additional data to support the elacestrant clinical development program anticipated at that time. We discontinued recruitment in the Part D cohort as the data was no longer required to support the final design of our Phase 3 study.

In December 2016 and June 2017, we reported positive results from this ongoing Phase 1 dose-escalation and expansion study. As of the study cut-off date of April 28, 2017, the elacestrant single agent ORR, was 23% with five confirmed partial responses in heavily pre-treated patients with advanced ER-positive breast cancer and in the 400-mg patient group of 26 patients with mature data, the median PFS was 4.5 months. These results showed that elacestrant

was well-tolerated with the most commonly reported adverse events being low grade nausea and dyspepsia. In December 2017, we reported additional updated data from this ongoing Phase 1 dose-escalation and expansion study, which included mature data from 40 patients treated at the 400 mg dose in Parts A through C of this study. As of the study cut-off date of October 30, 2017, the elacestrant

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single agent ORR, was 27.3% with six confirmed partial responses out of 22 patients with response evaluation criteria in solid tumors ("RECIST") measurable disease. The median PFS was 5.4 months and clinical benefit rate at 24 weeks was 47.4%. These results showed that elacestrant was well-tolerated with the most commonly reported adverse events being low grade nausea, dyspepsia and vomiting.

We initiated Part D of the Phase 1 dose-escalation and expansion study to evaluate the safety and preliminary efficacy of elacestrant at a 400 mg tablet dose in a population with different eligibility requirements from Parts A, B, and C of this study. In Part D, patients were required to have at least two prior lines of endocrine therapy for advanced/metastatic breast cancer, including fulvestrant, and prior treatment with a CDK 4/6 inhibitor. Ten patients of an originally planned thirty-six were enrolled in Part D, and as of January 3, 2019, one patient remained on treatment. A preliminary review of the data as of December 27, 2018 showed that overall the patients in Part D were more heavily pretreated and more likely to have visceral metastases than patients in Parts A through C of this study. In addition, out of the nine patients with measurable disease, four had a best response of stable disease, two of them for greater than 24 weeks. Combined data, as of December 27, 2018, from all four study Parts (A through D) at 400 mg showed that the overall elacestrant single agent ORR was 19.4% and the median PFS was 4.5 months.

Phase 1 - FES-PET Study

In December 2015, we commenced a FES-PET study in patients with metastatic breast cancer in the EU, which included the use of FES-PET imaging to assess estrogen receptor occupancy in tumor lesions following elacestrant treatment.

In December 2016, we reported positive results from the Phase 1 FES-PET study. The first three enrolled patients dosed at the 400-mg cohort had a tumor FES-PET signal intensity reduction ranging from 79% to 91% at day 14 compared to baseline. This study enrolled five additional patients in the 400-mg daily oral cohort, followed by eight patients in the 200-mg daily oral cohort. In December 2017, we reported updated data from the Phase 1 FES-PET study showing that elacestrant demonstrated robust reduction in tumor ER availability in patients with advanced ER+ breast cancer who progressed on prior endocrine therapy. Seven out of eight patients dosed at the 400-mg cohort, and four out of seven patients dosed at the 200-mg cohort, had a tumor FES-PET signal intensity reduction equal to, or greater than, 75% at day 14 compared to baseline. The reduction in FES uptake supports flexibility for both 200-mg and 400-mg elacestrant dose selection for further clinical development in combination studies with various targeted agents and was similar in patients harboring mutant or wild-type ESR1. The most commonly reported adverse events reported were grade 1 and 2 nausea and dyspepsia.

Potential for use in Combination Therapy

In July 2015, we announced that early but promising preclinical data showed that our investigational drug elacestrant, in combination with Pfizer's palbociclib, a cyclin-dependent kinase ("CDK 4/6 inhibitor") or Novartis' everolimus, an mTOR inhibitor, was effective in shrinking tumors. In preclinical patient-derived xenograft breast cancer models with either wild type or mutant ESR1, treatment with elacestrant resulted in marked tumor growth inhibition, and the combination of elacestrant with either agent, palbociclib or everolimus, showed anti-tumor activity that was significantly greater than either agent alone. We believe that this preclinical data suggests that elacestrant has the potential to overcome endocrine resistance, is well-tolerated, and has a profile that is well suited for use in combination therapy.

In December 2017, we announced additional preclinical data that continues to demonstrate elacestrant anti-tumor activity, as a single agent and in combination, in multiple models. In these preclinical models, elacestrant demonstrated marked tumor growth inhibition, as a single agent in models treated with multiple rounds of fulvestrant and in combination with CDK 4/6 inhibitors such as palbociclib and abemaciclib and with a phosphoinositide 3-kinase inhibitor, alpelisib. In December 2018, we announced additional preclinical data that showed that elacestrant demonstrated marked tumor growth inhibition as a single agent in models harboring ESR1 point mutations, models insensitive to fulvestrant, and models insensitive to CDK 4/6 inhibitors such as palbociclib, ribociclib, or abemaciclib.

Collaborations

We plan to enter into a worldwide co-development and co-commercialization strategic collaboration with a global oncology partner to broaden development of elacestrant to potentially address earlier lines of treatment in combination with other anti-cancer agents.

In July 2016, we entered into a preclinical collaboration with Takeda Pharmaceutical Company Limited to evaluate the combination of elacestrant with Takeda's investigational drug TAK-228, an oral mTORC 1/2 inhibitor in Phase 2b development for the treatment of breast, endometrial and renal cancer, with the goal of potentially exploring such combination in a clinical study. We and Takeda have each agreed to contribute resources and supply compound material necessary for studies to be

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conducted under the collaboration and will share third party out-of-pocket research and development expenses. Activities under this collaboration are ongoing. Upon completion, both parties will agree upon the appropriate communication of the results.

In January 2016, we entered into a worldwide clinical collaboration with Novartis Pharmaceuticals to evaluate the safety and efficacy of combining elacestrant with Novartis' investigational agent LEE011 (ribociclib), a CDK 4/6 inhibitor, and BYL719 (alpelisib), an investigational phosphoinositide 3-kinase inhibitor. In January 2018, we terminated this collaboration following the completion of preclinical studies. We are evaluating additional opportunities to collaborate with companies to evaluate the safety and efficacy of combining elacestrant with other agents for the treatment of breast cancer. We believe that such combinations may be suitable in earlier lines of treatment for patients with advanced disease.

RAD140

RAD140 is an internally discovered SARM. The androgen receptor ("AR") is highly expressed in many ER-positive, ER-negative, and triple-negative receptor breast cancers. Due to its receptor and tissue selectivity, potent activity, oral bioavailability, and long half-life, we believe RAD140 could have clinical potential in the treatment of breast cancer. We hold worldwide commercialization rights to RAD140.

In September 2017, we initiated a Phase 1 dose escalation study of RAD140 in patients with locally advanced or metastatic breast cancer. The clinical trial is designed to evaluate the safety and maximum tolerated dose of RAD140 in approximately 40 patients. Primary safety outcomes from the trial include rate of dose-limiting toxicities, adverse events related to treatment, and tolerability as measured by dose interruptions or adjustments. In addition, pharmacokinetics, pharmacodynamics and tumor response will also be evaluated. In November 2018, we provided an update on the Phase 1 study, noting that we had identified a provisional maximum tolerated dose and an additional cohort had been opened to further confirm tolerability, pharmacokinetics, and on-treatment pharmacodynamics effects of RAD140 at that dose. Enrollment in this study is expected to remain active through the first quarter of 2019.

In July 2016, we reported that RAD140 in preclinical xenograft models of breast cancer demonstrated potent tumor growth inhibition when administered alone or in combinations with CDK4/6 inhibitors. It is estimated that approximately 70% of breast cancers express the androgen receptor. Our data suggest that RAD140 activity at the androgen receptor leads to activation of AR signaling pathways including an AR-specific tumor suppressor and suppression of ER signaling. In April 2017, we presented these RAD140 preclinical results at a major scientific congress. In December 2018, we presented a preclinical poster further demonstrating anti-tumor activity of RAD140 in breast cancer models resistant to standard-of-care endocrine treatments.

Manufacturing

We do not own or operate manufacturing facilities for the production of our commercial product, TYMLOS, or any of our investigational product candidates, nor do we have plans to develop our own manufacturing operations in the foreseeable future.

Abaloparatide, the active pharmaceutical ingredient ("API") for both TYMLOS and abaloparatide-patch, is manufactured for us on a contract basis by Polypeptide Laboratories Holding (PPL) AB ("PPL"), as successor-in-interest to Lonza Group Ltd., using a solid phase peptide synthesis assembly process, and purification by high pressure liquid chromatography. Abaloparatide for TYMLOS is supplied as a liquid in a multi-dose cartridge for use in a pen delivery device. The components of the pen delivery device are manufactured by Ypsomed AG ("Ypsomed"). The multi-dose cartridges and pen delivery device are filled, assembled and packaged by Vetter International GmbH ("Vetter").

Abaloparatide-patch drug product is manufactured by 3M Company and 3M Innovative Properties Company, (together "3M"), based on their patented microneedle technology to administer drugs through the skin, as an alternative to subcutaneous injection.

Elacestrant API and drug product are manufactured for us on a contract basis by Patheon, Inc.

RAD140 API and drug product are manufactured for us on a contract basis by Alcami Corporation.

Manufacturing is subject to extensive regulations that impose various procedural and documentation requirements, which govern the methods used in, and the facilities and controls used for, the manufacture, processing, packing and holding of drugs. FDA and International Conference on Harmonisation ("ICH") current Good Manufacturing Practice

("cGMP") requirements include those pertaining to record keeping, manufacturing processes and controls, personnel, quality control and quality assurance, among others. Our contract manufacturing organizations are required to manufacture TYMLOS and our investigational product candidates under cGMP conditions. cGMP is a regulatory standard for the production of human pharmaceuticals that imposes extensive substantive, procedural and record keeping requirements on the manufacturing processes, testing methodology, and associated production and testing facilities.

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Intellectual Property

As of December 31, 2018, we owned or co-owned 13 issued U.S. patents, as well as 24 pending U.S. patent applications, 3 pending Patent Cooperation Treaty ("PCT") applications, 80 pending foreign patent applications in the European Patent Office and 14 other jurisdictions, and 83 granted foreign patents. As of December 31, 2018, we had licenses to 3 U.S. patents related to compositions and related uses thereof, as well as numerous foreign counterparts to many of these patents and patent applications. We own the federal trademark registration in the United States for Radius® in association with pharmaceuticals and TYMLOS® for use in the treatment of bone diseases. In addition, we have received a notice of allowance in Canada for TYMLOS and for trademarks on potential brand names for our product candidates in the U.S. and in other countries.

We strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining patents intended to cover our investigational product candidates and compositions, their methods of use and processes for their manufacture and any other inventions that are commercially important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will significantly depend on our ability to obtain and maintain patent and other proprietary protection for commercially important technology and inventions and know-how related to our business, defend and enforce our patents, preserve the confidentiality of our trade secrets, and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how and continuing technological innovation to develop and maintain our proprietary position.

Abaloparatide

We acquired and maintain exclusive worldwide rights, excluding development and commercialization rights for Japan, to certain patents, data and technical information related to abaloparatide through a license agreement with an affiliate of Ipsen Pharma SAS ("Ipsen"). Composition of matter of abaloparatide was claimed in the United States (U.S. Patent No. 5,969,095), Australia, Canada, China, Hong Kong, South Korea, New Zealand, Russia, Singapore, Mexico, and Taiwan. These patents expired in 2016. The subcutaneous formulation of abaloparatide for use in treating osteoporosis is covered by Patent No. 7,803,770 until the statutory term expires October 3, 2027, which we expect will be extended to March 26, 2028 (statutory term that may be extended with 175 days of patent term adjustment due to delays in patent prosecution by the United States Patent and Trademark Office, or USPTO) in the United States (not including any patent term extension under the Hatch-Waxman Act). The therapeutic formulation for abaloparatide-SC is covered by Patent No. 8,148,333 until October 3, 2027 in the United States (not including any patent term extension under the Hatch-Waxman Act) and Patent No. 8,748,382 (not including any patent term extension under the Hatch-Waxman Act). Related patents granted in Australia, China, Israel, Japan, South Korea, Mexico, New Zealand, Russia, Singapore, and Ukraine, and additional patent applications pending in Brazil, Canada, Hong Kong, India, and South Korea, will have a patent expiration date of 2027, not taking into account extension under any applicable laws. Patent applications covering various aspects of abaloparatide for microneedle application have been granted in Australia, Europe, Japan, and New Zealand, and additional patent applications are currently pending in the United States, Europe, Hong Kong, and Japan. The issued patents and any patents that might issue from the pending applications will have statutory expiration dates ranging from 2032 to 2037, not taking into account extension under any applicable laws. We have worldwide rights to commercialize abaloparatide-patch, including in Japan.

Elacestrant (RAD1901)

We exclusively licensed the worldwide rights to elacestrant from Eisai. U.S. Patent No. 7,612,114 (statutory term expires December 25, 2023 which may be extended up to August 18, 2026 with 967 days of patent term adjustment not taking into account any Hatch-Waxman patent term extensions) covers elacestrant as a composition of matter as well as the use of elacestrant for treatment of estrogen-dependent breast cancer. Corresponding patents issued in Australia, Canada, Japan, Poland, and Europe and pending in India will have a statutory expiration date in 2023, not taking into account extension under any applicable laws. We exclusively licensed US 9,421,264 (statutory term expires October 10, 2034) covering the treatment of ER+, SERM-resistant (such as tamoxifen and fulvestrant) breast cancer brain metastasis with elacestrant and related applications covering, more broadly, the use of elacestrant for the treatment of ER+ cancers, such as SERM-resistant ER+ breast cancer (statutory term expires October 10, 2034).

Corresponding applications pending in Europe and Canada will have a statutory expiration date in 2035. Polymorphic forms of elacestrant are covered in a U.S. application and a PCT application (filed January 2018) having a projected statutory expiration date in 2038, not taking into account any extension under any applicable laws. Elacestrant combination therapies with a CDK4/6 inhibitor (e.g., palbociclib) or an mTOR inhibitor (e.g., everolimus) for treatment of cancers that are drug-resistant and/or expressing mutant ER + are covered by applications pending in the U.S., Australia, Brazil, Canada, China, Europe, Israel, Japan, South Korea, Mexico, New Zealand, Russia, and Singapore (statutory expiration date in 2036, not taking into account any extension under any applicable laws).

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RAD140

The composition of matter of, and methods of using, RAD140 are covered by U.S. Patent No. 8,067,448 (statutory term expires February 19, 2029, which we expect will be extended to September 25, 2029, with potentially 218 days of patent term adjustment due to delays by the USPTO, not taking into account any Hatch Waxman patent term extensions) and U.S. Patent No. 8,268,872 (statutory term expires February 19, 2029 which may be extended to September 25, 2029 with patent term adjustment, subject to a terminal disclaimer of Patent Nos. 8,067,448 and 8,455,525). Related patents have been granted in Australia, Canada, Europe, Japan and Mexico and additional patent applications are pending in Brazil and India. Any patents issued from these filings will have a statutory expiration date in 2029. RAD140 for the treatment of breast cancer expressing the androgen receptor ("AR+ breast cancer") is covered in a PCT application (projected statutory expiration date in 2037, not taking into account extension under any applicable laws). The PCT application covers the use of RAD140 alone or in combination with a CDK4/6 inhibitor (e.g., palbociclib) or an mTOR inhibitor (e.g., everolimus) for the treatment of the AR+ breast cancer.

There can be no assurance that an issued patent will remain valid and enforceable in a court of law through the entire patent term. Should the validity of a patent be challenged, the legal process associated with defending the patent can be costly and time consuming. Issued patents can be subject to oppositions, interferences and other third-party challenges that can result in the revocation of the patent or that can limit patent claims such that patent coverage lacks sufficient breadth to protect subject matter that is commercially relevant. Competitors may be able to circumvent our patents. Development and commercialization of pharmaceutical products can be subject to substantial delays and it is possible that at the time of commercialization any patent covering the product has expired or will be in force for only a short period of time following commercialization. We cannot predict with any certainty if any third-party U.S. or foreign patent rights, or other proprietary rights, will be deemed infringed by the use of our technology. Nor can we predict with certainty which, if any, of these rights will or may be asserted against us by third-parties. Should we need to defend ourselves and our partners against any such claims, substantial costs may be incurred. Furthermore, parties making such claims may be able to obtain injunctive or other equitable relief, which could effectively block our ability to develop or commercialize some or all our products in the United States and abroad and could result in the award of substantial damages. In the event of a claim of infringement, we or our partners may be required to obtain one or more licenses from a third party. There can be no assurance that we can obtain a license on a reasonable basis should we deem it necessary to obtain rights to an alternative technology that meets our needs. The failure to obtain a license may have a material adverse effect on our business, results of operations and financial condition.

We also rely on trade secret protection for our confidential and proprietary information. No assurance can be given that we can meaningfully protect our trade secrets on a continuing basis. Others may independently develop substantially equivalent confidential and proprietary information or otherwise gain access to our trade secrets.

It is our policy to require our employees and consultants, outside scientific collaborators, sponsored researchers and other advisors who receive confidential information from us to execute confidentiality agreements upon the commencement of employment or consulting relationships. These agreements provide that all confidential information developed or made known to these individuals during the course of the individual's relationship with us is to be kept confidential and is not to be disclosed to third parties except in specific circumstances. The agreements provide that all inventions conceived by an employee shall be our property. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

Our success will depend in part on our ability to obtain and maintain patent protection, preserve trade secrets, prevent third parties from infringing upon our proprietary rights and operate without infringing upon the proprietary rights of others, both in the United States and other territories worldwide.

Competition

The development and commercialization of new products to treat the targeted indications of our marketed and investigational product candidates is highly competitive, and TYMLOS faces, and our product candidates, if approved, will face considerable competition from major pharmaceutical, biotechnology and specialty pharmaceutical companies, including Lilly, Amgen, UCB S.A., Novartis, Pfizer, Genentech, and Corium, that currently market and/or are seeking to develop products for similar indications. Many of our competitors have substantially more resources

than we do, including financial, manufacturing, marketing, research and drug development resources. In addition, many of these companies have longer operating histories and more experience than us in preclinical and clinical development, manufacturing, regulatory and global commercialization.

Abaloparatide

There are two main types of osteoporosis drugs currently available in the United States, anti-resorptive agents and anabolic agents. Anti-resorptive agents including bisphosphonates, estrogen, SERMs and Amgen's Prolia are the most common

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treatments for osteoporosis. Teriparatide, marketed by Lilly under the name Forteo/Forsteo (outside the U.S.), is the only other anabolic drug approved in the United States for the treatment of osteoporosis. We are aware of companies pursuing development in the United States of biosimilar and/or generic versions of teriparatide through various regulatory pathways, including Pfenex, Inc., under regulatory review; Teva Pharmaceutical Industries, Ltd., under regulatory review; and APOTEX, under regulatory review (in each case, with launch not expected until expiration of the applicable patents covering teriparatide, or if earlier, invalidation of such patents in connection with patent litigation and/or challenges, or settlements of such challenges). We believe other companies may be in earlier stages of development of a generic version of teriparatide.

Other organizations are also working to develop new therapies to treat osteoporosis. For example, Amgen and UCB are co-developing romosozumab, a humanized monoclonal antibody that inhibits the action of sclerostin, which received Japanese marketing approval in January 2019 and is under regulatory review in the United States.

In addition, we are aware that Corium is developing a transdermal formulation of parathyroid hormone ("PTH") (1-34) that is in Phase 2 clinical development and which, if approved, would compete with abaloparatide-patch, if approved.

Elacestrant (RAD1901)

Elacestrant for the treatment of hormone receptor positive breast cancer will face competition from SERDs, CNS-penetrant anti-cancer agents and from chemotherapy derivatives. AstraZeneca's Faslodex is the only SERD currently approved in the United States for the treatment of metastatic breast cancer. In addition, there are other organizations working to develop new therapies to treat metastatic hormone receptor-positive breast cancer, including Genentech, AstraZeneca, G1 Therapeutics, InventisBio, H3 Biomedicine, Novartis, and Sanofi, which are each developing oral SERD's that are currently in Phase 1 and/or Phase 2 clinical development.

RAD140

RAD140 is being developed for women with hormone receptor positive breast cancer. While no SARMs are currently approved as therapeutics in the United States, there are select competitive molecules in development across a range of indications, including in stress urinary incontinence (GTx), hip fractures (Viking Therapeutics), and cachexia (GSK).

We cannot assure you that any of our current investigational product candidates, if successfully developed and approved, will be able to compete effectively against these, or any other competing therapeutics that may become available on the market.

Collaborations and License Agreements

3M

In February 2018, we entered into a Scale-Up and Commercial Supply Agreement (the "Supply Agreement") with 3M, pursuant to which 3M has agreed to exclusively manufacture Phase 3 and global commercial supplies of abaloparatide-coated transdermal patch product ("Product") and associated applicator devices ("Applicator"). Under the Supply Agreement, 3M will manufacture Product and Applicator for us according to agreed-upon specifications in sufficient quantities to meet our projected supply requirements. 3M will manufacture commercial supplies of Product at unit prices that decrease with an increase in the quantity we order. We will pay 3M a mid-to-low single digit royalty on worldwide net sales of Product and reimburse 3M for certain capital expenditures incurred to establish commercial supply of Product. We are responsible for providing, at our expense, supplies of abaloparatide drug substance to be used in manufacturing Product. During the term of the Supply Agreement, 3M and Radius have agreed to work exclusively with each other with respect to the delivery of abaloparatide, PTH, and/or PTH related proteins via active transdermal, intradermal, or microneedle technology.

The initial term of the Supply Agreement began on its effective date and will continue for five years after the first commercial sale of Product. The Supply Agreement then automatically renews for successive three-year terms, unless earlier terminated pursuant to its terms or upon either party's notice of termination to the other 24 months prior to the end of the then-current term. The Supply Agreement may be terminated by either party upon an uncured material breach of its terms by the other party, or due to the other party's bankruptcy, insolvency, or dissolution. Radius may terminate the Supply Agreement upon the occurrence of certain events, including for certain clinical, technical, or commercial reasons impacting Product, if we are unable to obtain U.S. regulatory approval for Product within a certain time period, or if we cease development or commercialization of Product. 3M may terminate the Supply Agreement upon the occurrence of certain events, including if there are certain safety issues related to Product, if we

are unable to obtain U.S. regulatory approval for Product within a certain time period, or if we fail to order Product for a certain period of time after commercial launch of the Product in the U.S. Upon certain events of termination, 3M is required to transfer the manufacturing processes for Product and Applicator to us or a mutually agreeable third party and continue supplying Product and Applicator for a period of time pursuant to our projected supply requirements.

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In June 2009, we entered into a Development and Clinical Supplies Agreement with 3M, as amended (the "Development Agreement"), under which Product and Applicator development activities occur and 3M has manufactured phase 1 and 2 clinical trial supplies for us on an exclusive basis. The term of the Development Agreement runs until June 2019 and then automatically renews for additional one-year terms, unless earlier terminated, until the earliest of (i) the expiration or termination of the Supply Agreement, (ii) the mutual written agreement of the parties, or (iii) prior written notice by either party to the other party at least ninety days prior to the end of the then-current term of the Development Agreement that such party declines to extend the term. Either party may terminate the agreement in the event of an uncured material breach by the other party. We pay 3M for services delivered pursuant to the agreement on a fee-for-service or a fee-for-deliverable basis as specified in the agreement. The Company has paid 3M approximately $26.3 million, in the aggregate, through December 31, 2018 with respect to services and deliverables delivered pursuant to the Development Agreement.

Ipsen Pharma

In September 2005, we entered into a license agreement with Ipsen, as amended (the "License Agreement") under which we exclusively licensed certain Ipsen compound technology and related patents covering abaloparatide to research, develop, manufacture and commercialize certain compounds and related products in all countries, except Japan (where we have an option to negotiate a co-promotion agreement for abaloparatide-SC) and France (where our commercialization rights were subject to certain co-marketing and co-promotion rights exercisable by Ipsen, provided that certain conditions included in the License Agreement were met). We believe that Ipsen's co-marketing and co-promotion rights in France have permanently expired. Ipsen also granted us an exclusive right and license under the Ipsen compound technology and related patents to make and have made compounds or product in Japan. Ipsen further granted us an exclusive right and license under certain Ipsen formulation technology and related patents solely for purposes of enabling us to develop, manufacture and commercialize compounds and products covered by the compound technology license in all countries, except Japan and France (as discussed above).

In consideration for the rights to abaloparatide, and in recognition of certain milestones having been met to date, we have paid to Ipsen an aggregate amount of $13.0 million. The license agreement further requires us to make payments upon the achievement of certain future clinical and regulatory milestones. Total additional milestone payments that could be payable under the agreement as of December 31, 2017 are €24.0 million (approximately $28.7 million). The agreement provides that we or our sublicensees are obligated to pay to Ipsen a fixed five percent royalty based on net sales of products containing abaloparatide on a country-by-country basis until the later of the last to expire of the licensed patents or for a period of 10 years after the first commercial sale of the licensed products in such country. The date of the last to expire of the abaloparatide patents licensed from or co-owned with Ipsen, barring any extension thereof, is expected to be March 26, 2028. In the event that we sublicense abaloparatide to a third party, the agreement provides that we would pay a percentage of certain payments received from such sublicensee (in lieu of milestone payments not achieved at the time of such sublicense). The applicable percentage is in the low double digit range. In addition, if we or our sublicensees commercialize a product that includes a compound discovered by us based on or derived from confidential Ipsen know-how, the agreement provides that we would pay to Ipsen a fixed low single digit royalty on net sales of such product on a country-by-country basis until the later of the last to expire of our patents that cover such product or for a period of 10 years after the first commercial sale of such product in such country.

The License Agreement expires on a country-by-country basis on the later of (1) the date the last remaining valid claim in the licensed patents expires in that country, or (2) a period of 10 years after the first commercial sale of the licensed products in such country, unless it is sooner terminated in accordance with its terms.

The License Agreement may be terminated by us with prior notice to Ipsen. The License Agreement may be terminated by Ipsen upon notice to us with immediate effect, if we, in any country of the world, bring an action or proceeding to challenge any Ipsen patent. The License Agreement can also be terminated by Ipsen if we fail to use reasonable commercial efforts to develop the licensed product for sale and commercialization in those countries within the territory where it is commercially reasonable to do so as contemplated by the License Agreement, or fail to use reasonable commercial efforts to perform our obligations under the latest revised version of the development plan approved by the joint steering committee, or fail to use reasonable commercial efforts to launch and sell one licensed product in those countries within the territory where it is commercially reasonable to do so. Either party may also

terminate the License Agreement upon an uncured material breach by the other party. Ipsen may terminate the License Agreement if the License Agreement is assigned or sublicensed, if a third party acquires us, or if we acquire control over a PTH or a PTHrP compound that is in clinical development or is commercially available in the territory, and if following such assignment, sublicense, acquisition, or acquisition of control by us, such assignee, sublicensee, acquirer or we, fail to meet the timetable under the latest revised version of the development plan approved by the joint steering committee under the License Agreement.

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Prior to executing the License Agreement for abaloparatide with Radius, Ipsen licensed the Japanese rights for abaloparatide to Teijin Limited (“Teijin”) a Japanese pharmaceutical company. Teijin has initiated a Phase 3 clinical trial of abaloparatide in Japan for the treatment of postmenopausal osteoporosis.

Pursuant to a final decision in arbitration proceedings with Ipsen in connection with the License Agreement, we are obligated to pay Ipsen $5.0 million if abaloparatide receives marketing approval in Japan and a fixed mid single-digit royalty based on net sales of abaloparatide in Japan.

Eisai

In June 2006, we exclusively licensed rights to research, develop, manufacture and commercialize elacestrant and related products from Eisai in all countries, except Japan (the "Eisai Agreement"). In March 2015, we entered into an amendment to the Eisai Agreement in which Eisai granted us an exclusive right and license to research, develop, manufacture and commercialize elacestrant in Japan (the "Eisai Amendment"). Specifically, we licensed the patent application that subsequently issued as U.S. Patent No. 7,612,114 (statutory term expires December 25, 2023 which we expect will be extended to August 18, 2026 with 967 days of patent term adjustment due to delays by the USPTO), entitled "Selective Estrogen Receptor Modulator," the corresponding foreign patent applications and continuing patent applications. In consideration for the worldwide rights to elacestrant and in recognition of certain milestones having been met to date, we have paid to Eisai an aggregate amount of $1.9 million. We have also agreed to pay Eisai additional fees of up to $22.3 million payable upon the achievement of certain clinical and regulatory milestones.

Under the Eisai Agreement as amended, should a product covered by the licensed technology be commercialized, we will be obligated to pay to Eisai royalties in a variable mid-single digit range based on net sales of the product on a country-by-country basis. The royalty rate will be reduced, on a country-by-country basis, at such time as the last remaining valid claim in the licensed patents expires, lapses or is invalidated and the product is not covered by data protection clauses. In addition, the royalty rate will be reduced, on a country-by-country basis, if, in addition to the conditions specified in the previous sentence, lawful generic versions of such product account for more than a specified minimum percentage of the total sales of all products that contain the licensed compound during a calendar quarter. The latest licensed patent may expire, barring any patent term extension under any applicable laws, on August 18, 2026.

We were also granted the right to sublicense with prior written approval from Eisai. If we sublicense the licensed technology to a third party, we will be obligated to pay Eisai, in addition to the milestone fees referenced above, a fixed low double digit percentage of certain fees we receive from such sublicensee in addition to royalties in the low single digit range based on net sales of the sublicensee.

The license agreement expires on a country-by-country basis on the later of (1) the date the last remaining valid claim in the licensed patents expires, lapses or is invalidated in that country, the product is not covered by data protection clauses, and the sales of lawful generic versions of the product account for more than a specified percentage of the total sales of all pharmaceutical products containing the licensed compound in that country, or (2) a period of 10 years after the first commercial sale of the licensed products in such country, unless it is sooner terminated.

We can terminate the license agreement, with respect to the entire territory, with prior notice to Eisai if we reasonably determine that the medical/scientific, technical, regulatory or commercial profile of the licensed product does not justify continued development or marketing.

Eisai can terminate the license agreement, on a country-by-country basis, at any time prior to the date on which we have submitted for either an NDA approval or EMA marketing approval with respect to a licensed product, upon prior written notice to us, if Eisai makes a good faith determination, in accordance with certain provisions specified in the agreement, that we have not used commercially reasonable efforts to develop the licensed product in the territory.

Either party may also terminate the agreement upon an uncured material breach by the other party or upon the bankruptcy or insolvency of the other party. Eisai may terminate the license agreement, with prior written notice, in the event of certain changes of control involving us, if Eisai reasonably determines that the entity assuming control of us is not able to perform under the license agreement with the same degree of skill and diligence that we would use. Eisai shall further have the right to terminate if the acquiring entity has any material and active litigations with Eisai or is a hostile takeover bidder against us.

Duke

In December 2017, we and Duke University ("Duke") entered into a patent license agreement (the "Duke Agreement") pursuant to which we acquired the exclusive worldwide license to certain Duke patents associated with elacestrant (RAD1901) related to the use of elacestrant in the treatment of breast cancer as a monotherapy and in a combination therapy (collectively, the "Duke Patents").

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In consideration for these rights, we incurred non-refundable, non-creditable obligations to pay Duke, an aggregate of $1.3 million, which were expensed as research and development costs during 2017. We also agreed to pay Duke up to an additional $3.8 million upon the achievement of certain future regulatory and commercial milestones. The agreement provides that we would pay Duke a fixed low single-digit royalty based on net sales of a licensed product, on a country-by-country basis, beginning in August 2029 and ending upon expiration of the last licensed patent rights to expire in a country. The latest licensed patent is expected to expire, barring any extension thereof, on October 10, 2034.

If we sublicense the Duke Patents to a third party, the agreement provides that we will pay Duke a percentage of certain payments that we receive from such sublicensee(s). The applicable percentage is in the high single-digit range on certain payments received in excess a pre-specified amount. The Duke Agreement may be terminated by either party upon an uncured material breach of the agreement by the other party. We may terminate the Duke Agreement upon 60 days written notice to Duke, if we suspend our manufacture, use and sale of the licensed products.

Teijin Limited

In July 2017, we entered into a license and development agreement with Teijin for abaloparatide-SC in Japan (the "Teijin Agreement"). Teijin is developing abaloparatide-SC in Japan under an agreement with Ipsen and has initiated a Phase 3 trial in Japanese patients with osteoporosis. Pursuant to the Teijin Agreement, we granted Teijin (i) an exclusive payment bearing license under certain of our intellectual property to develop and commercialize abaloparatide-SC in Japan, (ii) a non-exclusive payment bearing license under certain of our intellectual property to manufacture abaloparatide-SC for commercial supply in Japan, (iii) a right of reference to certain of our regulatory data related to abaloparatide-SC for purposes of developing, manufacturing and commercializing abaloparatide-SC in Japan, (iv) a manufacture transfer package, upon Teijin’s request, consisting of information and our know-how that is necessary for the manufacture of abaloparatide-SC, (v) an obligation, at Teijin’s request, to manufacture (or arrange for a third party to manufacture) and supply (or arrange for a third party to supply) the active pharmaceutical ingredient for the clinical supply of abaloparatide-SC in sufficient quantities to enable Teijin to conduct its clinical trials in Japan, and (vi) an obligation, at Teijin’s request, to arrange for Teijin to directly enter into commercial supply agreements with our existing contract manufacturers on the same pricing terms and on substantially similar commercial terms to those set forth in our existing agreements with such contract manufacturers.

In consideration for these rights, Teijin agreed to pay us an upfront payment of $10.0 million, which we received in October 2017. The Teijin Agreement also provides for additional payments to us of up to an aggregate of $40.0 million upon the achievement of certain regulatory and sales milestones and requires Teijin to pay us a fixed low double-digit royalty based on net sales of abaloparatide-SC in Japan during the royalty term, as defined below. In addition, we have an option to negotiate a co-promotion agreement with Teijin for abaloparatide-SC in Japan.

Teijin granted us (i) an exclusive license under certain of Teijin’s intellectual property to develop, manufacture and commercialize abaloparatide-SC outside Japan and (ii) a right of reference to certain of Teijin’s regulatory data related to abaloparatide-SC for purposes of developing, manufacturing and commercializing abaloparatide-SC outside Japan. Pursuant to the Teijin Agreement, we and Teijin may further collaborate on new indications for abaloparatide-SC. We maintain full global rights to our development program for abaloparatide-patch, which is not part of the Teijin Agreement.

Unless earlier terminated, the Teijin Agreement expires on the later of the (i) date on which the use, sale or importation of abaloparatide-SC is no longer covered by a valid claim under our patent rights licensed to Teijin in Japan, (ii) expiration of marketing or data exclusivity for abaloparatide-SC in Japan, or (iii) 10th anniversary of the first commercial sale of abaloparatide-SC in Japan.

Supply and Manufacturing Agreements

In June 2016, we entered into a Supply Agreement with Ypsomed AG (“Ypsomed”), pursuant to which Ypsomed agreed to supply commercial and clinical supplies of a disposable pen injection device customized for subcutaneous injection of abaloparatide, the API for TYMLOS. We agreed to purchase a minimum number of devices at prices per device that decrease with an increase in quantity supplied. In addition, we made milestone payments for Ypsomed’s capital developments in connection with the initiation of the commercial supply of the device and paid a one-time capacity fee. All costs and payments under the agreement are delineated in Swiss Francs. The agreement has an initial term

of three years which began on June 1, 2017, after which, it automatically renews for two-year terms unless either party terminates the agreement upon 18 months' notice prior to the end of the then-current term. We or Ypsomed may terminate the agreement at any time by providing notice to the other party 18 months prior to the end of the then-current term. The agreement may also be terminated by either party upon material breach of the agreement, due to a party's bankruptcy, insolvency, or dissolution, or due to a change of control of either party under certain circumstances. We may terminate the agreement in the event that Ypsomed is unable to obtain regulatory or other approval for the manufacture and sale of Devices or if such approval is revoked. The Company will purchase the device

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subject to minimum annual quantity requirements over the initial three-year term of the agreement. The Company is required to purchase a minimum number of batches for CHF 2.4 million ($2.5 million) through the year ended December 31, 2022.

In June 2016, we entered into a Commercial Supply Agreement with Vetter Pharma International GmbH ("Vetter"), pursuant to which Vetter has agreed to formulate the finished abaloparatide-SC drug product, to fill cartridges with the drug product, to assemble the pen delivery device, and to package and label the pen for commercial distribution. We agreed to purchase the cartridges and pens in specified batch sizes at a price per unit. For labeling and packaging services, the Company has agreed to pay a per unit price dependent upon the number of pens loaded with cartridges that are labeled and packaged. These prices are subject to an annual price adjustment. The agreement has an initial term of five years, which began on January 1, 2016, after which, it automatically renews for two-year terms unless either party notifies the other party two years before the end of the then-current term that it does not intend to renew. Vetter may terminate the agreement effective upon written notice to us if we fail to maintain certain insurance required under the agreement, or breach provisions regarding ethical business practices, laws, and regulations. We may terminate the agreement effective upon written notice to Vetter if: (1) Vetter fails to obtain or maintain any material governmental licenses or approvals, (2) Vetter has breached provisions regarding ethical business practices, laws, and regulations, or (3) we fail to obtain certain regulatory approvals. Either party may terminate the agreement due to: (1) the other party's bankruptcy or insolvency, (2) the other party's uncured breach of the agreement, (3) a continuing force majeure event, or (4) a failure to reach mutual agreement on a change in the scope of work or services that Vetter reasonably believes it cannot perform because the change is in violation of applicable law.

In July 2016, we entered into a Manufacturing Services Agreement with Polypeptide Laboratories Holding AB ("PPL"), as successor-in-interest to Lonza Group Ltd., pursuant to which PPL has agreed to manufacture the commercial and clinical supplies of the API for abaloparatide. The Company has agreed to purchase the API in batches at a price per gram in euros, subject to an annual increase by PPL. The Company is also required to purchase a minimum number of batches annually, equal to €2.9 million ($3.4 million) per year and $17.2 million in total through the year ended December 31, 2022. The agreement has an initial term of six years, after which, it automatically renews for three-year terms unless either party provides notice of non-renewal 24 months before the end of the then-current term. PPL may terminate the agreement for any reason upon 30-months' notice. We may terminate the agreement for any reason upon 24-months' notice, if we fail to obtain regulatory marketing approval for abaloparatide upon 12-months' notice to PPL, or if abaloparatide is withdrawn from the market upon 12-months' notice to PPL. Either party may terminate the agreement for the other's uncured breach of the agreement due to a party's bankruptcy, insolvency, or dissolution, or due to certain force majeure events.

Government Regulation

United States—FDA Product Approval Process

The research, development, testing, manufacture, labeling, promotion, marketing, advertising, and distribution, among other things, of our product candidates are extensively regulated by governmental authorities in the United States and other countries. In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act (the "FDCA") and its implementing regulations. Failure to comply with the applicable United States requirements may subject us to administrative or judicial sanctions, such as FDA refusal to approve pending NDAs, imposition of clinical holds, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, and/or criminal prosecution. We expect abaloparatide-patch, elacestrant and RAD140 will each be subject to review by the FDA as a drug pursuant to the NDA process, and we currently only have active investigational new drug ("IND") applications in relation to abaloparatide, elacestrant and RAD140 in the United States.

Approval Process—None of our drugs may be marketed in the United States until the drug has received FDA approval of an NDA. The steps required to be completed before a drug may be marketed in the United States include, among others:

- preclinical laboratory tests, animal studies, and formulation studies, all performed in accordance with the FDA's Good Laboratory Practice ("GLP") regulations;

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submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials may begin and must be updated annually;

- adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug for each proposed indication to FDA's satisfaction;

- submission to the FDA of an NDA;

- satisfactory completion of an FDA pre-approval inspection of one or more clinical trial site(s) at which the drug was studied in a clinical trial(s) to assess compliance with Good Clinical Practices ("GCP") regulations;

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- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with cGMP regulations; and

- FDA review and approval of the NDA based on a determination that the drug is safe and effective for the proposed indication(s).

Preclinical tests include laboratory evaluation of product chemistry, toxicity, and formulation, as well as animal studies. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND application, which must become effective before human clinical trials may begin. An IND application will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about issues such as the conduct of the trials as outlined in the IND application. In such a case, the IND application sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. We cannot be sure that submission of an IND application will result in the FDA allowing clinical trials to begin.

Clinical trials involve the administration of the investigational drug to human subjects under the supervision of qualified investigators. Clinical trials are conducted under GCP pursuant to protocols detailing the objectives of the study, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND application. Detailed information about many clinical trials must be submitted to the National Institutes of Health ("NIH") for public disclosure on the government website ClinicalTrials.gov.

Clinical trials necessary for product approval are typically conducted in three sequential phases, but the Phases may overlap. The study protocol and informed consent information for study subjects in clinical trials must also be approved by an Institutional Review Board ("IRB") for each institution where the trials will be conducted, and each IRB must monitor the study until completion. Study subjects must provide informed consent and sign an informed consent form before participating in a clinical trial. Clinical testing also must satisfy the extensive GCP regulations for informed consent and privacy of individually identifiable information.

Phase 1 trials usually involves the initial introduction of the investigational drug into people to evaluate its short-term safety, dosage tolerance, metabolism, pharmacokinetics and pharmacologic actions, and, if possible, to gain an early indication of its effectiveness. Phase 1 studies are usually conducted in healthy individuals and are not intended to treat disease or illness. However, Phase 1b studies are conducted in healthy volunteers or in patients diagnosed with the disease or condition for which the study drug is intended, who present some biomarker, surrogate, or possibly clinical outcome that could be considered for "proof of concept." Proof of concept in a Phase 1b study typically confirms the hypothesis that the current prediction of biomarker, or outcome benefit is compatible with the mechanism of action.

Phase 2 studies usually involves trials in a limited patient population to: (1) evaluate dosage tolerance and appropriate dosage, (2) identify possible adverse effects and safety risks, and (3) evaluate preliminarily the efficacy of the drug for specific target indications. Several different doses of the drug may be looked at in Phase 2 to see which dose has the desired effects. Patients are monitored for side effects and for any improvement in their illness, symptoms, or both.

Phase 3 trials usually further evaluate clinical efficacy and test further for safety by using the drug in its planned commercial form in an expanded patient population. A Phase 3 trial usually compares how well the study drug works compared with an inactive placebo and/or another approved medication. One group of patients may receive the investigational new drug being tested, while another group of patients may receive the comparator drug (already approved drug for the disease being studied), or placebo. Phase 3 trials typically are relied upon as the primary basis for approval because they provide the safety and effectiveness information needed to evaluate the overall benefit-risk relationship of the drug and to create the physician labeling.

There can be no assurance that Phase 1, Phase 2 or Phase 3 testing will be completed successfully within any specified period of time, if at all. Furthermore, we, the FDA, or an Institutional Review Board (with respect to a particular study site) may suspend or terminate clinical trials at any time on various grounds, including a finding that the subjects or

patients are being exposed to an unacceptable health risk.

In addition, clinical trial sponsors are required to register and report results from certain applicable clinical trials for publication on www.clinicaltrials.gov. Until recently, disclosure of clinical trial results for unapproved drugs could be delayed until approval of the drug. The Department of Health and Human Services recently broadened these reporting requirements to also apply to unapproved drugs, regardless of whether FDA approval is or will be sought. The allowable delay period for submitting results for applicable clinical trials of unapproved drugs is one year after the primary completion date of the study, and potentially an additional two years beyond that after submission of a certification; in any event, not to exceed three years in

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total. Consequently, clinical trial information could be subject to posting even if a drug is not approved and does not make it to market.

Assuming successful completion of the required clinical testing, the results of the preclinical studies and of the clinical studies, together with other detailed information, including information on the manufacture and composition of the drug, are submitted to the FDA in the form of an NDA requesting approval to market the product for one or more proposed indications. The testing and approval process requires substantial time, effort and financial resources. Unless the applicant qualifies for an exemption, the filing of an NDA typically must be accompanied by a substantial payment to the FDA, referred to as a "user fee," which currently exceeds $2 million. The FDA reviews the application and may deem it to be inadequate, and companies cannot be sure that any approval will be granted on a timely basis, if at all. The FDA may also refer the application to an appropriate advisory committee, typically a panel of clinicians, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of the advisory committee, but the Agency historically has tended to follow such recommendations.

The FDA has various programs, including fast track designation, breakthrough therapy designation, priority review and accelerated approval, which are intended to expedite or simplify the process for reviewing drugs and/or provide for approval on the basis of surrogate endpoints. Generally, drugs that may be eligible for one or more of these programs are those intended to treat serious or life-threatening diseases or conditions, those with the potential to address unmet medical needs for those disease or conditions, and those that provide meaningful benefit over existing treatments. For example, a sponsor may be granted FDA designation of a drug candidate as a "breakthrough therapy" if the drug candidate is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. If a drug is designated as breakthrough therapy, FDA will take actions to help expedite the development and review of such drug. From time to time, we anticipate applying for such programs where we believe we meet the applicable FDA criteria. A company cannot be sure that any of its drugs will qualify for any of these programs, or even if a drug does qualify, that the review time will be reduced.

In addition to the existing programs described above, additional measures intended to expedite drug product development and review were also included in the 21st Century Cures Act ("Cures Act"). The Cures Act, which was enacted in December 2016, includes provisions intended to enhance and accelerate the FDA's processes for reviewing and approving new drugs and supplements to approved NDAs. These provisions include (1) requirements that FDA establish a program to evaluate the potential use of real world evidence to help to support the approval of a new indication for an approved drug and to help to support or satisfy post-approval study requirements, (2) requirements that FDA issue guidance for purposes of assisting sponsors in incorporating complex adaptive and other novel trial designs into proposed clinical protocols and applications for new drugs, and (3) authorizing FDA to rely upon qualified data summaries to support the approval of a supplemental application with respect to a qualified indication for an already approved drug.

Before approving an NDA, the FDA usually will inspect the facility or the facilities at which the drug is manufactured and will not approve the product unless the manufacturing and production and testing facilities are in compliance with cGMP regulations. If the NDA and the manufacturing facilities are deemed acceptable by the FDA, it may issue an approval letter, and, if not, the agency may issue a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for a specific indication(s). A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. Such a letter usually describes all the deficiencies that the FDA has identified in an NDA that must be satisfactorily addressed before it can be approved. A Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. The FDA could also require, as a condition of NDA approval, post-marketing testing and surveillance to monitor the drug's safety or efficacy or impose other conditions. Approval may also be contingent on a Risk Evaluation and Mitigation Strategy

("REMS") that may include both special labeling and controls, known as Elements to Assure Safe Use, on the distribution, prescribing, dispensing and use of a drug product. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-marketing studies or clinical trials. Once issued, the FDA may withdraw product approval if ongoing regulatory requirements are not met or if safety problems occur after the product reaches the market.
After approval, certain changes to the approved product, such as adding new indications, making certain manufacturing changes or making certain additional labeling claims, are subject to further FDA review and approval. Before a company can market products for additional indications, it must obtain additional approvals from the FDA. Obtaining approval for a new indication generally requires that additional clinical studies be conducted. A company cannot be sure that any additional approval for new indications for any investigational product candidate will be approved on a timely basis, or at all.

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Post-Approval Requirements—Often times, even after a drug has been approved by the FDA for sale, the FDA may require that certain post-approval requirements be satisfied, including the conduct of additional clinical studies. If such post-approval conditions are not satisfied, the FDA may withdraw its approval of the drug. In addition, holders of an approved NDA are required to, among other requirements: (1) report certain adverse reactions to the FDA within specific time frames, (2) comply with certain requirements concerning advertising and promotional labeling for their products, (3) continue to have quality control and manufacturing procedures conform to cGMP regulations after approval, (4) make periodic reports to FDA about the approved product, and (5) comply with requirements regarding distribution of the drug product. The FDA periodically inspects the sponsor's records related to safety reporting, distribution and/or manufacturing facilities; this latter effort includes assessment of ongoing compliance with cGMP regulations. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. We have used and intend to continue to use third-party manufacturers to produce our products in clinical and commercial quantities, and future FDA inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution or require substantial resources to correct. In addition, discovery of problems with a product after approval may result in restrictions on a product, including recall or withdrawal of the product from the market, labeling changes, imposition of REMS, or the requirement to conduct additional studies.

Hatch-Waxman Act-Under the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, Congress created an abbreviated FDA review process for generic versions of pioneer (brand name) drug products under section 505(j) of the FDCA. Section 505(j) provides for approval of an abbreviated new drug application ("ANDA") that contains information to show that the proposed product is identical in active ingredient, dosage form, strength, route of administration, labeling, quality, performance characteristics, and intended use, among other things, to a previously approved drug (commonly known as the reference drug). In considering whether to approve such a generic drug product, the FDA requires that an ANDA applicant demonstrate, among other things, that the proposed generic drug product's active ingredient is the same as that of the reference product, that the proposed generic is bioequivalent to the reference product, that any impurities in the proposed product do not affect the product's safety or effectiveness, and that its manufacturing processes and methods ensure the consistent potency and purity of its proposed product. In addition to the ANDA pathway, the Hatch-Waxman Act also established an abbreviated approval pathway under section 505(b)(2) of the FDCA for applications that contain full reports of investigations of safety and effectiveness, but where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Section 505(b)(2) permits approval of applications other than those for duplicate products and permits reliance for such approvals on literature or on FDA's finding of safety or effectiveness for an approved drug product.

The Hatch-Waxman Act provides five years of data exclusivity for new chemical entities ("NCE") referred to as NCE exclusivity, which generally (except as discussed below) prevents the FDA from accepting ANDAs and section 505(b)(2) applications containing the protected active ingredient or active moiety for five years after initial approval of the NCE. A drug is a NCE if the FDA has not previously approved an NDA for another drug that contains the same active moiety, which FDA defines to mean the molecule or ion (excluding certain specified appended portions) responsible for the physiological or pharmacological action of the drug substance. TYMLOS qualified as an NCE, thus received five years of NCE exclusivity following the FDA's approval in April 2017. Under FDA's "umbrella policy," NCE exclusivity protects all drug products that contain the qualifying NCE, so if abaloparatide-patch is approved prior to the expiration to the NCE exclusivity granted to TYMLOS, we would expect abaloparatide-patch to be protected by any remaining NCE exclusivity period.

The Hatch-Waxman Act also provides three years of exclusivity for applications (including supplements) containing the results of new clinical investigations (other than bioavailability studies) essential to the FDA's approval of new versions or conditions of use of previously approved drug products, such as new indications, delivery mechanisms, dosage forms, strengths, or other conditions of use. For example, if we are successful in performing a clinical trial of abaloparatide-patch that provides a new basis for approval (a different delivery mechanism) and that FDA considers essential to approval of the drug, it is possible that we may become eligible for a three-year period of market exclusivity for approval of an NDA for abaloparatide-patch. Any such three-year exclusivity period would protect

against the approval (but not the filing) of ANDAs and section 505(b)(2) applications referencing abaloparatide-patch for the protected transdermal route of administration. Such exclusivity period for abaloparatide-patch would generally not, however, prohibit the FDA from accepting or approving ANDAs or section 505(b)(2) applications referencing only abaloparatide-SC or section 505(b)(2) applications that reference abaloparatide-patch but that seek approval for a different route of administration or for a use other than for the indication that has been approved for abaloparatide-patch.

The Hatch-Waxman Act requires NDA applicants and NDA holders to submit certain information about patents related to their drugs for listing in the FDA's list of Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as the Orange Book). ANDA and section 505(b)(2) applicants generally must submit a certification or statement regarding each of the patents listed with the FDA for the reference product. A certification that a listed patent is invalid and/or will not be infringed by the marketing of the ANDA or section 505(b)(2) applicant's product is called a "Paragraph IV

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certification." If the sponsor of an ANDA or section 505(b)(2) application that references a drug with unexpired exclusivity provides a Paragraph IV certification for a patent for a reference product that is protected by NCE exclusivity, then the FDA may accept the ANDA or section 505(b)(2) application beginning four years after approval of the reference product's NDA (rather than five years). If an ANDA or section 505(b)(2) application containing a Paragraph IV certification is submitted to the FDA and accepted as a reviewable filing by the Agency, the ANDA or section 505(b)(2) applicant then must provide, within 20 days of FDA acceptance, notice to the NDA holder and patent owner stating that the application has been submitted and providing the factual and legal basis for the applicant's opinion that the patent is invalid and/or not infringed. The NDA holder or patent owner then may file suit against the ANDA or section 505(b)(2) applicant for patent infringement. If this is done within 45 days of receiving notice of the Paragraph IV certification, a 30-month stay of the FDA's ability to approve the ANDA or section 505(b)(2) application is triggered. The 30-month stay begins on the date of receipt of the Paragraph IV notice and, in the case where an ANDA or section 505(b)(2) application is submitted before a reference product's NCE exclusivity expires (i.e., four years after approval of the reference product), the 30-month period is extended to ensure that approval of the ANDA or section 505(b)(2) application cannot be granted for 7-$^1/_2$ years after initial approval of the reference product. Nevertheless, the FDA may approve the proposed product before the expiration of the 30-month stay (or 7-$^1/_2$ year period) if a court finds the patent invalid and/or not infringed or if the court shortens the period because the parties have failed to cooperate in expediting the litigation.

European Union—Product Approval Process

In the European Union, medicinal products are authorized following a similar demanding process as that required in the United States and applications for marketing authorization must be submitted based on the ICH Common Technical Document format. In the European Economic Area ("EEA") (comprising 28 EU Member States plus Iceland, Liechtenstein and Norway), medicines can be authorized by using either the centralized authorization procedure or national authorization procedures, albeit through the decentralized or mutual recognition procedure to gain access to two or more EEA Member States.

Centralized procedure—Under the centralized procedure governed by Regulation (EC) 726/2004, a single marketing authorization application is submitted to the EMA for its scientific evaluation of the safety, quality and efficacy. The CHMP then carries out a scientific assessment of the application and issues an opinion on the approvability of the medicine. Following adoption of the CHMP's opinion, the European Commission, as the EU licensing authority, will adopt a legally binding decision on granting of a centralized marketing authorization which is valid across the EU and through the EEA Treaty, the Member States of the EEA. The centralized procedure is mandatory for human medicines derived from certain biotechnology processes, advanced therapy medicinal products (such as gene therapy, somatic cell therapy and tissue engineered products), medicines containing a new active substance falling within the mandatory centralized procedure such as those which are indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, or neurodegenerative disorders, diabetes, autoimmune diseases and other immune dysfunctions, viral diseases, and orphan-designated medicines. The centralized procedure is optional for applicants seeking marketing authorizations for medicines which contain a new active substance which is not authorized in the EEA. Alternatively, a medicine which is shown to constitute a significant therapeutic, scientific or technical innovation, or if its authorization via the centralized procedure would be in the interest of public health in the EEA would be considered as eligible for centralized assessment.

National authorization procedure—Pure national authorization procedure is applicable where the applicant intends to market the product only in one Member State. However, if an applicant intends to market the product in two or more Member States, there are two other possible regulatory procedures for products that fall outside the scope of the mandatory or the optional centralized procedure:

- Decentralized procedure. Where a medicinal product has not been authorized anywhere in the EEA and the product does not fall within the mandatory centralized procedure, an applicant may request a Member State to act as the Reference Member State to lead the assessment of the marketing authorization for it to be considered by the selected number of Member States which are concerned by the procedure. A positive decision adopted during the decentralized procedure will result in national marketing authorizations being granted by the Reference and Concerned Member States.

- Mutual recognition procedure. Where the medicinal product has been authorized in a EU Member State, the applicant can request the Member State to act as the Reference Member State for the national marketing authorization to be recognized progressively in the other Concerned Member States.

Under both decentralized and mutual recognition procedures, the Reference Member State leads the assessment for it to be recognized by the national authorities in Member States concerned by the procedure. A satisfactory conclusion of a procedure will result in granting of a national marketing authorization.

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Good manufacturing practices—Like the FDA, the EMA, the competent authorities of the EU Member States and other regulatory agencies regulate and inspect equipment, facilities and processes used in the manufacture of pharmaceutical and biologic products. Prior to the CHMP adopting an opinion with respect to approvability of an application for marketing authorization, the EMA, acting upon the advice of the CHMP, may decide to coordinate an inspection to be undertaken by the designated EU Supervising Authority of the proposed manufacturing site to verify the manufacturer's compliance with EU GMP principles and guidelines or to investigate a specific GMP-related matter that may arise from the assessment of the application. If there is a material change in manufacturing equipment, location, or process, affecting the quality of the product, additional regulatory review and approval may be required from the relevant competent regulatory authority. Once we or our partners commercialize products, we will be required to comply with GMP with regard to manufacture and control, and product-specific requirements according to the terms of the marketing authorization. Also, like the FDA, the EMA (as a coordinating body for centrally authorized medicinal products), the competent authorities of the EU Member States and other regulatory agencies also conduct regular, periodic visits to re-inspect equipment, facilities, and processes following the initial approval of a product. If it is determined that the equipment, facilities, or processes used to manufacture our product do not comply with applicable regulations and conditions of product approval, regulatory agencies may seek civil, criminal or administrative sanctions, or enforcement actions and/or remedies against the manufacturer holding the requisite manufacturing authorization and us, including the suspension of our manufacturing operations or the withdrawal of our product from the market.

Data and market exclusivity—Similar to the United States, there is a process for approval of generic versions of innovator drug products in the European Union. Abridged applications for the authorization of generic versions of drugs authorized centrally by the European Commission can be submitted to the EMA through the centralized procedure referencing the innovator's non-clinical and clinical data to support generic approval provided always that the following conditions are met: the generic product has the same qualitative and quantitative composition in the active substances and the same pharmaceutical form as the reference innovator drug product and the generic product is shown to be bioequivalent to the reference product.

New medicinal products authorized according to the EU regulatory requirements will benefit from eight years of data protection within which the generic applicant cannot rely on the non-clinical and clinical data contained in the dossier of the reference product to support product approval, and two years of market protection within which the generic applicant is not permitted to place the generic product on the market even if it is approved. This period of data and market protection can be extended to a maximum of eleven years if during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which during the scientific assessment prior to their authorization are held to bring a significant benefit in comparison with existing therapies.

Other International Markets—Drug approval process

In some international markets (e.g., China or Japan), although data generated in U.S. or EU trials may be submitted in support of a marketing authorization application, additional clinical trials conducted in the host territory, or studying people of the ethnicity of the host territory, may be required prior to the filing or approval of marketing applications within the country.

Pricing and Reimbursement

In the United States and internationally, sales of products that we market in the future, and our ability to generate revenues on such sales, are dependent, in significant part, on the availability and level of coverage and reimbursement from third-party payors such as state and federal governments, pharmacy benefit managers and health insurance plans. Third-party payors have implemented cost-cutting and reimbursement initiatives and likely will continue to do so in the future. These include establishing formularies that limit and govern the drugs and biologics that will be offered, determining the evidence and documentation required to support medical need, setting the out-of-pocket obligations of member patients, and negotiating discounts, rebates and price concessions with manufacturers for such products. In addition, particularly in the United States and increasingly in other countries, we may be required to provide discounts, price concessions and pay rebates to state and federal governments and agencies in connection with purchases of our products that are reimbursed by such entities. It is possible that future legislation in the United States

and other jurisdictions could be enacted which could potentially impact the reimbursement rates for the products we are developing and may develop in the future, and also could further impact the levels of discounts, price concessions and rebates paid to federal and state government entities. Any legislation that impacts these areas could impact, in a significant way, our ability to generate revenues from sales of products that, if successfully developed, we bring to market.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (“MMA”) established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities to provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Parts A and B, Part D coverage may vary based on the Part D plan sponsor. Part D

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prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each Part D prescription drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, although not necessarily all of the drugs within each category or class and must cover all or substantially all medications within six protected classes of drugs: immunosuppressants, antidepressants, antipsychotics, anticonvulsants, antiretrovirals, and antineoplastics. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. A significant proportion of patients eligible for TYMLOS are Medicare beneficiaries and as of January 17, 2019, TYMLOS was covered for 67% of the covered lives under Medicare Part D.

Government payment for some of the costs of prescription drugs may increase demand for any of our products that are successfully developed and approved. However, any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, although the MMA applies only to drug benefits for Medicare beneficiaries, private payers often follow Medicare coverage policy and payment limitations in setting their own payment rates. Accordingly, any reduction in payment under Medicare may result in a similar reduction in payments from non-governmental payers.

We expect that there will continue to be a number of federal and state proposals to implement governmental pricing controls and limit the growth of healthcare costs, including the cost of prescription drugs. Currently, Medicare is prohibited from negotiating directly with pharmaceutical companies for drugs. However, the U.S. Congress may in the future consider legislation that would lift the ban on federal negotiations.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research would be developed by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes of Health, and periodic reports on the status of the research and related expenditures would be made to the U.S. Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payers, it is not clear whether research would have any effect on the sales of any of our products that is successfully developed and approved, if the product or the condition that it is intended to treat becomes the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits of a competitor's product could adversely affect the sales of any of our products that is successfully developed and approved. If third-party payers do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The Patient Protection and Affordable Care Act (the "ACA") as amended by the Health Care and Education Affordability Reconciliation Act of 2010, or collectively the ACA, is expected to have a significant impact on the health care industry. The ACA expands coverage for the uninsured while at the same time containing overall healthcare costs. Among other things, the ACA expands and increases industry rebates for drugs covered under Medicaid programs and make changes to the coverage requirements under the Medicare Part D program. In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. Any such legislative changes associated with healthcare reform, including the ACA, may have a significant impact on drug pricing, and could limit pricing flexibility or expand rebate liabilities of drug manufacturers.

On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2025 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012 (the "ATRA") was enacted, which among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers.

Several states enacted legislation in 2017 related to prescription drug pricing transparency. Savings projected under these proposals are targeted as a means to fund both health care expenditures and non-health care initiatives, or to

manage federal and state budgets. The Bipartisan Budget Act, enacted on February 9, 2018, will require manufacturers of brand name drugs, biologics, and biosimilars to pay a 70 percent discount in the Medicare Part D Coverage Gap, up from the current 50 percent discount. This increase in Coverage Gap discounts will be effective beginning in 2019. Decisions on pricing and reimbursement of medicinal products in the European Union are based upon national rules subject to the control of the Transparency Directive, (Council Directive 89/105/EEC) which aims to ensure the transparency of measures established by EU countries to control the pricing and reimbursement of medicinal products. It defines a series of procedural requirements designed to verify that national pricing and reimbursement decisions do not create obstacles to the

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pharmaceutical trade within the EU's Internal Market. The competent authorities of each of the 28 EU Member States have adopted individual national measures aimed at regulating the pricing and reimbursement of medicinal products in their territory. These measures often vary widely in nature, scope and application. However, a major element that they have in common is an increased move toward reduction in the reimbursement price of medicinal products, a reduction in the number and type of products selected for reimbursement, and an increased preference for generic products over innovative products. These efforts have mostly been executed through these countries' existing price-control methodologies, including price cuts, mandatory rebates, value-based pricing, and reference pricing (i.e., referencing prices in other countries and using those reference prices to set a price). It is increasingly common in many EU Member States for Marketing Authorization Holders to be required, in order to get support for reimbursement under national health schemes and, therefore, access to the market, to demonstrate the cost effectiveness or otherwise added value benefit of their products as compared to products (which are considered as standard of care) already subject to pricing and reimbursement in specific countries. In order for drugs to be evaluated positively under such criteria, pharmaceutical companies may need to re-examine, and consider altering, a number of traditional functions relating to the selection, study, and management of drugs, whether currently marketed, under development, or being evaluated as candidates for research and/or development.

Future legislation, including the current versions being considered at the federal and state level in the United States and at the national level in EU Member States, or regulatory actions implementing recent or future legislation may have a significant effect on our business. Our ability to successfully commercialize products depends in part on the extent to which coverage and reimbursement for the costs of our products and related treatments will be available in the United States and worldwide from government health administration authorities, private health insurers and other organizations. Substantial uncertainty exists as to the reimbursement status of newly approved healthcare products by third-party payors. In addition, negotiating prices with government authorities under current and proposed legislation can delay the commercialization of our product candidates.

Sales and Marketing

The FDA regulates all advertising and promotion activities for products under its jurisdiction both prior to and after approval. Generally, a company can make only those claims relating to safety and efficacy that are approved by the FDA following review and approval of an NDA. Physicians may prescribe legally available drugs for uses that are not described in the drug's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties, and often reflect a physician's belief that the off-label use is the best treatment for the patients. The FDA does not regulate the behavior of physicians in their choice of treatments, but FDA regulations and enforcement policies do impose stringent restrictions on manufacturers' communications regarding off-label uses. In addition, the FDA also regulates communications about investigational drugs, including with respect to the pre-approval promotion of investigational drugs. Recent case law suggests that pharmaceutical companies may have a First Amendment right to provide truthful and non-misleading information about off-label uses of their products to physicians and others, but the scope of this right remains unclear. Accordingly, failure to comply with applicable FDA requirements may subject a company to adverse publicity, enforcement action by the FDA, corrective advertising, consent decrees and the full range of civil and criminal penalties available to the FDA.

We may also be subject to various federal and state laws pertaining to healthcare "fraud and abuse," including anti-kickback laws and false claims laws. Anti-kickback laws make it illegal for a prescription drug manufacturer to solicit, offer, receive, or pay any remuneration in exchange for, or to induce, the referral of business, including the purchase or prescription of a particular drug. Due to the breadth of the statutory provisions and the absence of guidance in the form of regulations and very few court decisions addressing industry practices, it is possible that our practices might be challenged under anti-kickback or similar laws. Moreover, recent healthcare reform legislation has strengthened these laws. For example, the ACA, among other things, amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes, so that a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the ACA permits the government to assert that a claim that includes 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 statutes.

False claims laws prohibit anyone from knowingly and willingly presenting, or causing to be presented for payment, to third-party payors (including Medicare and Medicaid) claims for reimbursed drugs or services that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. Our activities relating to the sale and marketing of our products, if approved, may be subject to scrutiny under these laws. Violations of fraud and abuse laws may be punishable by criminal and civil sanctions, including fines and civil monetary penalties, the possibility of exclusion from federal healthcare programs (including Medicare and Medicaid) and corporate integrity agreements, which impose, among other things, rigorous operational and monitoring requirements on companies. Similar sanctions and penalties also can be imposed upon executive officers and employees, including criminal sanctions against executive officers under the so-called “responsible corporate officer” doctrine, even in situations where the executive officer did not intend to violate the law and was unaware of any wrongdoing.

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Given the significant penalties and fines that can be imposed on companies and individuals if convicted, allegations of such violations often result in settlements even if the company or individual being investigated admits no wrongdoing. Settlements often include significant civil sanctions, including fines and civil monetary penalties, and corporate integrity agreements. If the government were to allege or convict us or our executive officers of violating these laws, our business could be harmed. In addition, private individuals have the ability to bring similar actions. The majority of states also have anti-kickback and false claims laws, which establish similar prohibitions and, in some cases, may apply to items or services reimbursed by any third-party payor, including commercial insurers. Our activities could be subject to challenge for the reasons discussed above and due to the broad scope of these laws and the increasing attention being given to them by law enforcement authorities.

There has also been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The ACA, among other things, imposed new reporting requirements on drug manufacturers for payments made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties of up to an aggregate of $150,000 per year (or up to an aggregate of $1 million per year for “knowing failures”), for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Drug manufacturers are required to submit reports to the government by the 90th day of each calendar year. Certain states also mandate implementation of compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians. Many of these laws contain ambiguities as to what is required to comply with the laws. Given the lack of clarity in laws and their implementation, our actions could be subject to the penalty provisions of the pertinent state authorities.

Similar rigid restrictions are imposed on the promotion and marketing of medicinal products in the EU and other countries. Laws (including those governing promotion, marketing and anti-kickback provisions), industry regulations and professional codes of conduct often are strictly enforced. Even in those countries where we are not directly responsible for the promotion and marketing of our products, inappropriate activity by our international distribution partners can have adverse implications for us.

Other Laws and Regulatory Processes

We are subject to a variety of financial disclosure and securities trading regulations as a public company in the United States, including laws relating to the oversight activities of the Securities and Exchange Commission (“SEC”) and the regulations of the Nasdaq Global Market or any national securities exchange on which our capital stock may be traded. In addition, the Financial Accounting Standards Board (“FASB”) the SEC and other bodies that have jurisdiction over the form and content of our accounts, our consolidated financial statements and other public disclosure are constantly discussing and interpreting proposals and existing pronouncements designed to ensure that companies best display relevant and transparent information relating to their respective businesses.

Our international operations are subject to compliance with the Foreign Corrupt Practices Act