Regulus Therapeutics Inc.
Form 10-K
March 08, 2018
Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)
x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
FOR THE FISCAL YEAR ENDED DECEMBER 31, 2017
or
¨ 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: 001-35670

Regulus Therapeutics Inc.
(Exact name of registrant as specified in its charter)

Delaware (State or Other Jurisdiction of Incorporation or Organization)	26-4738379 (I.R.S. Employer Identification No.)
10614 Science Center Drive San Diego, CA (Address of Principal Executive Offices)	92121 (Zip Code)

(858) 202-6300
(Registrant's Telephone Number, Including Area Code)
Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, par value $0.001 per share	The NASDAQ Global Market

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No ý
Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ¨ 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 ¨
Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). Yes ý No ¨

Table of Contents

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the 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. ¨

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 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	¨	Accelerated filer ý
Non-accelerated filer	¨	Smaller reporting company ¨
		Emerging growth company ¨

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. o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes ¨ No ý

As of June 30, 2017, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's common stock held by non-affiliates of the registrant was approximately $51.5 million, based on the closing price of the registrant's common stock on the NASDAQ Global Market on June 30, 2017 of $0.99 per share.

The number of outstanding shares of the registrant's common stock, par value $0.001 per share, as of February 23, 2018 was 103,959,103.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's proxy statement to be filed with the Securities and Exchange Commission pursuant on Schedule 14A in connection with the registrant's 2018 Annual Meeting of Stockholders, which will be filed subsequent to the date hereof, are incorporated by reference into Part III of this Form 10-K. Such proxy statement will be filed with the Securities and Exchange Commission not later than April 30, 2018.

Table of Contents

REGULUS THERAPEUTICS INC.
TABLE OF CONTENTS

Table of Contents

PART I

Forward-Looking Statements

This Annual Report on Form 10-K and the documents incorporated by reference herein may contain "forward-looking statements" within the meaning of the federal securities laws made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth below under Part I, Item 1A, "Risk Factors" in this Annual Report. Except as required by law, we assume no obligation to update these forward-looking statements, whether as a result of new information, future events or otherwise. These statements, which represent our current expectations or beliefs concerning various future events, may contain words such as "may," "will," "expect," "anticipate," "intend," "plan," "believe," "estimate" or other words indicating future results, though not all forward-looking statements necessarily contain these identifying words. Such statements may include, but are not limited to, statements concerning the following:

- the initiation, cost, timing, progress and results of, and our expected ability to undertake certain activities and accomplish certain goals with respect to, our research and development activities, preclinical studies and clinical trials;
- our ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations;
- our plans to research, develop and commercialize our product candidates;
- the potential election of any strategic alliance or collaboration partner to pursue development and commercialization of any programs or product candidates that are subject to a collaboration with such partner;
- our ability to attract collaborators with relevant development, regulatory and commercialization expertise;
- future activities to be undertaken by our strategic alliance partners, collaborators and other third parties;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- our ability to successfully commercialize, and our expectations regarding future therapeutic and commercial potential with respect to, our product candidates;
- the rate and degree of market acceptance of our product candidates;
- our ability to develop sales and marketing capabilities, whether alone or with potential future collaborators;
- regulatory developments in the United States and foreign countries;
- the performance of our third-party suppliers and manufacturers;
- the success of competing therapies that are or may become available;
- the loss of key scientific or management personnel;
- our ability to successfully secure and deploy capital;
- our ability to satisfy our debt obligations;
- the accuracy of our estimates regarding future expenses, future revenues, capital requirements and need for additional financing; and
- the risks and other forward-looking statements described under the caption "Risk Factors" under Part I, Item 1A of this Annual Report on Form 10-K.

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

unduly rely upon these statements.

Item 1. Business

Overview

We are a clinical-stage biopharmaceutical company focused on discovering and developing first-in-class drugs targeting microRNAs to treat diseases with significant unmet medical need. We were formed in 2007 when Alnylam Pharmaceuticals, Inc., or Alnylam, and Ionis Pharmaceuticals, Inc., or Ionis, contributed significant intellectual property, know-how and financial and human capital to pursue the development of drugs targeting microRNAs pursuant to a license and collaboration agreement. Our two lead product candidates, RG-012 and RGLS4326, are currently in clinical development. RG-012 is an anti-miR targeting miR-21 for the treatment of Alport syndrome, a life-threatening kidney disease with no approved therapy available. RGLS4326 is an anti-miR targeting miR-17 for the treatment of autosomal dominant polycystic

Table of Contents

kidney disease, or ADPKD. In addition to these programs, we continue to develop a pipeline of preclinical drug product candidates.

microRNAs are naturally occurring ribonucleic acid, or RNA, molecules that play a critical role in regulating key biological pathways. Scientific research has shown that an imbalance, or dysregulation, of microRNAs is directly linked to many diseases. Furthermore, many different infectious pathogens interact and bind to host microRNA to survive. To date, over 500 microRNAs have been identified in humans, each of which can bind to multiple messenger RNAs that control key aspects of cell biology. Since many diseases are multi-factorial, involving multiple targets and pathways, the ability to modulate multiple pathways by targeting a single microRNA provides a new therapeutic approach for treating complex diseases.

RNA plays an essential role in the process used by cells to encode and translate genetic information from deoxyribonucleic acid, or DNA, to proteins. RNA is comprised of subunits called nucleotides and is synthesized from a DNA template by a process known as transcription. Transcription generates different types of RNA, including messenger RNAs that carry the information for proteins in the sequence of their nucleotides. In contrast, microRNAs are RNAs that do not code for proteins but rather are responsible for regulating gene expression by modulating the translation and decay of target messenger RNAs. By interacting with many messenger RNAs, a single microRNA can regulate the expression of multiple genes involved in the normal function of a biological pathway. Many pathogens, including viruses, bacteria and parasites, also use host microRNAs to regulate the cellular environment for survival. In some instances, the host microRNAs are essential for the replication and/or survival of the pathogen. For example, miR-122 is a microRNA expressed in human hepatocytes and is a key factor for the replication of the hepatitis C virus, or HCV.

We believe that microRNA therapeutics have the potential to become a new and major class of drugs with broad therapeutic application for the following reasons:

- microRNAs play a critical role in regulating biological pathways by controlling the translation of many target genes;
- microRNA therapeutics regulate disease pathways which may result in more effective treatment of complex multi-factorial diseases;
- many human pathogens, including viruses, bacteria and parasites, use microRNAs (host and pathogen encoded) to enable their replication and suppression of host immune responses; and
- microRNA therapeutics may be synergistic with other therapies because of their different mechanism of action.

We believe we have assembled the leading position in the microRNA field, including expertise in microRNA biology and oligonucleotide chemistry, a broad intellectual property estate, relationships with key opinion leaders and a disciplined drug discovery and development process. We are using our microRNA expertise to develop chemically modified, single-stranded oligonucleotides that we call anti-miRs to modulate microRNAs and address underlying disease. We believe microRNAs may play a critical role in complex disease and that targeting them with anti-miRs may become a source of a new and major class of drugs with broad therapeutic application, much like small molecules, biologics and monoclonal antibodies.

We believe that microRNA biomarkers may be used to select optimal patient segments in clinical trials and to monitor disease progression or relapse. We believe these microRNA biomarkers can be applied toward drugs that we develop and drugs developed by other companies with which we partner or collaborate.

Development Stage Pipeline

We currently have multiple programs in various stages of clinical and preclinical development.

RG-012: In the third quarter of 2017, we initiated HERA, the Phase II randomized (1:1), double-blinded, placebo-controlled study evaluating the safety and efficacy of RG-012 in 40 Alport syndrome patients. In parallel, a renal biopsy study was also initiated in the third quarter of 2017 to evaluate RG-012 renal tissue pharmacokinetics, or PK, target engagement and downstream effects on genomic disease biomarkers. In connection with the initiation of HERA and the renal biopsy study, we completed enrollment of additional Alport syndrome patients in our global ATHENA natural history of disease study. In May 2017, we completed a Phase I multiple-ascending dose, or MAD,

study in 24 healthy volunteers (six-week repeat dosing) to determine safety, tolerability and PK of RG-012 prior to chronic dosing in patients. In Phase I clinical studies to date, RG-012 was well-tolerated, and there were no serious adverse events, or SAEs, reported. RG-012 has received orphan designation in both the United States and Europe.

Table of Contents

RGLS4326: In December 2017, we initiated a Phase I randomized, double-blind, placebo-controlled, single ascending dose study designed to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of RGLS4326 administered subcutaneously in healthy volunteers. RGLS4326 is a novel oligonucleotide designed to inhibit miR-17 using a unique chemistry designed to preferentially deliver to the kidney. Preclinical studies with RGLS4326 have demonstrated a reduction in kidney cyst formation, improved kidney weight/body weight ratio, decreased cyst cell proliferation, and preserved kidney function in mouse models of ADPKD.

RG-101: In July 2017, we discontinued clinical development of RG-101 for the treatment of chronic HCV infection. Comprehensive preclinical investigation and detailed analysis of clinical data from the RG-101 program identified the direct inhibition of a hepatocyte conjugated bilirubin transporter as the likely mechanism for the cases of hyperbilirubinemia in the RG-101 program. We believe that a combination of factors, including inhibition of conjugated bilirubin transport by RG-101, impaired baseline bilirubin transport in HCV patients and the preferential uptake of RG-101 by hepatocytes contributed to this mechanism. Additional patient-specific contributing factors cannot be excluded. Applying the learnings from the RG-101 program, alternative compounds targeting miR-122 have been identified that maintain potent HCV antiviral activity while lacking inhibition of the bilirubin transporter. We believe these compounds have the potential for rapid clinical proof-of-concept of a novel, markedly shortened treatment regimen for HCV and will be considered for further development.

RG-125(AZD4076): In June 2017, AstraZeneca AB, or AstraZeneca, delivered written notice of their election to terminate the collaboration and license agreement. Effective upon the termination of the agreement, AstraZeneca's rights with respect to RG-125(AZD4076) for the treatment of non-alcoholic steatohepatitis, or NASH, in Type 2 Diabetes/Pre-diabetes will revert to us. In accordance with the agreement, the termination will become effective in June 2018.

Preclinical Pipeline

A major focus of our preclinical research is targeting dysregulated microRNAs implicated in diseases of high unmet medical need where we know we can effectively deliver to the target tissue or organ, such as the liver and kidney. For example, multiple microRNAs have been identified as being dysregulated in NASH and these are in the process of target validation including the evaluation of tool compounds in animal models of NASH. Profiling of primary tumor cells from glioblastoma multiforme, or GBM, a rapidly fatal form of brain cancer, has identified miR-10b as a microRNA target with the potential to inhibit tumor growth. We are investigating local and systemic delivery of anti-miR-10b oligonucleotides in preclinical models to evaluate potential for advancing this program to clinical testing in GBM. We also have early discovery programs investigating additional microRNA targets for infectious diseases, immunology and indications for which there is microRNA dysregulation or in disease settings where the host microRNAs are essential for the replication and/or survival of the pathogen.

Our microRNA product platform

We believe we are the leading company in the field of microRNA therapeutics and are uniquely positioned to leverage oligonucleotide technologies developed by us and our founding companies.

We view the following as providing a competitive advantage for our microRNA product platform:

- a mature platform selectively producing multiple development candidates advancing to the clinic;
- scientific advisors who are pioneers in the microRNA field;
- exclusive access to proven RNA therapeutic technologies through our founding companies, such as GalNac conjugation and the corresponding manufacturing rights licensed to us from Alnylam;
- a leading microRNA intellectual property estate with over 300 patents and patent applications covering compositions and therapeutic uses related to microRNA and microRNA drug products, as well as access to numerous patents and patent applications relating to RNA technologies, including patent and patent applications relating to chemical modification of oligonucleotides that are useful for microRNA therapeutics;
- development expertise and financial resources provided by our strategic alliance; and
- numerous academic collaborations that help us identify new microRNA targets and support our early stage discovery efforts.

The disciplined approach we take for the discovery and development of microRNA therapeutics is as important as the assets assembled to execute our plans and is based on the following four steps:

Step 1 - Evaluation of microRNA therapeutic opportunities

Table of Contents

The initiation of our microRNA discovery and development efforts is based on rigorous scientific and business criteria, including:

- existence of significant scientific evidence to support the role of a specific microRNA in a disease;
- availability of predictive preclinical disease models to test our microRNA development candidates;
- ability to effectively deliver anti-miRs to the diseased cells or tissues; and
- existence of a significant unmet medical need and commercial opportunity.

Step 2 - Identification of microRNA targets

We identify microRNA targets through bioinformatic analysis of public and proprietary microRNA expression profiling data sets from samples of diseased human tissues. The analysis of such data sets can immediately highlight a potential role for specific microRNAs in the disease being studied. Further investigation of animal models that are predictive of human diseases in which those same microRNAs are also dysregulated provides additional data to support a new program. We have applied this strategy successfully in our existing programs and we believe that this approach will continue to help us identify clinically relevant microRNA targets.

Step 3 - Validation of microRNA targets

Our validation strategy is based on two distinct steps. First, using genetic tools, we determine whether up-regulation, or overproduction, of the microRNA in healthy animals can create the specific disease state and inhibition of the microRNA can lead to a therapeutic benefit. Second, using animal models predictive of human diseases, we determine whether pharmacological modulation of the up-regulated microRNA target with our anti-miRs can also lead to a therapeutic benefit. This validation process enables us to prioritize microRNA targets that appear to be key drivers of disease and not simply correlating markers.

Step 4 - Optimization of microRNA development candidates

We have developed a proprietary process that allows us to rapidly generate an optimized development candidate. Unlike traditional drug classes, such as small molecules, in which thousands of compounds must be screened to identify prospective leads, the fact that anti-miRs are complementary to (thereby pairing with) the target microRNA allows for a more efficient rational design process. The optimization process incorporates our extensive knowledge base around oligonucleotide chemistry and anti-miR design to efficiently synthesize a starting pool of rationally designed anti-miRs to be evaluated in a series of proven assays and models. We are able to enhance our anti-miRs for distribution in certain tissues, such as the liver and kidney, where the specific microRNA target is causing disease.

Our development candidates

We are developing single-stranded oligonucleotides, which are chemically synthesized chains of nucleotides that are complementary to (thereby pairing with) the target microRNA. We incorporate proprietary chemical modifications to enhance drug properties such as potency, stability and tissue distribution. We refer to these chemically modified oligonucleotides as anti-miRs. Each anti-miR is designed to bind with and inhibit a specific microRNA target that is up-regulated in a cell and that is involved in the disease state. In binding to the microRNA, anti-miRs correct the dysregulation and return diseased cells to their healthy state. We have demonstrated the therapeutic benefit of inhibiting microRNA-122 in humans with RG-101 in HCV patients. In addition to these human proof-of-concept results, we have demonstrated therapeutic benefits of our anti-miRs in over 20 different preclinical models of human diseases.

We have identified and validated several microRNA targets across a number of disease categories and are working independently and with our strategic alliance partner to optimize anti-miR development candidates. We intend to pursue a balanced approach between product candidates that we develop ourselves and those that we develop with partners. We intend to focus our own resources on proprietary product opportunities in therapeutic areas where development and commercialization activities are appropriate for our size and financial resources. In therapeutic areas where costs are more significant, development timelines are longer or markets are too large for our capabilities, we may seek to secure partners with requisite expertise and resources.

6

Table of Contents

*Sanofi will have the exclusive option, exercisable after proof-of-concept, to take over further development and commercialization of these programs. At this stage, we will have the option to co-promote any microRNA therapeutic product in the United States.

Our strategy

The key elements of our strategy are to (i) build a meaningful clinical portfolio by advancing our current clinical programs and rapidly advancing our preclinical programs into clinical development; (ii) focus our resources on developing drugs for indications that represent significant unmet medical need and where the development and commercialization activities are appropriate for our size and financial resources; (iii) selectively form strategic alliances to augment our expertise and accelerate development and commercialization; (iv) develop microRNA biomarkers to support our therapeutic product candidates; and (v) maintain our scientific and intellectual leadership in the microRNA field.

Our strategy has been validated to date by the following strategic alliances and collaborations with large pharmaceutical companies:

In June 2010, we formed a strategic alliance with Sanofi to discover and develop microRNA therapeutics for fibrotic diseases. In July 2012, we expanded the alliance to include potential microRNA therapeutics in oncology. The original research term for this strategic alliance expired in June 2013, upon which we and Sanofi entered into an option agreement pursuant to which we granted Sanofi an exclusive right to negotiate the co-development and commercialization of certain of our unencumbered microRNA programs, for which Sanofi paid us an upfront option fee of $2.5 million. In addition, Sanofi granted us an exclusive option to negotiate the co-development and commercialization of miR-21. In February 2014, we and Sanofi extended our strategic alliance and Sanofi concurrently made a $10.0 million investment in our common stock. Under the terms of our extended alliance, Sanofi has opt-in rights to our RG-012 clinical fibrosis program targeting miR-21 for the treatment of Alport syndrome, our preclinical program targeting miR-21 for hepatocellular carcinoma, or HCC, and kidney fibrosis, and our preclinical programs targeting miR-221/222 for oncology indications, each of which is being led by us. If Sanofi chooses to exercise its option on any of these programs, Sanofi will reimburse us for a significant portion of our preclinical and clinical development costs and will also pay us an option exercise fee for any such program, provided that $1.25 million of the $2.5 million upfront option fee paid to us by Sanofi in connection with the June 2013 option agreement will be creditable against such option exercise fee. In addition, we will be eligible to receive clinical and regulatory milestone payments under these programs and potentially commercial milestone payments. We also continue to be eligible to receive royalties on microRNA therapeutic products commercialized by Sanofi and have the right to co-promote these products. For additional information, see Note 5 to our financial statements under Item 8 of Part II of this Annual Report.

Table of Contents

In August 2012, we formed a strategic alliance with AstraZeneca to discover and develop microRNA therapeutics for cardiovascular diseases, metabolic diseases and oncology. In March 2015, we and AstraZeneca nominated RG-125(AZD4076), a GalNAc-conjugated anti-miR 103/107 oligonucleotide that has been shown to improve insulin sensitivity and glucose tolerance in animal models as a clinical development candidate in NAFLD in patients with type 2 diabetes/pre-diabetes. In December 2015, AstraZeneca commenced the first-in-human dosing of RG-125(AZD4076) in healthy volunteers and commenced dosing patients in a Phase IIa clinical trial in the third quarter of 2016. In June 2017, AstraZeneca informed us that it intends to terminate the clinical development program for AZD4076(RG-125) for the treatment of NASH in Type 2 Diabetes/Pre-diabetes. Pursuant to the terms of our collaboration and license agreement with AstraZeneca, AstraZeneca's rights with respect to AZD4076(RG-125) will revert to us when the termination becomes effective in June 2018. For additional information, see Note 5 to our financial statements under Item 8 of Part II of this Annual Report.

- Under our collaboration and license agreement with Sanofi, we are eligible to receive up to approximately $430.3 million in aggregate milestone payments upon successful commercialization of microRNA therapeutics, in addition to royalties on net sales for the programs contemplated by the agreement. These payments include up to $105.3 million upon achievement of preclinical and investigational new drug, or IND, milestones, up to $25.0 million upon achievement of clinical development milestones, up to $180.0 million upon achievement of regulatory milestones and up to $120.0 million upon achievement of commercialization milestones.

Our Intellectual Property and Technology Licenses

Intellectual property

We strive to protect and enhance the proprietary technologies that we believe are important to our business, including seeking and maintaining patents intended to cover our products and compositions, their methods of use and any other inventions that are 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 objective is to continue to expand our intellectual property estate through our multiple layer approach in order to protect our microRNA therapeutics and to maintain our leading position in the microRNA therapeutics field.

We believe that we have a leading intellectual property position and substantial know-how relating to the development and commercialization of microRNA therapeutics, composed of:

- over 300 patents and patent applications that we own or have in-licensed from academic institutions and third parties including our founding companies, Alnylam and Ionis, related to microRNA and microRNA drug products; and
- numerous patents and patent applications exclusively licensed from our founding companies, Alnylam and Ionis, related to RNA technologies, including patent and patent applications relating to chemical modification of oligonucleotides that are useful for microRNA therapeutics, including chemical modifications incorporated into our clinical candidates.

We have exclusively licensed patent rights from Julius-Maximilians-Universität Würzburg and Bayerische Patent Allianz GmBH, which we collectively refer to herein as the University of Würzburg, which rights encompass the use of anti-miR therapeutics targeting miR-21 for the treatment of fibrosis, including kidney, liver, lung and cardiac fibrosis. In collaboration with us, investigators at the University of Würzburg demonstrated that targeting miR-21 in a disease model resulted in beneficial phenotypic effects, including the inhibition of the development of fibrosis. The Würzburg-licensed patent portfolio includes more than 25 U.S. and foreign patents and patent applications. Based on a typical patent term ending 20 years from the date of filing of the application, patents within this portfolio that have issued or may yet issue would have a statutory expiration date in 2029.

We have an exclusive license from Stanford University, or Stanford, to patent rights concerning the use of anti-miR therapeutics targeting miR-122 for the treatment of HCV infection. This patent portfolio is based upon research conducted by Peter Sarnow, Ph.D. and colleagues at Stanford, demonstrating that miR-122 is required for HCV replication in mammalian cells. The Stanford-licensed portfolio includes 15 U.S. and foreign patents and patent applications. Based on a typical patent term ending 20 years from the date of filing of the application, patents within this portfolio that have issued or may yet issue would have a statutory expiration date in 2025.

We have an exclusive license from ETH Zürich to patent rights related to the use of anti-miR therapeutics targeting miR-103/107 for the treatment of metabolic disorders, including type 2 diabetes. In collaboration with us, Dr. Markus Stoffel and colleagues demonstrated that inhibition of miR-103/107 in disease models of diabetes and obesity resulted in beneficial

Table of Contents

phenotypic effects, including improved insulin sensitivity and glucose homeostasis. The ETH Zurich-licensed portfolio includes more than 10 U.S. and foreign patents and patent applications. Based on a typical patent term ending 20 years from the date of filing of the application, patents within this portfolio that have issued or may yet issue would have a statutory expiration date in 2030.

Our portfolio of exclusively and jointly owned patent and patent applications is currently composed of over 200 U.S. and foreign patents and patent applications with claims to compositions-of-matter or methods related to our microRNA drug products and microRNA product platform. Based on the patents and patents that may issue from pending applications within our portfolio, patent protection for our microRNA drug products and their methods of use is currently expected to expire between 2024 and 2036.

Our founding companies, Alnylam and Ionis, each own or otherwise have rights to numerous patents and patent applications concerning oligonucleotide technologies and a substantial number of these patents and applications have been exclusively licensed to us for use in the microRNA field. The technologies covered in these patents and applications include various chemical modifications that are applicable to microRNA therapeutics. Due to patent expiration and strategic patent portfolio decisions, the total number licensed to Regulus will fluctuate from year to year. Among the licensed patents or patent applications, those covering key chemical modifications for use in microRNA drug products are currently expected to expire in 2023, 2027 and 2029.

We have a co-exclusive license to the patent portfolio owned by Max-Planck-Gesellschaft, or MPG, which has been granted to us by Max-Planck-Innovation GmbH, or MI, a wholly-owned subsidiary of MPG acting as MPG’s technology transfer agency. MPG and MI are collectively referred to herein as Max-Planck. This patent portfolio is based on the pioneering microRNA research conducted by Thomas Tuschl, Ph.D. and colleagues at the Max-Planck Institute of Biophysical Chemistry, which led to the discovery of over 100 human microRNA sequences, including microRNAs that are the focus of several of our programs. The patent rights encompass the microRNA gene sequences as well as the antisense sequences that are complemen