MERRIMACK PHARMACEUTICALS INC
Form 10-K
March 12, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

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 001-35409

Merrimack Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

Delaware	04-3210530
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
One Kendall Square, Suite B7201	
Cambridge, MA	02139
(Address of principal executive offices)	(Zip Code)

Registrant’s telephone number, including area code: (617) 441-1000

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Name of each exchange on which registered
Common Stock, $0.01 par value	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

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 No

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 No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate website, 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 No

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 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, 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		Accelerated filer
Non-accelerated filer	(Do not check if a smaller reporting company)	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.

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the last sale price for such stock on June 30, 2017, was $157,909,117.

As of March 7, 2018, there were 13,342,784 shares of Common Stock, $0.01 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A in connection with its 2018 Annual Meeting of Stockholders. Portions of such proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward looking statements. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “c expressions are intended to identify forward looking statements, although not all forward looking statements contain these identifying words.

The forward looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- our plans to develop and commercialize our clinical stage product candidates and diagnostics;
- our ongoing and planned discovery programs, preclinical studies and clinical trials;
- the timing of the completion of our clinical trials and the availability of results from such trials;
- our ability to establish and maintain collaborations for our product candidates;
- our receipt of payments related to the milestone events under the asset purchase and sale agreement with Ipsen S.A. or under the license and collaboration agreement between Baxalta Incorporated, Baxalta US Inc., Baxalta GmbH and Ipsen S.A., when expected or at all;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of our product candidates;
- our intellectual property position;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the potential advantages of our approach to drug research and development; and
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in Part I, Item 1A. Risk Factors, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments that we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

NOTE REGARDING TRADEMARKS

ONIVYDE® is a registered trademark of Ipsen S.A. Any other trademarks, trade names and service marks referred to in this Annual Report on Form 10-K are the property of their respective owners.

PART I

Item 1. Business

Overview

We are a clinical stage biopharmaceutical company based in Cambridge, Massachusetts that is outthinking cancer by targeting biomarker-defined cancers. Our vision is to ensure that cancer patients and their families live fulfilling lives. Our mission is to transform cancer care through the smart design and development of targeted solutions based on a deep understanding of cancer pathways and biological markers. All of our development programs, including four clinical trials and six candidates in preclinical development, fit into our strategy of (1) understanding the biological problems we are trying to solve, (2) designing specific solutions against the problems we are trying to solve and (3) developing those solutions for biomarker-selected patients. This three-pronged strategy seeks to ensure optimal patient outcomes.

We currently own worldwide development and commercial rights to all of our clinical and preclinical programs. The following table summarizes our clinical programs as of March 1, 2018, each of which is described in further detail below.

A further description of our clinical programs is as follows:

- MM-121 (seribantumab): MM-121 is a fully human monoclonal antibody that binds to the ErbB3 (HER3) receptor and targets heregulin positive cancers. There are two active development programs for MM-121, each in a Phase 2 clinical trial. We are currently conducting the global, open-label, biomarker-selected, Phase 2 randomized SHERLOC clinical trial, evaluating MM-121 in combination with docetaxel in patients with heregulin positive non-small cell lung cancer, or NSCLC. We are also conducting the global, double-blinded, placebo-controlled, biomarker-selected, Phase 2 randomized SHERBOC clinical trial evaluating MM-121 in combination with fulvestrant in patients with heregulin positive, hormone receptor positive, ErbB2 (HER2) negative, metastatic breast cancer.
- MM-141 (istiratumab): MM-141 is a fully human tetravalent bispecific antibody designed to block tumor survival signals by targeting receptor complexes containing the insulin-like growth factor 1, or IGF-1, receptor and ErbB3 (HER3) cell surface receptor. We are currently conducting and have completed enrollment of the global, double-blinded, placebo-

controlled, Phase 2 randomized CARRIE clinical trial evaluating MM-141 in combination with nab-paclitaxel and gemcitabine in patients with previously untreated metastatic pancreatic cancer with high serum levels of free IGF-1.

- MM-310: MM-310 is an antibody-directed nanotherapeutic that targets the ephrin receptor A2, or EphA2, receptor and contains a novel prodrug of the highly potent chemotherapy docetaxel. The EphA2 receptor is highly expressed in most solid tumor types, such as prostate, ovarian, bladder, gastric, pancreatic and lung cancers. We initiated a Phase 1 clinical trial to evaluate safety and preliminary activity of MM-310 and to identify the maximum tolerated dose in the first quarter of 2017.

The table below summarizes our preclinical pipeline as of March 1, 2018. We have six preclinical programs that we are actively working to advance into the clinic. Our preclinical programs focus on three areas of expertise: disruption of growth factor pathways, disruption of cellular proliferation and repair, and immuno-oncology.

We are also developing in vitro diagnostics for use with each of our oncology product candidates. Our in vitro diagnostics employ biophysical or biochemical markers of cancer, or biomarkers. We believe that our biomarker-driven development strategy utilizing companion diagnostics will allow us to improve the efficiency and productivity of our clinical development and enhance the potential efficacy and pharmacoeconomic benefit of our product candidates.

On April 3, 2017, we completed the sale, or the asset sale, to Ipsen S.A., or Ipsen, of all of our right, title and interest in the non-cash assets, equipment, inventory, contracts and intellectual property primarily related to or used in our business operations and activities involving or relating to developing, manufacturing and commercializing ONIVYDE, our first commercial product, and MM-436, or the commercial business. Additional information about the asset sale is described in Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations. Our non-commercial assets, including our clinical and preclinical development programs described above, or the pipeline business, were not included in the asset sale and remain assets of ours.

Our Approach to Cancer Research

We are executing a three-pronged strategy as the basis for our approach to drug development. Our process begins with identifying the problems we are trying to solve and developing a fundamental understanding of how cancer cell signaling pathways

and drug metabolism affect those problems. We then engineer product candidates, which include both antibodies and antibody-directed nanotherapeutics, which are designed to match the problem and fit our understanding of the target. Finally, we test our product candidates in biomarker-defined populations that are more homogenous than the general unselected disease population. This strategy improves our ability to detect a clear signal early in clinical development and enables us to pursue smaller, shorter, more personalized studies with lower development costs and a potentially accelerated timeframe to clinically meaningful data.

Step 1: Understand the problem

To understand the problems we are trying to solve, we begin by developing a deep understanding of how cancer pathways and drug metabolism affect those problems. Using systems biology and systems pharmacology, our goal is to understand how the complex molecular interactions that occur within cell signaling pathways, or networks, lead to cancer. Our approach utilizes proprietary, dynamic biological data generated in a high-throughput method in which we test multiple biological or chemical parameters using engineering, analytical and modeling expertise, and from which we build computational models of cell biology to further our drug discovery, design and predictive development. We have developed an expertise in generating kinetic data, describing molecular changes or interactions over time, to illuminate the dynamic interactions that occur within biological systems. We apply those insights throughout the research and development process, including for target identification, lead compound design and optimization, diagnostic discovery and the design of clinical trial protocols.

Our models are constructed and validated using internally generated and proprietary data sets. Following the validation of a comprehensive model of a cell signaling network, we are able to use the model for drug discovery. A significant portion of our discovery work takes place in silico, or using the model for computer simulation, which we believe is a more efficient and productive approach for drug discovery and development than traditional approaches.

Step 2: Design a specific solution

Once we understand the problem that we are trying to solve and have developed a clear target, we design a very specific solution to fit our deep understanding of the target, using two internal platforms: our engineered antibody platform and our antibody-directed nanotherapeutics platform.

Human monoclonal antibodies

Human antibodies are a key component of many of our targeted therapies based on a range of favorable attributes, including significant target specificity and avidity relative to small molecules and well-understood pharmacokinetic properties. Our human monoclonal antibody engineering platform provides us with the ability to create antibodies that are designed to inhibit specific nodes responsible for tumor growth and survival, or to address inherent drug resistance by simultaneously targeting redundant signaling pathways. We have designed antibodies both for use as stand-alone therapeutics and as targeting or docking agents for our antibody-directed nanotherapeutics. We have worked with several antibody formats, including:

- fully human recombinant monoclonal antibodies and fragments of fully human recombinant monoclonal antibodies that include the antibody binding domain. Monoclonal antibodies and antibody fragments are proteins that bind specifically to one defined site on a cell surface protein or receptor;
- stabilized ligand-fusions, either alone or in a bispecific targeted format with an antibody domain;
- multi-specific antibody formats, which are comprised of two or more antibodies or antibody fragments linked to a common scaffold molecule to produce a single molecule that binds to distinct epitopes on two or more target cell surface proteins or receptors; and
-

- oligoclonal antibody mixtures, which are comprised of defined ratios of two or more recombinant human monoclonal antibodies that target two or more distinct epitopes on a single cell surface protein or receptor.

Antibody-directed nanotherapeutics

Our antibody-directed nanotherapeutics platform is a next-generation antibody drug conjugate, or ADC, that enables us to create actively targeted liposomes that can contain different chemotherapeutic agents. Our targeted nanotherapeutics are lipidic particles constructed to stably encapsulate active drug payloads. Nanoscale objects typically, though not exclusively, have dimensions on the order of 100 nanometers or smaller. We believe that our nanotherapeutics offer the following potentially favorable attributes:

- a multi-layered targeting strategy that includes an antibody targeting ligand against a preferentially expressed cell-surface receptor on tumor cells, size-controlled accessibility to the tumor microenvironment but not to most normal tissues, and a selective active payload for delivery;

- a uniform nanoscale size, which is intended to enable targeting and preferential deposition within tumors by taking advantage of the enhanced permeability and retention effect to selectively enter, and subsequently accumulate in, tumors with leaky vasculature;
- a formulation designed to minimize the leakage of active drug payload out of the particle before the nanotherapeutic has reached the tumor, with the goal of limiting systemic exposure and the associated occurrence of adverse events, while maximizing the amount of active drug that reaches the target;
- encapsulation of small molecules or nucleic acids in lipidic nanoparticles, designed to protect the active drug payload as it passes through the circulation and organs of the body, such as the liver, and to prevent premature clearance or metabolism of the active drug, and thereby extend the pharmacokinetic profile and enable more convenient dosing regimens; and
- a customizable payload by which our nanotherapeutics can contain a variety of drug payloads, including chemotherapies, cytotoxics, molecularly targeted small molecule drugs, and nucleic acids, such as siRNA and genes. Unlike conventional ADCs, our antibody-directed nanotherapeutics do not require the use of ultra-high potency drugs or direct conjugation to the antibody, both of which can constitute considerable limitations to the conventional ADC platform.

Step 3: Test the solution in a homogenous patient population

With a clear understanding of the problem and a custom-designed solution, we target our product candidates to biomarker-defined populations. Every program must utilize a biomarker signature, and accordingly our companion diagnostics are being designed to test for such biomarkers and thereby provide prognostic and predictive value for enrichment of the patient populations. Utilizing companion diagnostics to identify the biomarker-defined population, our clinical trials are designed to test our product candidates in more homogenous patient populations.

Ultimately, we believe that our approach will result in better treatments for complex diseases by incorporating the identification of biomarkers and the development of associated companion diagnostics into the drug development process. We believe this may enable physicians to better deliver the right drug to the right set of patients at the right time, which may in turn improve patient outcomes, reduce the overall costs of treating and caring for cancer patients, and ultimately may provide a basis for seeking favorable reimbursement of approved drugs from payors.

Our Most Advanced Product Candidates

The table and descriptions below summarize key information about our clinical stage product candidate assets, MM-121, MM-141 and MM-310. Each of these product candidates is a targeted therapy, designed to efficiently act on selected cancer cells. These targeted therapies are either monoclonal antibodies or monoclonal antibody-derived molecules that are designed to block oncogenic signaling pathways, such as MM-121 and MM-141, or an antibody-directed nanotherapeutic designed to selectively deliver a large cytotoxic payload to the tumor tissue, such as MM-310. None of our product candidates is approved for any indication by the U.S. Food and Drug Administration, or FDA, or any other regulatory agency.

Product Candidate	Development Program Status	Commercial Rights (Territory)
MM-121 (seribantumab) (ErbB3 (HER3) targeted monoclonal antibody)	• Conducting a Phase 2 clinical trial in patients with heregulin positive NSCLC in combination with docetaxel. We refer to this trial as the SHERLOC trial. • Top-line results are expected in the second half of 2018.	Merrimack (worldwide)
MM-121 (seribantumab) (ErbB3 (HER3) targeted monoclonal antibody)	• Conducting a Phase 2 clinical trial in patients with heregulin positive, hormone receptor positive, ErbB2 (HER2) negative, metastatic breast cancer in combination with fulvestrant. We refer to this trial as the SHERBOC trial.	Merrimack (worldwide)
MM-141 (istiratumab) (IGF-1R and ErbB3 (HER3) targeted tetravalent bispecific antibody)	• Conducting a Phase 2 clinical trial in patients with previously untreated metastatic pancreatic cancer with high serum levels of free IGF-1 in combination with nab-paclitaxel and gemcitabine. Enrollment is complete for this clinical trial. We refer to this trial as the CARRIE trial. • Top-line results are expected in the first half of 2018.	Merrimack (worldwide)
MM-310 (antibody-directed nanotherapeutic; EphA2 targeted docetaxel pro-drug)	• Conducting a Phase 1 clinical trial to evaluate safety and preliminary activity in patients with solid tumors. • Safety data and a maximum tolerated dose are expected in the second half of 2018.	Merrimack (worldwide)

MM-121 (seribantumab)

MM-121 overview

MM-121 is a fully human monoclonal antibody that targets ErbB3 (HER3), a cell surface receptor that is activated by its ligand heregulin. Heregulin-driven ErbB3 (HER3) signaling has been implicated as a mechanism of tumor growth and broad resistance to cytotoxic, anti-endocrine, targeted and immuno-oncology therapies. When used in combination with anti-cancer drugs, MM-121 is designed to block heregulin-driven ErbB3 (HER3) signaling and enhance the anti-tumor effect of combination therapy partners.

Heregulin is the cognate ligand of the ErbB3 (HER3) receptor and a powerful driver of cell survival signaling. Based on the central role of heregulin and ErbB3 (HER3) in cancer growth and survival, we believe that MM-121 may be applicable to a broad range of metastatic tumors, including lung, breast, prostate, ovarian, head and neck, colon and

pancreatic cancers, among others. Our preclinical studies of several hundred tumor samples and the analysis of tumor samples from our Phase 2 clinical trials suggest that MM-121 may be able to target heregulin-dependent ErbB3 (HER3) signaling that is relevant in approximately 35-50% of cancer patients with these types of tumors, defining a highly drug-tolerant cancer cell phenotype potentially contributing to poor prognosis and thus potentially addressing a high unmet medical need.

In 2017, we obtained orphan drug designation in the United States for MM-121 for the treatment of heregulin positive non-small cell lung cancer.

Our three-pronged drug development strategy informs our approach to our MM-121 program:

Understand the problem. The ErbB3 (HER3) pathway is a drug resistance pathway, allowing cancer cells to escape death and survive the effect of other drugs. The ErbB3 (HER3) pathway is activated by its ligand heregulin, which binds to the ErbB3 (HER3) receptor. We have identified this pathway as a key node in cellular signaling networks and a prime target for cancer drug development.

Design a specific solution. MM-121 is an engineered monoclonal antibody designed to block the ErbB3 (HER3) pathway by preventing the binding between heregulin and the ErbB3 (HER3) receptor.

Test the solution in a homogenous patient population. Consistent with cell biology data, human clinical trials in three different cancers (lung, breast and ovarian) have independently pointed to the potential value of investigating MM-121 in tumors with a high expression of heregulin. Our SHERLOC and SHERBOC randomized Phase 2 clinical trials are designed to prospectively test the therapeutic effect of MM-121 in lung and breast cancer patients, respectively, whose tumors have high expression of heregulin.

MM-121 Phase 2 clinical trial in non-small cell lung cancer

In February 2015, we initiated the global, open-label, biomarker-selected, Phase 2 randomized SHERLOC clinical trial evaluating MM-121 in combination with docetaxel, versus docetaxel alone, in patients with heregulin positive non-small cell lung cancer. The trial was amended in 2017 into a proof-of-concept study in a more defined patient population, namely second or third-line heregulin positive adenocarcinoma of the lung. In March 2018, we announced an amendment to the SHERLOC clinical trial to increase the number of patients from 80 to 100. The primary endpoint of the trial is progression free survival, or PFS, and secondary endpoints include overall survival, objective response rate, safety and tolerability. We expect to report top-line results from the SHERLOC clinical trial in the second half of 2018.

MM-121 Phase 2 clinical trial in breast cancer

In August 2017, we initiated the global, double-blinded, placebo-controlled, biomarker-selected, Phase 2 randomized SHERBOC clinical trial of MM-121 in combination with fulvestrant, versus fulvestrant alone, in patients with heregulin positive, hormone receptor positive, ErbB2 (HER2) negative, metastatic breast cancer. This is a double-blinded, placebo-controlled randomized trial, and we plan to enroll 80 patients. The primary endpoint of the trial is investigator-assessed PFS and secondary endpoints include overall survival, time to progression, objective response rate, safety and pharmacokinetics.

MM-121 previous clinical trials

We have evaluated MM-121 in multiple Phase 1 and Phase 2 clinical trials in combination with both chemotherapies and other targeted agents across a wide spectrum of solid tumor patient populations, including patients with ovarian, breast and lung cancers. Over 700 patients were treated with MM-121 in those previous clinical trials. The goal of these clinical trials was to explore the efficacy and safety of MM-121 in combination with other agents and to establish and validate clinically meaningful biomarkers to identify patients most likely to benefit from MM-121.

Three such previous Phase 2 clinical trials of MM-121 in unselected patient populations with NSCLC, ovarian cancer and breast cancer enrolled a total of 464 patients and evaluated whether MM-121 in combination with a standard of care therapy was more effective than the standard of care therapy alone in prolonging PFS. In the NSCLC trial, two of the three cohorts (Groups A and C) did not meet their primary endpoints, and the third cohort (Group B) did not pass its planned interim analysis and ceased enrolling patients. Additionally, the previous Phase 2 clinical trials of MM-121 in patients with ovarian cancer and in patients with breast cancer did not meet the primary endpoints. However, retrospective biomarker analysis of each of these three trials identified heregulin as a key biomarker for MM-121. In 2014, we announced biomarker results from a meta-analysis of these three trials. This meta-analysis highlighted heregulin as the principal biomarker for MM-121 efficacy. High levels of heregulin mRNA correlated with favorable hazard ratios in all three of these trials. A hazard ratio, or HR, is a measure of how often a particular event happens in one group compared to how often it happens in another group over time. In cancer research, hazard ratios are often used in clinical trials to measure survival at any point in time in a group of patients who have been given a specific treatment compared to a control group given another treatment or a placebo. A hazard ratio of one means that there is no difference in survival between the two groups, while a hazard ratio of greater than one or less than one means that survival was better in one of the groups. The confidence interval, or CI, given after the HR reflects the amount of

certainty in the estimate of the HR. A HR value that is not contained within a 95% CI is unlikely to be the true HR.

In the lung cancer clinical trial, heregulin-high patients had a PFS HR of 0.35 (95% CI [0.16–0.76]) (37 of 69 evaluable patients were heregulin positive;