MERRIMACK PHARMACEUTICALS INC
Form 10-K
March 20, 2013

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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, 2012

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 001-35409

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. o Yes ý 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. o Yes ý 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. ý Yes o 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). ý Yes o 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. o

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

Large accelerated filer o	Accelerated filer o	Non-accelerated filer ý (Do not check if a smaller reporting company)	Smaller reporting company o

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

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, 2012: $630,064,672.

As of February 28, 2013, there were 95,901,025 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 2013 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," "continue" and similar 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 most advanced product candidates and companion diagnostics;
- our ongoing and planned discovery programs, preclinical studies and clinical trials;
- our collaborations with PharmaEngine, Inc. related to MM-398 and with Sanofi related to MM-121;
- our ability to establish and maintain additional collaborations;
- 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 products;
- our intellectual property position;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the potential advantages of our Network Biology approach to drug research and development;
- the potential use of our Network Biology approach in fields other than oncology; 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 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.

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PART I

Item 1. Business

Overview

We are a biopharmaceutical company discovering, developing and preparing to commercialize innovative medicines consisting of novel therapeutics paired with companion diagnostics. Our mission is to provide patients, physicians and the healthcare system with the medicines, tools and information to transform the approach to care from one based on the identification and treatment of symptoms to one focused on the diagnosis and treatment of illness through a more precise mechanistic understanding of disease. We seek to accomplish our mission by applying our proprietary systems biology-based approach to biomedical research, which we call Network Biology. Our vision is to apply Network Biology to become a global healthcare enterprise that is founded on leading science and driven to deliver integrated healthcare solutions that improve both the quality of outcomes and the efficiency of care. Our initial focus is in the field of oncology. We have six programs in clinical development. In our most advanced program, we are conducting a Phase 3 clinical trial.

Network Biology is an interdisciplinary approach to drug discovery and development. It focuses on understanding how the complex molecular interactions that occur within cell signaling pathways, or networks, regulate cell decisions and how network dysfunction leads to disease. Our approach integrates proprietary, dynamic biological data generated in a high-throughput, or rapid and automated, method in which we test multiple biological or chemical parameters using engineering, analytical and modeling expertise. Our capabilities allow us to build computational models of cell biology as a basis for drug discovery, design and predictive development. We apply Network Biology throughout the research and development process, including for target identification, lead compound design and optimization, diagnostic discovery, *in vitro* and *in vivo* predictive development and the design of clinical trial protocols. We believe that drug discovery and development using Network Biology is more efficient and productive than traditional approaches.

We currently have six targeted therapeutic oncology candidates in clinical development. Additionally, we have multiple product candidates in preclinical development and a discovery effort advancing additional candidate medicines. We have tailored each of our six most advanced product candidates to target specific disease mechanisms that our research suggests are common across many solid tumor types. We believe that these product candidates have the potential to address major unmet medical needs.

Our most advanced product candidates are MM-398, MM-121, MM-111, MM-302, MM-151 and MM-141.

MM-398 is a novel, stable nanotherapeutic encapsulation, or enclosed sphere carrying an active drug, of the marketed chemotherapy drug irinotecan. MM-398 achieved its primary efficacy endpoints in two Phase 2 clinical trials, one in pancreatic cancer patients and one in gastric cancer patients. We are conducting a Phase 3 clinical trial of MM-398 in patients with metastatic pancreatic cancer whose cancer has progressed on treatment with the chemotherapy drug gemcitabine. In July 2011, the U.S. Food and Drug Administration, or FDA, granted MM-398 orphan drug designation for the treatment of pancreatic cancer. In September 2011, the European Medicines Agency, or EMA, granted MM-398 orphan medicinal product designation for the treatment of pancreatic cancer. We believe that MM-398 may have potential uses in a number of other solid tumor indications, including colorectal cancer, lung cancer and glioma. There are multiple ongoing Phase 1 and Phase 2 clinical trials of MM-398.

MM-121 is a fully human monoclonal antibody that targets ErbB3, a cell surface receptor, or protein, attached to the cell membrane that mediates communication signals that are critical in cell growth and function. Signaling of this receptor is often implicated in cancer. A monoclonal

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antibody is a type of protein normally produced by cells of the immune system that binds to just one epitope, or chemical structure, on a protein or other molecule. Research suggests that ErbB3 signaling is often critical to the growth and survival of tumors, and that the use of ErbB3 signaling as a resistance mechanism by cancer cells to a variety of cancer therapies often occurs across patient populations and tumor types. MM-121 is designed to inhibit cancer growth directly, restore a tumor's sensitivity to drugs to which it has become resistant, and delay the development of resistance by a tumor to other agents. In collaboration with Sanofi, we are conducting a research and development program to test MM-121 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. There are multiple ongoing Phase 1 and Phase 2 clinical trials of MM-121.

MM-111 is a bispecific antibody designed to inhibit ErbB3 signaling in cancer cells that are characterized by overexpression of the ErbB2 cell receptor, also referred to as HER2. A bispecific antibody is a type of antibody that is able to bind simultaneously to two distinct proteins or receptors. Research suggests that a complex including ErbB2 (HER2) and ErbB3 is a powerful promoter of tumor growth and survival when stimulated by signaling molecules called ligands. MM-111 is designed to uniquely address the signaling from this complex of molecules. We believe that MM-111 is potentially applicable across a broad range of solid tumors. We are preparing to initiate a Phase 2 clinical trial of MM-111 and are currently conducting multiple Phase 1 clinical trials of MM-111 in combination therapy settings.

MM-302 is a nanotherapeutic encapsulation of doxorubicin with attached antibodies that target the ErbB2 (HER2) receptor. We designed MM-302 to bind to cancer cells that overexpress ErbB2 (HER2) and thereby release doxorubicin at the site of the tumor. Our goal is for MM-302 to retain the safety profile of liposomal doxorubicin, in particular with respect to cardiac safety, but to have better efficacy than liposomal doxorubicin in ErbB2 (HER2) positive tumors. We are conducting a Phase 1 clinical trial of MM-302 in patients with advanced ErbB2 (HER2) positive breast cancer.

MM-151 is an oligoclonal therapeutic consisting of a mixture of three fully human monoclonal antibodies designed to bind to non-overlapping epitopes of the epidermal growth factor receptor, or EGFR. EGFR is also known as ErbB1. An oligoclonal therapeutic is a mixture of two or more distinct monoclonal antibodies. EGFR (ErbB1) has long been recognized as an important drug target in several malignancies, including lung, breast, colon, pancreatic and head and neck cancers. We are conducting a Phase 1 clinical trial of MM-151 in patients with solid tumors.

MM-141 is a fully human tetravalent bispecific antibody designed to inhibit signaling of the PI3K/AKT/mTOR pathway initiated by the insulin-like growth factor 1 receptor, or IGF-1R, and ErbB3. A tetravalent bispecific antibody is a single molecule that has four binding sites, two for each of two different target cell surface receptors. PI3K/AKT/mTOR signaling is often activated in cancers in response to stress induced by chemotherapies or targeted anti-cancer medicines and is believed to play a significant role in promoting tumor cell survival. We are conducting a Phase 1 clinical trial of MM-141 in patients with solid tumors as a monotherapy and in a combination therapy setting.

We are developing *in vitro* and *in vivo* companion diagnostics for use with each of our therapeutic oncology product candidates. We use Network Biology in identifying biomarkers, which are biophysical or biochemical markers of cancer, and developing them into *in vitro* companion diagnostic agents for use with our therapeutic products. The *in vivo* companion diagnostics that we are developing take the form of imaging agents that may help identify patients likely to benefit from our therapeutic products by measuring deposition of our products in the tumor. We believe that 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 therapeutics.

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Our Strategy

Our goal is to build a global healthcare enterprise founded on a leading understanding of complex biology through the use of our Network Biology approach. Key elements of our strategy to achieve this goal are:

Strengthen and expand our core Network Biology capabilities. Network Biology is critical to our ability to explore, model and understand complex biology and is the core of our drug discovery and development efforts. We apply Network Biology across all of our development programs. We intend to increase our investment in the technologies, methods and know-how that comprise our Network Biology capabilities. We also plan to expand the scope of the therapeutic areas and biological processes we explore with Network Biology.

Foster an integrated, multidisciplinary model of drug discovery, clinical development, manufacturing and commercialization. We believe that an integrated, multidisciplinary team approach is essential to our productivity, innovation and retention of knowledge across all of our processes from research through manufacturing. To continue to foster this collaborative environment, we plan to invest in recruiting and retaining top talent and professional development for all of our employees and to focus on establishing and maintaining strong relationships with researchers, physicians and patients. We intend to extend our multidisciplinary team approach into our planned commercial organization and to market our product candidates with the same science and information-based passion with which they are developed.

Develop a companion diagnostic for each of our therapeutic oncology product candidates. We are investing in the development of companion diagnostics to support our therapeutic oncology product candidates so as to guide their use and enhance their benefit for patients and the healthcare system. It is our long-term vision to combine these individual tests into a unified cancer diagnostic that can aid in the prescription of multiple therapeutics and treatment combinations based on the profile of a tumor.

Establish sales and marketing capabilities. We generally expect to retain commercial rights in the United States and Europe for our oncology product candidates, other than MM-121. Subject to receiving marketing approvals, we plan to commence commercialization activities by building a focused sales and marketing organization to establish relationships with the community of oncologists who are the key specialists in treating solid tumors.

Network Biology

Merrimack was founded by a team of scientists from The Massachusetts Institute of Technology and Harvard University seeking to develop a systems biology-based approach to biomedical research. Fundamentally, systems biology is the study of the complex molecular interactions that regulate the cellular processes that drive the functioning of living organisms. The core of our approach to systems biology is to apply multidisciplinary and multitechnology capabilities to build functional and predictive computational models of biological systems, such as cell signaling networks, that allow us to engineer treatments that are directed at the mechanisms of disease.

Network Biology Compared to Traditional Molecular Biology

Traditionally, the search for new drugs has been based on the identification of individual molecules in diseased cells that appear to be abnormal relative to individual molecules in healthy cells. Using traditional biomedical research methods, researchers label as "targets" the molecules that appear to be abnormal, typically either in amount, which is commonly referred to as expression, or make-up, which is commonly referred to as mutation status. These researchers then seek to validate a target by creating cells that either lack the target, overexpress the target, or express an abnormal version of the target to

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verify that the target contributes to the diseased state of the cell. Following positive validation, companies using traditional biomedical research methods then develop drugs to treat the target and test those various drugs in experimental models of the disease. If effective in animal studies that replicate the disease characteristics, these companies then consider the new drug candidate for human clinical testing. Unfortunately, new drug candidates developed with the traditional approach have a very high rate of clinical failure. We believe that the failure of traditional research methods to account for the complexity of biological systems underlying disease has contributed to this high rate of clinical failure. Additionally, we believe that few complex disease states are caused and perpetuated by only one molecular component.

Our view is that traditional research methods for drug discovery are suboptimal. First, they generally focus on individual molecules as determinants of cell decisions. We believe that the governance of cells is a function of the interactions of many molecules, which is referred to as systems dynamics. Individual molecules are simply contributors to signaling networks that process many parallel signals. We focus on networks because it is the outcome of the network that determines cell behavior, both normal and abnormal. We believe that the overexpression of many molecules in a diseased cell is merely symptomatic of abnormal cell processes, rather than causal. Second, we believe that the focus on individual molecules and their relationship to disease states does not account for the inherent complexity of signaling. Cellular signaling networks often have redundant signaling routes, any one of which can compensate for the other. In addition, networks are replete with feedback loops, or a signaling relationship in which the output of one communication path returns to regulate or affect the input of its own or other communication paths. This complexity often confounds efforts to ascribe specific cellular behavior to one molecule or one signaling relationship. Although a molecule may be involved in a signaling pathway, the degree of its importance depends on its signaling contribution and the state of other contributors in the system. Lastly, traditional biomedical research has focused on one-dimensional measures of a molecule's impact on signaling, such as the increase or decrease in the expression of a protein at a specific time point. We believe that traditional methods fail to recognize the dynamic nature of biology in which the duration and intensity of signaling is essential. Our view is that the duration and the degree of signaling is a more important contributor to cell signaling networks than the expression of a molecule.

Network Biology Methods

The goal of Network Biology is to understand how systems dynamics govern cell behavior. The methodology underpinning Network Biology is an integrated, multidisciplinary technology platform that incorporates biology, simulation and mathematics to enable the construction of computational models of cell signaling pathways. To execute Network Biology, 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. Our data sets differ from traditional data sets in that they focus on quantitative measures of signaling, and not qualitative measures of molecular activity and interaction. Our data also focus on time, and not simply intensity, as a critical variable in understanding the impact of a signal.

We initiate our Network Biology discovery efforts by identifying the biological signaling networks that are engaged in a disease state. For example, in order to identify the signaling networks that are used by cancer cells for growth and survival, we perform experiments that we refer to as Critical Network Identification. We conduct these experiments using our expertise in high-density protein array technology to measure the impact of dozens of factors that are thought to cause or promote cancer across many different tumor types. The experimental output identifies which cell signaling networks are activated in response to various stimuli across different disease models. In one such experiment, we studied 54 types of solid tumor cells from the National Cancer Institute's panel of tumor cell lines. This analysis revealed that, while there are many different types of cancer reflecting diverse genetic

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backgrounds, these cancers rely on a relatively limited number of cell signaling networks for growth and survival.

Once we identify the critical networks, we initiate a program of mapping, measuring and constructing a detailed biochemical model of each individual signaling network for use in drug discovery. We construct our network models using proprietary data sets. We generate our data sets utilizing high-throughput, multiplexed microarray technology or automated, high-throughput biological assays. These experiments are executed over time-courses on cultured cells. Within each cell, at specific time intervals, we simultaneously measure the signaling and interaction status of a large panel of proteins to generate this kinetic data. We then convert the kinetic parameters drawn from the data sets into mathematical equations that describe the relationship between each molecular entity in the network. The individual equations are then assembled into a network model. Once constructed, we then test the model for accuracy in many different and varied experimental settings. We use the model to make predictions of network behavior within a cell under a varied set of experimental conditions. Following this, we test these predictions in actual laboratory experiments and use the data to refine and validate the model.

We believe that our models differ from other models in the industry because of their level of specificity and detail. Models that we have seen in other drug discovery settings often seek to correlate activity from external cellular stimuli directly to disease state. In contrast, we build models that describe each of the individual molecular interactions starting with external stimuli, but continuing with the hundreds of interactions that occur from the cell surface to the nucleus of the cell. In academic settings, this level of detailed molecular interaction modeling is often referred to as biochemical modeling. We believe our accuracy in predicting cell behavior from our models is driven by the precision and details of our approach.

Our models are constructed and validated using internally generated and proprietary data sets. We do not rely on outside databases. The data generated from our Critical Network Identification experiments is also proprietary and generated in-house.

Following the validation of a comprehensive model of a cell signaling network, we are able to use the model for drug discovery. Contrary to traditional methods, our discovery work takes place *in silico*, or using the model for simulation. One example of our discovery approach is to execute a sensitivity analysis across an entire signaling network to identify drug targets that have the greatest impact on signal transduction in the network. We believe that the best targets are those most involved in signaling, and not necessarily those that are most abnormal, which is more likely a symptom of irregular cell processes.

As one example, we identified ErbB3, the target of MM-121, using our proprietary model of the ErbB signaling network after conducting a sensitivity analysis on its signaling process. Although the ErbB pathway has been extensively targeted by cancer therapeutics, we believe that understanding the relative importance of the different components of the ErbB network is central to identifying an attractive drug target and a therapeutic directed at this target. In this case, we built a computational model of the ErbB signaling network that includes the most potent ErbB receptor ligands, as well as known and novel ErbB inhibitors. We populated the model with proprietary dynamic data that we generated from our Critical Network Identification experiments. The model describes in mathematical equations 700 biochemical reactions representing the ErbB signal transduction network. The model identified ErbB3 as the key node in response to both ErbB3- and EGFR (ErbB1)-binding ligands. We then used this insight to develop MM-121.

Network Biology and Patient Care

The goal of Network Biology is to deliver better treatments for complex diseases. We use Network Biology to obtain an understanding of the dynamics that govern cell signaling networks and how

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dysfunction in these networks leads to and perpetuates disease. We believe that Network Biology may provide broader insight into disease and the potential therapeutic alternatives for physicians and patients. In particular, we believe that Network Biology may provide three key benefits:

- stratification of disease by the underlying mechanisms promoting tumor growth and survival;
- novel medicines designed to take into account the complexity of cell signaling networks within a tumor cell; and
- integrated medicines that provide a therapeutic and diagnostic to help guide treatment.

Stratification of disease by the underlying mechanisms promoting tumor growth and survival

To date, much of the study of cancer has focused on tumors characterized by a single, overexpressed receptor or a mutated gene, also known as oncogene-driven cancers. While these types of cancer are relatively easy to discern, we believe that they are actually somewhat rare across solid tumors.

Our research suggests that identifying the cell signaling networks that are used by a patient's tumor will enable more precise mechanistic diagnosis. Based on our research on the mechanisms underlying cancer, we believe that the abnormal growth of tumor cells is due to the development of addictions to one or more signaling networks in response to stressors in the tumor environment. Once a cell has been stressed, its systems begin to compensate, in particular by activating additional growth and survival signaling.

As an example, the results of one of our Critical Network Identification experiments revealed that, while there are many different types of cancer reflecting diverse genetic backgrounds, these cancers rely on a relatively limited number of cell signaling networks for growth and survival. We believe that developing drugs that effectively inhibit these signaling mechanisms, independent of the type or nature of the stressor, may provide an improved basis of treatment.

Novel medicines designed to take into account the complexity of cell signaling networks within a tumor cell

All cells function by means of signaling networks. Critical signals related to functions, such as growth and survival, are regulated via complex networks of extracellular and intracellular molecular entities that are organized into individual biological pathways. These pathways compete and cooperate with one another to drive particular cellular decisions or outcomes. We use the detailed understanding of the most active signaling networks within a tumor cell that we obtain from Network Biology to guide the design of targeted therapeutics that we believe will intervene and affect the activity of these networks.

As discussed above, a Critical Network Identification screen confirmed that one of these networks, the ErbB pathway, is a significant survival network utilized by tumor cells. This pathway is made up of four receptors: EGFR (ErbB1), ErbB2 (HER2), ErbB3 and ErbB4. Several currently approved therapies are directed at targets in the ErbB pathway. In particular, EGFR (ErbB1) and ErbB2 (HER2) have been the focus of modern pharmaceutical efforts due to their overexpression or abnormal function due to mutation in many tumor cells relative to their expression in normal tissue. However, using Network Biology to understand the complex signaling dynamics that govern this pathway, our research suggested that ErbB3 is the most sensitive target in the ErbB pathway. This was an unconventional conclusion because, in contrast to EGFR (ErbB1) and ErbB2 (HER2), ErbB3 does not have an active kinase domain, a common drug target. A kinase domain is part of an enzyme-like protein often involved in the activation or deactivation of other proteins. In addition, ErbB3 is not expressed in tumors at levels nearly as high as those seen with EGFR (ErbB1) and ErbB2 (HER2), and it rarely harbors mutations that could impact its normal function.

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Thus, despite being aware of the existence of ErbB3, scientists previously largely ignored ErbB3 as a drug target. In our research, we found that within the ErbB pathway, blocking ErbB3 had the largest impact on inhibiting the survival signal that perpetuates the growth of tumor cells addicted to this network. Our analysis assessed signal transmission and communication, which we believe is a more accurate measure of disease mechanism than simply examining the characteristics of different proteins, such as expression level or mutation status, in isolation.

Integrated medicines that provide a therapeutic and diagnostic to help guide treatment

Using Network Biology, we are incorporating the identification of biomarkers and the development of companion diagnostics into the drug development process. We believe that a companion diagnostic for a therapeutic agent should provide a precise molecular assessment of the nature of the tumor, rather than simply identifying the qualitative overexpression of a protein. We are also of the view that cancer continues to alter its means of growth and survival over time, often in response to the additional stress of drug treatments. As a result, we believe that frequent assessment of patients' cancers during treatment are helpful to gain insight into which resistance mechanism a cancer defers to once treatment has altered the tumor's mechanism of growth and survival.

Ultimately, we intend all of our oncology candidates to be integrated medicines consisting of:

a therapeutic designed to work in tumors with a specific molecular profile;

diagnostics that measure the biochemical and biophysical properties that characterize the molecular profiles of tumors; and

analytical algorithms to translate quantitative diagnostic data into treatment information.

We are currently developing predictive tests for companion diagnostics to identify patient populations who would preferentially respond to our therapeutic product candidates. In our preclinical work, we have used predictive development, which involves modeling and simulation, in an effort to understand and eventually predict how a tumor cell will respond to treatment. For example, in designing our ErbB3 inhibitor, MM-121, we utilized predictive development to understand how blocking signaling through ErbB3 would impact cell growth in several tumor cell lines. We quantitatively measured the expression level of multiple biomarkers to predict the activity of MM-121 in specific xenograft models, which are human tumors that have been implanted in mice. Based on our simulations and biomarker analysis, we were able to successfully and accurately predict response to MM-121 using 20 different xenograft tumor models. We are now actively translating this predictive test into a companion diagnostic that can be investigated for potential use with MM-121 for human treatment.

Our current diagnostic development efforts are focused on developing assays and algorithms that support a physician's determination of whether an individual therapeutic is appropriate for a given patient population. We intend to develop and commercialize future diagnostics that combine our research understanding across multiple cell signaling networks and in multiple tumors with varying biophysical characteristics to support physician treatment decisions for all classes of cancer therapeutics.

In another example of our application of the Network Biology systems modeling approach, we built a model of the biophysical characteristics of tumors to explore the variables most important to drug activity. The model examined the complex relationship between the pharmacokinetics of a drug and physical characteristics of a tumor, such as the nature of the vascularization, or blood vessel development, supporting a tumor's survival. The analysis demonstrated that the variability of the physical characteristics of the tumor had tremendous impact on the activity of the drug in treating the tumor. The analysis supports the insight of using our nanotherapeutics as a means to localize the activity of a drug by utilizing differences in vascularization between normal tissues and the tumor. Additionally, in some cases, we attach antibodies to the outside of our nanotherapeutics to promote

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active transport of the nanotherapeutics into the cell. The model also led directly to our efforts to use our nanoliposome technology to diagnose the biophysical characteristics of a tumor as a means of guiding the choice of a therapeutic and the appropriate dose.

We believe that integrated medicines may enable physicians to deliver the right drug to the right set of patients at the right time. If we are successful, we may be able to:

- improve patient outcomes by providing improved therapeutics along with the diagnostic information to guide physician treatment decisions;
- reduce the overall costs of treating and caring for cancer patients; and
- provide a basis for seeking favorable reimbursement of approved drugs from payors because of the benefits to patients.

Network Biology's Potential Impact on the Drug Development Process

In addition to improving patient care, we believe that Network Biology can increase the productivity of biomedical research, increase the probability of approval for new drugs and produce more precisely targeted therapeutics. We believe that our therapeutic oncology product candidates will have a greater probability of success than product candidates based on conventional drug development because Network Biology provides us with:

- a multidisciplinary, integrated approach to understanding complex biology;
- simulation and modeling capabilities that aid in the efficiency and productivity of development; and
- the capability to design and build a broad range of therapeutic product candidates without being limited to a particular drug design technology or target class.

A multidisciplinary, integrated approach to understanding complex biology

Network Biology incorporates biology, modeling, simulation and mathematics, which we use to build computational models of cell signaling pathways. This requires a focus on new types of data to understand the dynamic interactions that occur within biological systems. This biological data must be quantitative, kinetic and multiplexed to capture the breadth and depth of the parallel and often redundant signaling processes that occur within cells. We also use this approach to construct computational models that explain biophysical distribution of drugs, pharmacokinetics, which is the process by which a drug is absorbed, distributed and metabolized by the body, and pharmacodynamics, which is the biochemical and physiological effect of the drug on the body. Using our robust quantitative understanding of the complexity of cell signaling, we design drugs and drug combinations that we believe will effectively inhibit tumor growth and survival.

Simulation and modeling capabilities that aid in the efficiency and productivity of development

We believe that Network Biology improves our decision making throughout the research and development process by providing our scientists with tools to simulate hypotheses in computer models and then test these hypotheses in preclinical and clinical settings. This process provides a comprehensive view of the biological system that we are addressing and facilitates knowledge retention throughout the project. For example, as is the industry standard, preclinical development of our therapeutic product candidates includes testing our drugs in xenograft tumor models. However, our ability to model cell signaling pathways allows us to choose which xenograft tumor models we believe will be well suited for a particular program, as we did for both MM-121 and MM-111.

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Another example of our use of simulation capabilities to identify novel biology and design a therapy is our product candidate MM-151. MM-151 is an oligoclonal antibody mixture directed at inhibiting EGFR (ErbB1) signaling. EGFR (ErbB1) is one of four cell surface receptors in the ErbB network. EGFR (ErbB1) is overexpressed in several types of solid tumors, including lung and colorectal cancer. Currently, there are several approved products that target EGFR (ErbB1). Unfortunately, these therapies are limited in their efficacy because they have relatively low response rates in patients who overexpress EGFR (ErbB1). Further, even when they are effective, tumors often develop resistance. Our model of the ErbB network revealed that current drugs failed to account for a high degree of signal amplification downstream of EGFR (ErbB1). Only tumors with low amplification, even when EGFR (ErbB1) was overexpressed, were impacted by the current therapies. Moreover, we noted that the current therapies were only effective at blocking signaling when initiated by low affinity ligands that bind to EGFR (ErbB1). Noting the importance of understanding amplification and the role of high affinity ligands as a potential escape route for tumors, we sought to develop a comprehensive EGFR (ErbB1) inhibitor. Using the model, we identified key specifications of an optimal inhibitor and set about engineering MM-151.

We believe that our simulation and modeling capabilities enable us to:

- assess our product candidates within a broad range of biological conditions so that we can make informed judgments as to which indications and patient populations to pursue;
- based on these judgments, select appropriate preclinical tests for the cost-effective and expeditious development of our product candidates; and
- initiate clinical development programs that are based on hypotheses validated in the preclinical setting.

The capability to design and build a broad range of therapeutic product candidates without being limited to a particular drug design technology or target class

We apply the insights about cell signaling dynamics that we gain from our Network Biology approach across a range of therapeutic technologies to design product candidates that we believe can be efficiently delivered to the selected molecular target. We believe that the best drugs for the oncology indications that are the initial focus of our business are targeted therapies that, in contrast with conventional chemotherapies, are highly selective for the molecular mechanisms that we are seeking to affect and, therefore, offer the potential for significant efficacy and safety benefits.

The breadth of our therapeutic design capabilities is shown by the six different designs of our six most advanced product candidates. These product candidates consist of a nanotherapeutic, a monoclonal antibody, a bispecific antibody designed to simultaneously bind to two different target cell surface receptors, an antibody-targeted nanotherapeutic, an oligoclonal antibody consisting of a mixture of three different antibodies, and a tetravalent bispecific antibody designed to simultaneously bind to two different target cell surface receptors. Each of these product candidates is designed with specific characteristics that we believe are well suited for the type of disease mechanism that we are targeting.

Application of Network Biology Beyond Cancer

We believe that our Network Biology approach is applicable to a broad range of therapeutic areas beyond cancer, including bone and joint conditions, infectious disease, inflammation, central nervous system disease and other areas of medicine with high unmet needs. While we may pursue some of these disease areas directly ourselves, because of the potential of very broad applicability of our Network Biology approach, our plan is to pursue many or all of these other areas through collaborations, licenses and other arrangements with third parties. As an example, in 2010, we established Silver Creek Pharmaceuticals, Inc., or Silver Creek, to apply our Network Biology approach

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to the research, development and commercialization of pharmaceuticals in the regenerative medicine field. Silver Creek is now a majority-owned subsidiary of ours with the minority equity held by third party investors.

Our Most Advanced Product Candidates

The following table summarizes key information about our six most advanced therapeutic product candidates. All of these product candidates are designed for intravenous administration.

Program	Indication	Stage of development	Commercial rights
MM-398 (nanotherapeutic encapsulation of irinotecan)	Monotherapy and MM-398 plus fluorouracil, or 5-FU, and leucovorin in pancreatic cancer	Phase 3 ongoing	Merrimack worldwide, except Taiwan
	MM-398 plus 5-FU, leucovorin and bevacizumab in colorectal cancer	Phase 2 ongoing	
	Monotherapy in pancreatic cancer	Phase 2 complete	
	Monotherapy in gastric cancer	Phase 2 complete	
	Monotherapy in glioma	Phase 1 ongoing	
	Translational study in colorectal, lung and breast cancers	Phase 1 ongoing	
	Monotherapy in colorectal cancer	Phase 1 complete	
MM-121 (ErbB3 targeted monoclonal antibody)	MM-121 plus paclitaxel in platinum resistant/refractory ovarian cancer	Phase 2 ongoing	Sanofi worldwide; Merrimack holds option to co-promote in United States
	MM-121 plus exemestane in hormone receptor positive breast cancer	Phase 2 ongoing	
	MM-121 plus erlotinib in non-small cell lung cancer	Phase 2 ongoing	
	Neoadjuvant MM-121 plus paclitaxel in ErbB2 (HER2) negative breast cancer	Phase 2 ongoing	
	MM-121 plus paclitaxel in ErbB2 (HER2) negative breast, ovarian and other gynecological cancers	Phase 1 ongoing	
	MM-121 plus cetuximab and irinotecan in solid tumors	Phase 1 ongoing	

MM-121 plus multiple anti-cancer therapies in solid tumors	Phase 1 ongoing
Monotherapy in solid tumors	Phase 1 complete

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Program	Indication	Stage of development	Commercial rights
MM-111 (ErbB3 and ErbB2 (HER2) targeted bispecific antibody)	M-111 plus paclitaxel with or without trastuzumab in gastric cancers	Phase 2 planned	Merrimack worldwide
	MMM-111 plus trastuzumab in ErbB2 (HER2) positive breast cancer	Phase 1 ongoing	
	MM-111 plus multiple anti-cancer therapies in ErbB2 (HER2) positive solid tumors	Phase 1 ongoing	
	Monotherapy in ErbB2 (HER2) positive solid tumors	Phase 1 complete	
MM-302 (ErbB2 (HER2) targeted nanotherapeutic encapsulation of doxorubicin)	Monotherapy and MM-302 plus trastuzumab in ErbB2 (HER2) positive breast cancer	Phase 1 ongoing	Merrimack worldwide
MM-151 (EGFR (ErbB1) targeted oligoclonal antibody)	Monotherapy in solid tumors	Phase 1 ongoing	Merrimack worldwide
MM-141 (IGF-1R and ErbB3 targeted tetravalent antibody)	Monotherapy and MM-141 plus everolimus and docetaxel in solid tumors	Phase 1 ongoing	Merrimack worldwide

We are developing companion diagnostics for each of the above therapeutic candidates. We plan to file an Investigational Device Exemption, or IDE, with the FDA prior to initiating clinical trials of each of our *in vitro* companion diagnostics to validate their prospective use.

Cancer

The initial focus of our business is to apply our Network Biology approach to the development of therapeutics and companion diagnostics for the treatment of solid tumor cancers. Cancer is the second most common cause of death in the United States, exceeded only by heart disease. In the United States, cancer accounts for almost one of every four deaths. The National Institutes of Health estimates that the direct medical cost of cancer of all types, including solid tumors, in the United States in 2010 was more than $100 billion.

Solid Tumor Market

The following table sets forth information about some of the solid tumor cancers for which we are developing therapeutic product candidates and companion diagnostics. The U.S. estimated annual incidence and five year relative survival rates are based on information from the American Cancer Society, *Cancer Fact & Figures 2013*. Relative survival compares survival among cancer patients to that of people not diagnosed with cancer who are of the same age, race and sex. It represents the

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percentage of cancer patients who are alive after a designated time period relative to persons without cancer.

Tumor type	U.S. annual incidence	Five year relative survival rate	Selected marketed therapies
Breast	234,580	89%	trastuzumab (Herceptin®); docetaxel (Taxotere®); paclitaxel (Taxol®, Abraxane®); capecitabine (Xeloda®); anastrazole (Arimidex®); letrozole (Femara®); exemestane (Aromasin®); ado-trastuzumab emtansine (Kadcyla®); everolimus (Afinitor®)
Lung and bronchus	228,190	16%	docetaxel (Taxotere); gemcitabine (Gemzar®); pemetrexed (Alimta®); gefitinib (Iressa®); erlotinib (Tarceva®); bevacizumab (Avastin®); paclitaxel (Taxol)
Colorectal	142,820	64%	oxaliplatin (Eloxatin®); irinotecan (Camptosar®); bevacizumab (Avastin); cetuximab (Erbitux®); panitumumab (Vectibix®)
Pancreatic	45,220	6%	gemcitabine (Gemzar); erlotinib (Tarceva)
Liver	30,640	15%	sorafenib (Nexavar®)
Brain and other nervous system cancers	23,130	36%	temozolomide (Temodar®); carmustine (BiCNU®); polifeprosan 20 with carmustine implant (Gliadel®); bevacizumab (Avastin)
Ovarian	22,240	44%	liposomal doxorubicin (Doxil®); bevacizumab (Avastin); paclitaxel (Taxol, Abraxane)
Gastric	21,600	27%	capecitabine (Xeloda); trastuzumab (Herceptin); docetaxel (Taxotere)

In addition to the marketed therapies listed above, there are many generic chemotherapies and regimens commonly used to treat these cancers. Although the various marketed therapies and regimens provide benefits to some patients when given as monotherapies or in combination with other therapies, each has efficacy and adverse event limitations and none of them are successful in treating all patients. The level of morbidity and mortality from these cancers remains high.

Outcome Measures

There are a number of standard efficacy endpoints that clinicians use to measure outcomes for clinical trials for cancer therapies. The following are explanations of the meanings of the various efficacy endpoints that we are using in our ongoing and planned clinical trials for our product candidates, as described in more detail below:

Overall survival (OS): time to death from the initiation of treatment.

Complete response (CR): disappearance of all target tumors and non-target tumors.

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Pathologic complete response (pCR): complete response as determined by a pathologist and defined by the absence of any cancer cells in the tumor sample.

Partial response (PR): overall tumor regression based on a decrease of at least 30% in the sum of measured tumor diameters with no new tumors.

Progression free survival (PFS): time to tumor progression from the initiation of treatment based on an increase of at least 20% in the sum of measured tumor diameters with no new tumors.

Progressive disease (PD): growth of at least 20% in the sum of measured tumor diameters or spread of the tumor since beginning of treatment.

Stable disease (SD): neither sufficient decrease in tumor size to qualify for partial response (PR) nor sufficient increase in tumor size to qualify for progressive disease (PD) and no new tumors.

Objective response rate (ORR): complete response (CR) rate plus partial response (PR) rate.

Disease control rate (DCR): complete response (CR) rate plus partial response (PR) rate plus stable disease (SD) rate for a specified period of time, also known as clinical benefit rate.

Duration of response: amount of time a patient shows an objective tumor response.

Adverse Event Grading

Clinicians typically classify adverse events observed in clinical trials of cancer therapies based on a standard grading system as follows:

Grade 1 mild.

Grade 2 moderate.

Grade 3 severe.

Grade 4 potentially life-threatening or disabling.

Grade 5 death.

MM-398

Overview

MM-398 is a novel, stable nanotherapeutic encapsulation of the marketed chemotherapy drug irinotecan. MM-398 achieved its primary efficacy endpoints in two Phase 2 clinical trials, one in pancreatic cancer patients and one in gastric cancer patients. We are conducting a Phase 3 clinical trial of MM-398 in patients with metastatic pancreatic cancer whose cancer has progressed on treatment with the chemotherapy drug

gemcitabine. In July 2011, the FDA granted MM-398 orphan drug designation for the treatment of pancreatic cancer. In September 2011, the EMA granted MM-398 orphan medicinal product designation for the treatment of pancreatic cancer. We are simultaneously working to develop an imaging agent that can be used as a companion diagnostic to identify the patient population likely to respond to treatment with MM-398. We believe that MM-398 may have potential uses in a number of other solid tumor indications, including colorectal cancer, lung cancer and glioma.

Gemcitabine is the current standard of care in the first-line treatment of metastatic pancreatic cancer. Multiple studies of gemcitabine published in peer reviewed medical journals in the first-line setting for this indication have shown median overall survival (OS) in the range of five to seven months, with median progression free survival (PFS) of two to four months and 12-month survival of approximately 20%. Celgene Corporation also recently announced results from a Phase 3 clinical trial comparing gemcitabine to gemcitabine in combination with albumin-bound paclitaxel in treatment-naïve patients with metastatic pancreatic cancer, which found a statistically significant improvement in overall survival in patients receiving the combination regimen. The results of this trial may cause some health care professionals to modify their clinical practice and adopt this regimen as a first-line treatment.

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There are currently no approved treatments for gemcitabine refractory metastatic pancreatic cancer, nor is there a consensus on standard of care treatment for such patients. A limited amount of data suggest that, without further treatment, metastatic pancreatic cancer patients whose cancer progressed while on gemcitabine on average can expect to live approximately two months. If these patients receive additional treatment, they typically receive chemotherapy combinations containing one or more of gemcitabine, capecitabine, oxaliplatin, irinotecan, 5-FU or leucovorin.

There are a number of agents currently being tested in combination regimens as therapies for metastatic pancreatic cancer. In a recent Phase 3 clinical trial in first-line metastatic pancreatic cancer comparing gemcitabine with the regimen known as FOLFIRINOX, which is a combination of oxaliplatin, irinotecan, 5-FU and leucovorin, published in *The New England Journal of Medicine*, patients dosed with FOLFIRINOX showed a statistically significant increase in objective response rate (ORR) and overall survival (OS) compared to patients dosed with gemcitabine. However, the results in this trial suggested that FOLFIRINOX is most appropriate for patients with good performance status, or general well-being, because of adverse events observed in the FOLFIRINOX group. Patients dosed with FOLFIRINOX showed statistically significant increases in grade 3 and grade 4 adverse events, including neutropenia, febrile neutropenia, thrombocytopenia, diarrhea and sensory neuropathy, and higher rates of hospitalization, compared to patients treated with gemcitabine.

Design and potential advantages of MM-398

MM-398 is designed to stably retain and protect irinotecan while in circulation in the body and enable efficient accumulation of the drug in solid tumors. Our nanotherapeutics consist of lipidic particles, which are enclosed spheres of lipid membranes, and are designed to encapsulate active drug payloads. The encapsulated ingredient of MM-398, irinotecan, is a well known and widely used chemotherapy. Irinotecan is a pro-drug of the active agent SN-38. SN-38 potently arrests cell growth by inhibiting topoisomerase 1, an enzyme involved in cell replication. Typically, free irinotecan is metabolized in the liver into SN-38, and from there SN-38 circulates throughout the body and is rapidly cleared. Dosing with irinotecan, as with other chemotherapies, is limited by severe adverse effects that, in turn, limit efficacy. In addition, as with other chemotherapies, the efficacy of irinotecan is limited by tumor resistance mechanisms.

We believe that the nanotherapeutic encapsulation of irinotecan yields a number of favorable attributes that will lead to increased efficacy and fewer adverse events in comparison with free irinotecan.

We believe that the encapsulation technology prevents the premature metabolism of the active drug and thereby reduces systemic exposure and increases the amount of active drug available to be delivered at the tumor site.

The specific size and stability characteristics of MM-398 are designed to enable the preferential deposition of the drug within tumors relative to normal tissue. Specifically, we believe that, as a nanotherapeutic, MM-398 is able to utilize the enhanced permeability and retention, or EPR, effect to selectively enter, and subsequently be trapped in, tumors with leaky vasculature.

MM-398 is designed for the irinotecan inside the molecule to be converted into SN-38 locally by tumor-resident macrophages, rather than being converted in the liver, as occurs with free irinotecan. We believe that MM-398 utilizes tumor macrophages to both break down the nanotherapeutic and convert the irinotecan into SN-38 in the local tumor environment, resulting in a sustained pool of SN-38 in the tumor. Overall, the design of MM-398 is intended to increase the local concentration of active drug so as to improve its anti-tumor effects, especially for hard to treat tumors.

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Clinical development of MM-398

We are planning to pursue two approaches in the ongoing clinical development of MM-398:

Identify specific patients and tumor types that will respond to MM-398. In clinical practice, the chemotherapy drug irinotecan is used as a monotherapy or combination therapy in multiple cancer indications, including pancreatic, colorectal, lung, ovarian, stomach, breast, leukemia, lymphoma and cervical cancers. It has been difficult for clinicians to predict which patients will respond best to irinotecan, however. One of our clinical development strategies is to identify biomarkers based on drug deposition, activation and tumor sensitivity that will predict which patients are most likely to derive a greater benefit from MM-398 than from conventional chemotherapy.

Expand into new indications. The use of chemotherapies, including irinotecan, is limited by severe adverse effects that, in turn, limit their efficacy. Our second clinical development strategy is to expand the use of MM-398 into indications for which irinotecan is currently not being used by demonstrating that MM-398 has favorable efficacy and safety characteristics compared to the current standard of care.

Prior to May 2011, our collaborator, PharmaEngine, Inc., or PharmaEngine, led the clinical development of MM-398 under the designation PEP02. In May 2011, we entered into an agreement with PharmaEngine through which we now hold the development and commercialization rights to MM-398 worldwide, other than in Taiwan. As a result, we expect that we or third party investigator sponsors will conduct all future clinical trials of MM-398, including the Phase 3 clinical trial of MM-398 for the treatment of metastatic pancreatic cancer.

Pancreatic cancer

Phase 3 clinical trial

We are conducting a randomized, open label, controlled Phase 3 clinical trial of MM-398 in patients with metastatic pancreatic cancer whose cancer has progressed on treatment with gemcitabine. The trial is designed to compare the efficacy of MM-398, alone or in combination with 5-FU and leucovorin, against a common control arm of the combination of 5-FU and leucovorin, which is one of the drug combinations that clinicians use to treat patients with metastatic pancreatic cancer whose cancer progresses after treatment with gemcitabine. We expect this trial to enroll approximately 405 patients at approximately 90 sites in North America, South America, Europe, Asia and Africa. The primary efficacy endpoint of this trial is a statistically significant difference in overall survival (OS) between MM-398 or the combination of MM-398 with 5-FU and leucovorin against the combination of 5-FU and leucovorin. The secondary endpoints of this trial are objective response rate (ORR) and progression free survival (PFS).

Phase 2 clinical trial

MM-398 was evaluated in an open label, single arm Phase 2 clinical trial in 40 patients with metastatic pancreatic cancer whose cancer had progressed on treatment with gemcitabine. Patients received 120 mg/m^2 of MM-398 every three weeks. The trial was conducted at three sites, two in Taiwan and a third at the University of California, San Francisco, and was conducted by PharmaEngine.

The primary efficacy endpoint of this trial was the three month survival rate. The hypothesis was that absent further therapies, 40% of the patients would survive three months. Success in the MM-398 Phase 2 clinical trial was defined as achieving a three month survival rate of 65%. The trial was successful as 75% of patients survived three months or longer. The secondary efficacy endpoints in this trial were objective response rate (ORR), progression free survival (PFS) and overall survival (OS). The objective response rate (ORR) was 7.5%, with three patients achieving a partial response (PR).

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The median progression free survival (PFS) was 9.6 weeks, and median overall survival (OS) was 22.4 weeks.

The trial had the following additional results as of May 31, 2011, as reported at the 2011 Annual Meeting of the American Society of Clinical Oncology:

16 patients survived longer than six months and eight of those patients, or 20% overall, survived for greater than one year. Two additional patients reached the one year time point after May 31, 2011, for a 25% one year survival rate. Although cross-trial comparisons must be interpreted with caution as numerous factors may be different between studies, gemcitabine was approved as a first-line treatment for pancreatic cancer based on a one year survival rate of 18%.

Initially, one of the eight patients who survived one year had a tumor that was not able to be surgically removed. However, while receiving treatment with MM-398, the tumor shrank sufficiently that the patient could undergo surgery, and the tumor was surgically removed. As of May 31, 2011, this patient was still alive.

Three patients achieved a partial response (PR) and 16 patients had stable disease (SD) at six weeks, resulting in a disease control rate (DCR) at six weeks of 47.5%.

The chart below shows the overall survival (OS) of each patient in this trial as of May 31, 2011. Each bar represents a different patient, and the height of the bar represents how long that patient survived. The black bars represent patients who had died as of May 31, 2011, while the gray bars represent those who were still alive.

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The following table summarizes the grade 3 and grade 4 adverse events observed in this trial.

Adverse event	Patients (n = 40)
Neutropenia	12 (30.0)%
Leucopenia	9 (22.5)%
Anemia	6 (15.0)%
Diarrhea	3 (7.5)%
Fatigue	3 (7.5)%
Nausea	2 (5.0)%
Vomiting	2 (5.0)%
Thrombocytopenia	2 (5.0)%

Colorectal cancer

Phase 2 clinical trial

MM-398 is currently being evaluated in a randomized, open label Phase 2 clinical trial in second-line metastatic colorectal cancer, which is being conducted by GERCOR, a cooperative research group of physicians based in France. This trial was initially designed to compare the efficacy of a regimen of 5-FU, leucovorin and MM-398 and FOLFIRI, which is a regimen of 5-FU, leucovorin and irinotecan. Roche recently announced results from a Phase 3 clinical trial in second-line metastatic colorectal cancer being conducted in Europe comparing chemotherapy to chemotherapy plus bevacizumab. The results of this trial by Roche have caused some medical institutions and physicians in France to modify their clinical practice. As a result, GERCOR amended the Phase 2 clinical trial of MM-398 to include bevacizumab in both arms. The amended trial resumed accrual of patients in July 2012 and is currently ongoing. We expect this trial to enroll up to 88 patients at approximately six sites in France. The primary efficacy endpoint of this trial is objective response rate (ORR). Secondary endpoints include progression free survival (PFS) and overall survival (OS). The safety data from this trial will be evaluated after the first ten patients are dosed in each arm after the addition of bevacizumab.

Phase 1 clinical trial

MM-398 is currently being evaluated in an open label, dose escalation Phase 1 clinical trial of MM-398 in patients with colorectal cancer whose cancer has progressed on treatment with the chemotherapy drug oxaliplatin. The trial has enrolled 18 patients, and recruitment is complete. The purpose of this trial is to assess safety and determine the maximum tolerated dose. The National Institute of Cancer Research, National Health Research Institutes in Taiwan is conducting this trial. To date, MM-398 has been well tolerated at doses of 80 mg/m^2, 90 mg/m^2 and 100 mg/m^2 every two weeks in this trial, and preliminary signs of anti-tumor activity have been observed in certain patients. Consistent with the design of this Phase 1 clinical trial to principally test for safety and dosage tolerance, this Phase 1 trial was not designed to test for statistical significance of anti-tumor activity.

Gastric cancer

Phase 2 clinical trial

MM-398 was evaluated in a randomized, blinded Phase 2 clinical trial comparing the efficacy of MM-398 to each of irinotecan and docetaxel in 132 patients with metastatic gastric or gastroesophageal junction adenocarcinoma who had failed one previous therapy. The patients were randomized into three groups of 44 patients each. Patients were dosed at 22 sites in six countries in Europe and Asia. Patients were randomized to receive 120 mg/m^2 of MM-398 every three weeks, 300 mg/m^2 of irinotecan every three weeks or 75 mg/m^2 of docetaxel every three weeks.

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The primary efficacy endpoint of this trial was objective response rate (ORR). Success was prospectively defined as five or more patients in an arm achieving a complete or partial response. MM-398 (six patients) and docetaxel (seven patients) met the primary endpoint, but free irinotecan did not. The most common grade 3 and grade 4 hematological adverse events observed in each of the MM-398, irinotecan and docetaxel groups were, respectively: neutropenia (11.4%, 15.9%, 15.9%), febrile neutropenia (6.8%, 11.3%, 4.6%) and anemia (4.5%, 4.5%, 6.8%). The most common grade 3 and grade 4 non-hematological adverse events observed in each of the MM-398, irinotecan and docetaxel groups were, respectively: diarrhea (27.3%, 18.2%, 2.3%), nausea (11.4%, 4.6, 0.0%), vomiting (4.6%, 13.6%, 6.8%) and anorexia (6.8%, 6.8%, 0.0%).

Initial Phase 1 clinical trials

Several additional Phase 1 clinical trials of MM-398 have been conducted or are ongoing to evaluate safety and determine dosing for Phase 2 clinical trials of MM-398. Key findings from these trials include the following:

In a multi-center, open label dose escalation trial of MM-398 as a monotherapy at 60 mg/m^2, 120 mg/m^2 and 180 mg/m^2 every three weeks in 11 patients with advanced solid tumors, MM-398 exhibited a sustained release profile and longer circulation time in the blood than free irinotecan, based on a comparison of pharmacokinetic data from this trial and the product label for irinotecan. In addition, systemic exposure to irinotecan released by MM-398 was negligible across the range of doses tested, indicating that most MM-398 was present as the encapsulated form in the plasma and that leakage of irinotecan was minimal during circulation. In addition, preliminary signs of anti-tumor activity were observed in certain patients. Consistent with the design of this Phase 1 clinical trial to principally test for safety and dosage tolerance, this Phase 1 trial was not designed to test for statistical significance of anti-tumor activity.

In a multi-center, open label dose escalation trial of MM-398 at 60 mg/m^2, 80 mg/m^2, 100 mg/m^2 and 120 mg/m^2 every three weeks in combination with 5-FU and leucovorin in 16 advanced solid tumor patients, MM-398 exhibited a longer circulation time in the blood than free irinotecan, based on a comparison of pharmacokinetic data from this trial and the product label for irinotecan.

In an ongoing investigator sponsored, open label, dose escalation Phase 1 clinical trial of MM-398 in patients with glioma being conducted by the University of California, San Francisco, MM-398 has been well tolerated at doses of up to 180 mg/m^2 every three weeks by patients within a subgroup defined by the presence of a specific genetic marker of irinotecan metabolism.

Companion diagnostic development

We believe that deposition of MM-398 in the tumor is important to efficacy. We are developing an *in vivo* liposome-based imaging agent to measure deposition in the tumor in an effort to exclude those patients whose tumors are unlikely to respond to MM-398 treatment. We are currently evaluating in preclinical testing nanotherapeutic formulations of various agents imaged by PET scan and other modalities to assess the potential for measuring significant deposition. We are also investigating functional *in vitro* biomarkers that we believe may be predictive of efficacy in poorly vascularized tumors, such as pancreatic cancer.

Phase 1 clinical trial

We are currently conducting a translational study designed to identify predictive biomarkers associated with MM-398 in advanced colorectal, lung and triple-negative breast cancers. A translational study is a clinical trial where biomarker investigation is performed, with a goal of identifying biomarkers that predict patients' response to the therapy. Specifically, this study aims to establish the

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feasibility of collecting specialized magnetic resonance-based images (MRI) and tissue-based biomarkers for the purpose of estimating drug delivery to the tumor and patient response to MM-398. We are conducting this trial at one site in the United States.

MM-121

Overview

MM-121 is a fully human monoclonal antibody that targets the ErbB3 cell surface receptor. We are currently evaluating MM-121 in multiple Phase 1 and Phase 2 clinical trials in combination with chemotherapies and targeted therapies. We believe that MM-121 was the first ErbB3 inhibitor to enter clinical development. We are developing a companion diagnostic that is focused on multiple biomarker assays to determine whether a tumor is dependent on ErbB3 signaling and amenable to treatment with MM-121. We are performing initial research on this assay in our ongoing MM-121 clinical trial program to determine whether to pursue its validation in future clinical trials. We have established a worldwide collaboration with Sanofi for the development and commercialization of MM-121. We are developing MM-121 for a wide range of solid tumor indications, including ovarian, breast and lung cancers.

Design and potential advantages of MM-121

We identified the importance of ErbB3 through Network Biology. Our research recognized the previously unappreciated role of ErbB3 as being critical in combinatorial ligand-induced activation of the ErbB pathway, which can lead to tumor cell growth and survival in the cancer setting.

In designing MM-121, we:

- generated a human antibody antagonist as opposed to a small molecule therapeutic because the ErbB3 receptor does not have an active kinase domain and therefore ErbB3 signaling cannot be blocked by a small molecule kinase inhibitor;
- generated a human antibody that binds to a specific portion of the ErbB3 molecule so as to block the binding of ErbB3's activating ligand, known as heregulin, and inhibit growth and survival signaling;
- designed the antibody to inhibit ErbB3-induced activation by ligands other than heregulin;
- designed MM-121 to cause the ErbB3 receptor to be internalized into the tumor cell so that it is no longer available for the signaling process that can drive cancer growth and survival; and
- designed MM-121 as a specific type of antibody, called an IgG2, that minimizes immune activation that can cause off-target adverse events in order to potentially reduce drug associated toxicities.

Based on the central role of ErbB3 in cancer growth and survival, we believe that MM-121 potentially is applicable to a broad range of tumors, including lung, prostate, breast, ovarian, colon and pancreatic cancers. Our preliminary study of several hundred tumor samples suggests that MM-121 may be able to target ErbB3 signaling that is relevant in 30% or more of cancer patients with these types of tumors.

Research suggests that ErbB3 is associated with the development of resistance to other therapies. Therefore, we believe that MM-121 may be especially effective when given in combination with chemotherapies and other targeted therapies and potentially offers the following advantages compared to existing therapies:

- the ability to synergistically or additively attack tumor growth, based on our preclinical research involving a broad range of combination therapies;

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the ability to delay the development of resistance to other agents, based on research by us and others demonstrating that ErbB3 signaling is upregulated in response to treatment with other therapies; and

the ability to restore sensitivity to drugs, based on our preclinical research involving several cell types and xenograft models that are resistant to targeted therapies or chemotherapies.

Clinical development of MM-121

We and Sanofi are conducting a broad clinical program to test MM-121 in combination with a range of other therapies across a wide spectrum of solid tumor patient populations. The goal of this program is to explore the effect and efficacy of MM-121 in combination with other targeted ErbB agents, such as erlotinib, chemotherapies, such as paclitaxel, and anti-hormonal agents, such as exemestane. We plan to assess whether efficacy is improved by measuring the ability of various MM-121 combinations to enhance anti-tumor activity or to delay resistance or restore sensitivity to the other therapies.

Phase 2 clinical trial of MM-121 in combination with paclitaxel for platinum resistant or refractory advanced ovarian cancer

We are currently conducting a randomized, open label Phase 2 clinical trial of MM-121 in combination with paclitaxel in patients with advanced ovarian cancer who are resistant or refractory to treatment with platinum-based chemotherapies, which are frequently used to treat ovarian cancer. Enrollment in this trial is complete with a total of 223 patients enrolled. We are conducting this trial at multiple sites in North America and Europe. The primary efficacy endpoint of this trial is progression free survival (PFS). The secondary endpoints include overall survival (OS), objective response rate (ORR) and duration of response.

Phase 2 clinical trial of MM-121 in combination with exemestane for hormone receptor positive breast cancer

We are currently conducting a randomized, double blind Phase 2 clinical trial to compare the efficacy of MM-121 in combination with exemestane to exemestane alone. Exemestane is a widely used aromatase inhibitor for the treatment of breast cancer. Aromatase is an enzyme implicated in breast cancer. The trial protocol calls for enrollment of approximately 130 postmenopausal women with metastatic hormone receptor positive breast cancer who have tested negative for overexpression of ErbB2 (HER2) and whose cancer progressed on treatment with another aromatase inhibitor or other anti-estrogen therapy. We are conducting this trial at multiple sites in North America and Europe. The primary efficacy endpoint of this trial is progression free survival (PFS). The secondary endpoints are overall survival (OS), objective response rate (ORR), duration of response and disease control rate (DCR).

Phase 1/2 clinical trial of MM-121 in combination with erlotinib for non-small cell lung cancer

We are currently conducting a Phase 1/2 clinical trial of MM-121 in patients with metastatic non-small cell lung cancer. The Phase 1 portion of the trial was an open label, dose escalation study in which successive groups of patients were enrolled. The purpose of the Phase 1 portion of the trial was to assess the safety of MM-121 in combination with erlotinib and determine the optimal dose and dosing schedule of this combination for the Phase 2 portion of the trial. Erlotinib is a marketed small molecule directed at EGFR (ErbB1). Enrollment in the Phase 1 portion of the trial is complete with a total of 32 patients enrolled. Clinical activity observed in this trial included one patient with a partial response (PR) and 14 patients with stable disease (SD). The most common toxicities observed of any grade were diarrhea (82%), rash (64%) and fatigue (64%). Consistent with the design of this Phase 1

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clinical trial to principally test for safety and dosage tolerance, this Phase 1 trial was not designed to test for statistical significance of anti-tumor activity.

We are also currently conducting the Phase 2 portion of the trial, which involves testing three separate hypotheses in three different populations of non-small cell lung cancer patients, at multiple sites in North America, Europe and Asia. The Phase 2 portion of the trial is an open label study in which we plan to enroll approximately 229 patients in parallel across the three different patient populations. The primary efficacy endpoint of the Phase 2 portion of the trial is progression free survival (PFS). The three populations of non-small cell lung cancer patients to be included in the study are:

Group A: patients whose tumors do not have an EGFR (ErbB1) activating mutation, whose cancer has recurred or progressed following at least one chemotherapy-containing regimen and who have not received prior EGFR (ERbB1) targeted therapy will be randomized to receive either MM-121 in combination with erlotinib or erlotinib alone;

Group B: patients whose tumors have an EGFR (ErbB1) activating mutation and who have not received prior EGFR (ErbB1) targeted therapy will be randomized to receive either MM-121 in combination with erlotinib or erlotinib alone; and

Group C: patients whose tumors had responded to an EGFR (ErbB1) targeted therapy and subsequently acquired resistance will receive MM-121 in combination with erlotinib.

Phase 2 neoadjuvant clinical trial of MM-121 in combination with paclitaxel for ErbB2 (HER2) negative breast cancer

We are currently conducting a randomized, open label Phase 2 neoadjuvant clinical trial of MM-121 in combination with paclitaxel, an established chemotherapy, in patients with ErbB2 (HER2) negative breast cancer. We expect to enroll patients in this trial at approximately 35 to 40 sites in North America. The primary efficacy endpoint of this trial is pathologic complete response (pCR) rate at time of surgery. We expect this trial to enroll approximately 200 patients in parallel across the following two populations of ErbB2 (HER2) negative breast cancer patients:

Group A: patients whose tumors are estrogen receptor, or ER, positive and ErbB2 (HER2) negative and have not undergone prior treatment or surgery; and

Group B: patients whose tumors are ER negative, ErbB2 (HER2) negative and progesterone receptor negative, often referred to as triple negative breast cancer, and have not undergone prior treatment or surgery.

Each population of patients is being randomized at a two to one ratio to receive either MM-121 in combination with paclitaxel or paclitaxel alone. Following treatment with MM-121 and/or paclitaxel, patients will receive standard treatment with doxorubicin and cyclophosphamide, two marketed chemotherapies, prior to surgical resection.

Phase 1 clinical trial of MM-121 in combination with paclitaxel for ErbB2 (HER2) negative breast cancer and gynecological cancers

We are currently conducting an open label, dose escalation Phase 1 clinical trial of MM-121 in combination with paclitaxel in patients with the following cancers:

advanced ovarian and other gynecological cancers; or

metastatic ErbB2 (HER2) negative breast cancer.

We are conducting this trial at multiple sites in the United States. The purpose of the trial is to assess the safety of MM-121 in combination with paclitaxel, determine the recommended dose for a

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subsequent Phase 2 clinical trial and evaluate the potential utility of the predictive biomarkers for MM-121. The dose escalation portion of the trial is complete, and several expansion cohorts continue to enroll patients. To date, preliminary data regarding safety and anti-tumor activity from this trial suggest that further investigation of the combination of MM-121 and paclitaxel is warranted in Phase 2 clinical development, which we are currently pursuing in multiple indications. Consistent with the design of this Phase 1 clinical trial to principally test for safety and dosage tolerance, this Phase 1 trial was not designed to test for statistical significance of anti-tumor activity.

Phase 1 clinical trial of MM-121 in combination with cetuximab and irinotecan for multiple solid tumor types

We are currently conducting an open label, dose escalation Phase 1 clinical trial of MM-121 in combination with cetuximab and irinotecan in patients with the following cancers:

advanced colorectal cancer;

squamous cell head and neck cancer;

non-small cell lung cancer;

triple negative breast cancer; or

other types of solid tumors that are believed to depend on EGFR (ErbB1) activity.

We are conducting this trial at multiple sites in the United States. The purpose of the trial is to assess the safety and pharmacokinetics of MM-121 in combination with cetuximab and MM-121 in combination with cetuximab and irinotecan.

Phase 1 clinical trial of MM-121 in combination with multiple anti-cancer therapies for advanced solid tumor types

We are currently conducting an open label, dose escalation Phase 1 clinical trial of MM-121 in combination with one of multiple standard anti-cancer therapies. We are conducting this trial at multiple sites in North America and the European Union. The purpose of this trial is to evaluate the safety and pharmacokinetics of MM-121 in patients with advanced solid tumors when administered in combination with each separate anti-cancer therapy.

Phase 1 clinical trial of MM-121 in advanced solid tumors

We have completed an open label, dose escalation Phase 1 clinical trial of MM-121 in 25 patients with advanced tumors that were refractory to other treatments. The purpose of this trial was to study the safety and pharmacokinetic properties, determine the maximum tolerated dose and evaluate the effect of MM-121 on tumor growth. There were six successive cohorts of three to six patients each in this trial. Each cohort received different weekly doses of MM-121 that increased after each cohort. In the last cohort, a dosing regimen known as a loading dose regimen was tested in which the first dose received was higher than subsequent weekly dosing. We did not identify a maximum tolerated dose in this trial.

We have completed an expansion cohort of this trial which was designed to further characterize safety and explore clinical biomarkers. The patients in the expansion cohort were biopsied before and after dosing. This trial focused on enrolling patients with ErbB2 (HER2) negative breast cancer, ovarian cancer and other tumor types in which the ErbB3 pathway may play an important role. The

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following table summarizes the grade 3 and grade 4 adverse events observed in the dose escalation and expansion phases of this trial as of December 31, 2010.

Adverse event	Patients (n = 38)
Fatigue	4 (10.5)%
Nausea	1 (2.6)%
Vomiting	1 (2.6)%

In the dose escalation portion of this trial, five of 25 patients (20%) achieved a clinical benefit, as demonstrated by stable disease (SD), partial response (PR) or complete response (CR). In the expansion portion of this trial, four of 13 patients (29%) enrolled as of December 31, 2010 had stable disease (SD) for eight weeks or longer.

Preclinical development of MM-121

We have conducted a comprehensive program of preclinical testing of MM-121, including several *in vitro* analyses and *in vivo* xenograft studies. Key findings from this preclinical program include the following:

Administration of MM-121 resulted in dose-dependent growth inhibition in a broad range of cancer xenograft models, including those of lung, ovarian, breast, prostate and renal cancer.

MM-121 demonstrated synergistic or additive effects when combined with a number of other therapies, including both chemotherapies and other targeted therapies.

Companion diagnostic development

Using our Network Biology approach, we derived a predictive biomarker profile that identifies tumors that are responsive to MM-121 in animal models. This test measures the levels of five proteins involved in the ErbB pathway and predicts the activated state of ErbB3 and, therefore, the potential responsiveness of the tumor to MM-121 based on those levels. Using this approach, we have been able to successfully predict whether a tumor in a preclinical xenograft study will respond to MM-121. We now plan to investigate whether and at what levels these biomarkers can predict MM-121 response in human tumor samples. As part of our ongoing clinical development of MM-121, we are taking biopsies from patients in order to measure levels of biomarkers in the tumors treated with MM-121.

MM-111

Overview

MM-111 is a bispecific antibody designed to inhibit ErbB3 signaling in cancer cells that overexpress the ErbB2 (HER2) cell surface receptor, which are also referred to as ErbB2 (HER2) positive. Bispecific antibodies are antibodies designed to simultaneously bind to two different target cell surface proteins or receptors. In the case of MM-111, these targets are the ErbB2 (HER2) receptor and the ErbB3 receptor. We are preparing to initiate a Phase 2 clinical trial of MM-111 and are currently conducting multiple Phase 1 clinical trials in combination therapy settings. We are working to develop a companion diagnostic based on a multiple biomarker assay to identify patient populations likely to respond to treatment with MM-111. This diagnostic is in preclinical development. We are developing MM-111 for a wide range of solid tumors, including breast, gastric, ovarian and bladder cancers.

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Design and potential advantages of MM-111

MM-111 is designed to inhibit growth and survival signaling through ErbB3 in cancer cells characterized by high levels of ErbB2 (HER2). The complex of ErbB2, ErbB3 and its ligand, heregulin, promotes tumor growth in ErbB2 (HER2) positive cancer cells. MM-111 consists of a targeting arm that binds to ErbB2 (HER2) and a therapeutic arm that binds to ErbB3. The ErbB3 arm is designed to disrupt the ErbB2/ErbB3/heregulin complex and therefore inhibit tumor cell growth and survival.

Based on our preclinical research, we believe that MM-111 may offer the following advantages compared to existing treatments:

In patients with ErbB2 (HER2) positive cancers, we believe that the bispecific design of MM-111 may more effectively inhibit ErbB3 than combinations of separate ErbB2 (HER2) and ErbB3 targeted antibodies. Multiple published studies indicate that the affinity of heregulin for the ErbB2/ErbB3 receptor complex on ErbB2 (HER2) positive tumor cells is very high. Our research suggests that this makes it difficult to inhibit signaling with single drugs or combinations in patients that express high levels of ErbB2. MM-111 is designed to utilize an ErbB2 (HER2) targeting arm to greatly increase the local concentration of the ErbB3 therapeutic arm on the surface of ErbB2 (HER2) positive tumor cells, thus enabling the molecule to disrupt the high affinity complex and inhibit signaling.

We believe that MM-111 may be particularly effective in combination with both ErbB2 (HER2) targeted and conventional chemotherapies, as MM-111 may be able to enhance anti-tumor activity, delay the development of resistance to other agents and restore sensitivity to drugs to which a tumor has become resistant.

In breast cancer and additional tumor types, such as gastric and ovarian cancer, we believe that MM-111 may be effective in patients whose tumors express ErbB2 (HER2) at lower levels than those needed for currently marketed ErbB2 (HER2) targeted agents that inhibit the ErbB2 (HER2) receptor directly.

We believe that MM-111 will have a more favorable safety profile than currently marketed ErbB2 (HER2) targeting agents because it is not designed to block ErbB2 (HER2) cell signaling, which is associated with cardiac adverse events.

Clinical development of MM-111

We are conducting a clinical program to evaluate MM-111 as a monotherapy and in combination with a range of other therapies across ErbB2 (HER2) positive solid tumors. We are currently evaluating MM-111 for the treatment of breast and gastric cancer, for which ErbB2 (HER2) directed agents are currently approved, in addition to ErbB2 (HER2) positive solid tumors for which there are no approved therapies, such as bladder cancer.

Phase 2 clinical trial of MM-111 in combination with paclitaxel with or without trastuzumab for gastric cancers

We are preparing to initiate a randomized, open label Phase 2 clinical trial of MM-111 with paclitaxel with or without trastuzumab in patients with gastric, gastroesophageal junction and esophageal cancers. We expect to enroll patients in this trial at approximately 40 to 60 sites in North America, Europe, Africa and Asia. The primary efficacy endpoint of this trial is progression free survival (PFS). The secondary endpoints include overall survival (OS), objective response rate (ORR)

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and duration of response. We expect this trial to enroll up to 180 patients in parallel across the following two patient populations:

Group A: patients who have traditional ErbB2 (HER2) positive tumors, meaning that their tumors measure HER2 3+ or HER2 2+/FISH+ using conventional cancer testing methods, will receive either MM-111, paclitaxel and trastuzumab or paclitaxel and trastuzumab; and

Group B: patients who have non-traditional ErbB2 (HER2) positive tumors, meaning that their tumors measure HER2 2+/FISH- using conventional cancer testing methods, will receive either MM-111 and paclitaxel or paclitaxel alone.

Phase 1 clinical trial of MM-111 in combination with trastuzumab for advanced refractory ErbB2 (HER2) positive breast cancer

We are currently conducting an open label, dose escalation Phase 1 clinical trial of MM-111 in patients with ErbB2 (HER2) positive breast cancer. The purpose of the trial is to assess the safety of MM-111 in combination with trastuzumab and determine the optimal dose and dosing schedule of this combination. Trastuzumab is an approved therapy directed at ErbB2 (HER2) positive cancer cells. We are conducting this trial in 16 patients at approximately three sites in the United States.

Phase 1 clinical trial of MM-111 in combination with multiple anti-cancer therapies for ErbB2 (HER2) positive solid tumors

We are conducting an open label, dose escalation Phase 1 clinical trial of MM-111 in patients with advanced ErbB2 (HER2) positive solid tumors. The trial protocol calls for enrollment of up to approximately 85 patients. We are conducting this trial at approximately 14 sites in the United States. The purpose of the trial is to determine the maximum tolerated dose and any dose limiting adverse events of MM-111 in combination with multiple treatment regimens. The trial includes five combination therapies with MM-111:

capecitibine, cisplatin and trastuzumab;

lapatinib with or without trastuzumab;

paclitaxel and trastuzumab;

lapatinib, paclitaxel and trastuzumab; and

docetaxel and trastuzumab.

This trial also will assess the pharmacokinetics of MM-111 with each combination, safety and tolerability of each combination and the anti-tumor activity of each combination as indicated by objective response rate (ORR), duration of response and progression free survival (PFS). Exploratory endpoints include an analysis of serum and tissue markers and their correlation with anti-tumor activity. To date, the combination of MM-111 and each of the first three treatment regimens described above has been well tolerated in this trial, and preliminary signs of anti-tumor activity have been observed in certain patients receiving each of these treatment regimens. Consistent with the design of this Phase 1 clinical trial to principally test for safety and dosage tolerance, this Phase 1 trial was not designed to test for statistical significance of anti-tumor activity.

Phase 1 clinical trial of MM-111 in advanced, refractory ErbB2 (HER2) positive solid tumors

We have completed an open label, dose escalation Phase 1 clinical trial of MM-111 in patients with ErbB2 (HER2) positive solid tumors. We enrolled 20 patients in this trial at four sites in the United States. The purpose of this trial was to assess the safety and clinical activity of MM-111, to determine the maximum tolerated dose or the maximum feasible dose of MM-111 and to identify any

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dose limiting adverse events. We also designed the trial to assess objective response rate (ORR) and progression free survival (PFS). The final data from this trial are currently being reviewed.

Preclinical development of MM-111

We have conducted a comprehensive program of preclinical testing of MM-111, including several *in vitro* analyses and *in vivo* xenograft studies. Key findings from this preclinical program include the following:

MM-111 was active in several ErbB2 (HER2) positive xenograft models, including breast, lung and gastric cancer. Tumor size was reduced in all tumor types.

In cell-based and animal model tests, the anti-proliferative activity of MM-111 resulted in a tumor shrinkage that positively correlated with ErbB2 (HER2) expression levels. MM-111 had a synergistic effect on the inhibition of tumor growth in a breast cancer xenograft model when combined with trastuzumab or lapatinib or both. We believe these data suggest a potential benefit of adding MM-111 to existing agents that target ErbB2 (HER2) and have marginal activity as monotherapies in ErbB2 (HER2) positive cancers.

In cell-based and animal models, MM-111 had a synergistic effect on the growth of heregulin expressing models of breast and gastric cancer in combination with paclitaxel, or trastuzumab and paclitaxel. These data suggest that there is a potential benefit of adding MM-111 to paclitaxel-based regimens, especially in patients that overexpress heregulin.

In cell-based and animal model tests, the combination of MM-111 with anti-estrogen therapy showed superior activity to either drug as a monotherapy, indicating the potential for a combination of MM-111 with endocrine therapies to overcome acquired resistance to endocrine therapies in ER positive, ErbB2 (HER2) positive breast cancer patients. For example, in an estrogen-stimulated, estrogen positive and ErbB2 (HER2) positive breast cancer cell assay, MM-111 as a monotherapy showed growth inhibitory effects similar to the anti-estrogen drugs tamoxifen and fulvestrant. In the presence of heregulin, MM-111 maintained its growth inhibitory activity. In contrast, the inhibitory effect of tamoxifen and fulvestrant was diminished in the presence of heregulin. This suggests that activation of ErbB3 may confer tumor cell resistance to anti-estrogen therapies.

Companion diagnostic development

We are working to develop a diagnostic tool that will allow rapid identification of patients likely to respond to treatment with MM-111 based on their expression levels of ErbB2 (HER2), ErbB3, heregulin and other factors that we anticipate identifying from ongoing clinical trials. Our goal is to develop a diagnostic tool that offers significant improvement over the qualitative tests that are currently used to identify potentially responsive patients based on ErbB2 (HER2) overexpression alone.

The current focus of this program is the development of quantitative assays to assess ErbB2 (HER2), ErbB3 and heregulin levels in archived and pretreatment patient biopsies from our clinical trials to generate data to support our biomarker hypotheses. We are also evaluating other potential biomarkers through collaborative work with a third party.

MM-302

Overview

MM-302 is a nanotherapeutic encapsulation of doxorubicin with attached antibodies that target ErbB2 (HER2). We are conducting a Phase 1 clinical trial of MM-302 in patients with advanced ErbB2 (HER2) positive breast cancer. We are designing a companion diagnostic for MM-302 to predict which

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patients have tumors that will exhibit high uptake of MM-302. We also plan to pursue the use of MM-302 as an earlier line of therapy in the adjuvant setting, which means use in conjunction with radiotherapy or surgery, and the neoadjuvant setting. In addition, we plan to pursue the use of MM-302 as a therapy for other ErbB2 (HER2) positive tumors.

Doxorubicin is a marketed chemotherapy that is a member of the anthracycline class of chemotherapies. The addition of anthracyclines to the treatment of both solid and liquid tumors has historically improved outcomes for patients. Specifically, anthracyclines have served as the backbone of breast cancer therapy for decades. Free doxorubicin is currently approved and used in adjuvant and neoadjuvant breast cancer alone and in combination with other chemotherapies and targeted agents. Consistent clinical benefit has been observed with anthracycline-based regimens in breast cancer. However, significant adverse events, including acute and chronic heart dysfunction, have limited their use.

Liposomal doxorubicin, marketed as Doxil, is currently approved and used in ovarian cancer and multiple myeloma. Although liposomal doxorubicin exhibits a better cardiac adverse event profile than free doxorubicin, its use also has been limited by hand-foot syndrome, which is an adverse event that produces redness and peeling on the hands and feet. In addition, the incremental efficacy benefits of liposomal doxorubicin compared with free doxorubicin are not clear, with direct comparisons between the two therapies in some tumor subtypes demonstrating equivocal results. In a pivotal clinical trial of women with breast cancer, liposomal doxorubicin was no more effective than free doxorubicin.

Design and potential advantages of MM-302

We designed MM-302 to bind to cancer cells that overexpress ErbB2 (HER2) and thereby release doxorubicin at the site of the tumor. Our goal is for MM-302 to retain the safety profile of liposomal doxorubicin, in particular with respect to cardiac safety, but to have better efficacy in ErbB2 (HER2) positive tumors.

We believe that MM-302 may offer the following advantages in comparison with free doxorubicin and liposomal doxorubicin:

MM-302 is designed to utilize nanotherapeutic encapsulation to protect the heart from cardiac adverse events associated with free doxorubicin.

The specific size and stability characteristics of MM-302 are designed to enable the preferential deposition of the drug within tumors relative to normal tissue. Specifically, we believe that, as a nanotherapeutic, MM-302 is able to utilize the EPR effect to selectively enter, and subsequently be trapped in, tumors with leaky vasculature.

MM-302 is designed with attached antibodies so as to use the ErbB2 (HER2) receptor as a binding mechanism to induce the internalization of the nanotherapeutic encapsulated drug particle, and thereby provide drug delivery directly into the cell and increase the potential efficacy of doxorubicin.

MM-302 is designed with an ErbB2 (HER2) antibody that binds to but does not shut down the signaling activity of ErbB2 (HER2). We believe that this will minimize the severity and frequency of adverse events associated with suppressing ErbB2 (HER2) and allow for more clinical benefit for patients with lower levels of ErbB2 (HER2) than is provided by current ErbB2 (HER2) directed treatments.

MM-302 may provide anti-tumor benefit for patients who have failed other ErbB2 (HER2) targeted therapies, but who have not been exposed to anthracyclines.

Based on our preclinical research, we believe that MM-302 may synergize effectively in combination with a number of approved therapies, such as trastuzumab and possibly lapatinib,

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chemotherapy, hormonal therapy and our own drugs, MM-111 and MM-121. The current concerns about the severity and frequency of adverse events associated with doxorubicin and liposomal doxorubicin prevent them from being used in many combination regimens.

Clinical development of MM-302

We have two key strategies for the clinical development of MM-302:

Replace doxorubicin in ErbB2 positive settings. Doxorubicin remains a widely used chemotherapy drug notwithstanding concerns of adverse events, particularly cardiac adverse events. One of our clinical development strategies is to replace the use of doxorubicin with MM-302 by demonstrating that MM-302 has favorable efficacy and safety compared to doxorubicin.

Expand into indications where anthracyclines are no longer used. We believe that there is the potential to expand MM-302 into indications, such as late-line therapy, where anthracyclines are viewed as effective but are not used due to safety concerns. If we are able to demonstrate that MM-302 has a favorable safety profile compared to doxorubicin, we believe that we can expand into these settings.

Phase 1 clinical trial of MM-302 in ErbB2 (HER2) positive breast cancer

We are conducting an open label, dose escalation Phase 1 clinical trial of MM-302 in patients with advanced ErbB2 (HER2) positive breast cancer. The purpose of this trial is to assess the safety of MM-302 and identify the maximum tolerated dose. Enrollment in the monotherapy portion of this trial is complete with a total 34 patients enrolled at four sites in the United States. To date, MM-302 has been well tolerated in this trial, and preliminary signs of anti-tumor activity have been observed in certain patients. Consistent with the design of this Phase 1 clinical trial to principally test for safety and dosage tolerance, this Phase 1 trial was not designed to test for statistical significance of anti-tumor activity.

We recently amended this trial to evaluate MM-302 in combination with trastuzumab. We expect to enroll between 15 and 30 additional patients in this portion of the trial at four sites in the United States.

Preclinical development of MM-302

We have conducted a comprehensive program of preclinical testing of MM-302, including several *in vitro* analyses and *in vivo* xenograft studies. Key findings from this preclinical program include the following:

In studies of human heart muscle cells known as cardiomyocytes, MM-302 did not measurably impact ErbB2 (HER2) signaling, which we believe suggests a potential for low cardiac adverse event occurrence in the clinic.

In multiple cell culture experiments, MM-302 bound with and was internalized into ErbB2-expressing cells more effectively than liposomal doxorubicin.

MM-302 demonstrated measurable activity in cultured cells expressing a lower level of ErbB2 (HER2) receptors than are indicated for treatment with currently marketed therapies.

In multiple xenograft experiments, MM-302 was significantly more potent than free doxorubicin in inhibiting tumor growth.

Pretreatment of mice with cyclophosphamide significantly enhanced the amount of MM-302 that targeted the tumor and resulted in increased anti-tumor activity compared to treatment with either MM-302 or cyclophosphamide alone.

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Companion diagnostic development

We are conducting preclinical research on a companion diagnostic for MM-302 that will help to determine which patients will derive benefits from the drug alone or in combination with other therapies, while experiencing a satisfactory safety profile. This research is focused on:

Developing an *in vivo* liposome-based imaging agent to measure deposition in the tumor in an effort to exclude those patients whose tumors are unlikely to respond to MM-302 treatment. We are currently evaluating in preclinical testing nanotherapeutic formulations of various agents imaged by PET scan and other modalities to assess the potential for measuring significant deposition.

Assessing the association of ErbB2 (HER2) levels, measured *in vitro*, with how much MM-302 can bind and enter cells. As part of these efforts, we may incorporate inclusion and exclusion criteria into our Phase 1 clinical trials of MM-302 to enrich our study population with patients who we believe are likely to benefit from MM-302, including those with high ErbB2 (HER2) expression.

MM-151

Overview

MM-151 is an oligoclonal therapeutic consisting of a mixture of three fully human monoclonal antibodies designed to bind to non-overlapping regions, or epitopes, of the EGFR (ErbB1) receptor. EGFR (ErbB1) has long been recognized as an important drug target in several malignancies, including lung, breast, colon, pancreatic and head and neck cancers. We are conducting a Phase 1 clinical trial of MM-151 in patients with solid tumors. We are focusing our diagnostic efforts for MM-151 on the identification of key biomarkers that will indicate which patient populations are likely to benefit from MM-151 treatment. We plan to develop MM-151 for a range of solid tumor indications, including lung, breast, colorectal, pancreatic and head and neck cancers.

Design and potential advantages

We believe that MM-151 may offer the following advantages over other EGFR (ErbB1) inhibitors:

MM-151 is designed to block the signal amplification that our research suggests occurs in the EGFR (ErbB1) pathway. We believe that binding to multiple epitopes of EGFR (ErbB1) may result in superior signal inhibition compared to currently marketed EGFR (ErbB1) therapies, which only bind to one epitope.

MM-151 is designed to inhibit the signaling that results from the binding of a full range of EGFR (ErbB1) ligands. In contrast, currently marketed therapies block the signaling of only a subset of these ligands. As a result, we believe that a broader patient population may derive clinical benefit from MM-151 than from currently marketed therapies.

Tumors treated with marketed monoclonal antibodies directed at EGFR (ErbB1), such as cetuximab and panitumumab, often develop resistance to these therapies. We hypothesize that this resistance often results from the production by the tumor of a different type of ligand that binds to EGFR (ErbB1). Because MM-151 is designed to block a full range of EGFR (ErbB1) ligands, we believe that resistance to treatment with MM-151 may be delayed or reduced compared to existing therapies.

In preclinical models, MM-151 inhibited tumor cell growth of mutated lung cancer cell lines with acquired resistance to erlotinib. As a result, we believe that MM-151 may provide a longer duration of response than small molecules, such as erlotinib, that target mutated EGFR (ErbB1).

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Clinical development of MM-151

We have two key strategies related to the clinical development of MM-151:

Replace EGFR (ErbB1) therapies. The FDA approved the EGFR (ErbB1) therapy erlotinib in lung and pancreatic cancer and cetuximab in colon and head and neck cancer. In clinical practice, erlotinib is used as a monotherapy or combination therapy in multiple cancer indications, including non-small cell lung, colorectal, breast and head and neck cancers. One of our clinical development strategies is to replace the use of erlotinib with MM-151 by demonstrating that MM-151 has better efficacy and comparable safety.

Expand the EGFR (ErbB1) market using Network Biology. Based on Network Biology insights, we believe that current EGFR (ErbB1) therapies are not being used in indications in which patients would benefit from them. Our second clinical development strategy is to expand the use of MM-151 into indications in which targeted EGFR (ErbB1) therapies are not currently approved, but which our preclinical research indicates should contain patients who will respond to these therapies. Potential indications include lung cancer, for which there is no currently approved targeted antibody therapy, and triple negative breast cancer, for which there is no currently approved EGFR (ErbB1) targeted therapy.

Phase 1 clinical trial of MM-151 in solid tumors

We are conducting an open label, dose escalation Phase 1 clinical trial of MM-151 in patients with solid tumors. The trial protocol calls for enrollment of approximately 63 patients at four sites in the United States. The purpose of this trial is to assess the initial safety and tolerability of escalating doses of MM-151 in patients, including a determination of the maximum tolerated dose and any dose limiting adverse events. We also will assess pharmacokinetics, immunogenicity and the response to treatment after the administration of MM-151 based on objective response rate (ORR).

Preclinical development of MM-151

We have conducted a comprehensive program of preclinical testing of MM-151, including several *in vitro* analyses and *in vivo* xenograft studies. Key findings of this preclinical program include the following:

In *in vitro* experiments, MM-151 exhibited near complete inhibition of EGFR (ErbB1)-induced signaling in a dose-dependent manner. Subsequent *in vitro* studies confirmed that each of the three antibodies comprising MM-151 bound to EGFR (ErbB1) with differential avidity and affinity.

In *in vitro* experiments, the inhibitory effects of MM-151 on signaling and proliferation were more profound than those of cetuximab, as evidenced by the virtually complete inhibition of signaling by MM-151 compared to the partial inhibition of signaling with cetuximab.

MM-151 reduced tumor cell growth in multiple xenograft animal models. Furthermore, MM-151 exhibited better activity than cetuximab at reducing cell growth lung cancer models with acquired resistance to erlotinib.

Companion diagnostic development

We are focusing our diagnostic efforts for MM-151 on the identification of key biomarkers that will indicate which patient populations are likely to benefit from MM-151 treatment. Our goal is to be able to identify patient populations who will respond to MM-151 and who may be unresponsive to other EGFR (ErbB1) inhibitors. This program is in preclinical development.

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MM-141

Overview

MM-141 is a fully human tetravalent bispecific antibody designed to inhibit signaling of the PI3K/AKT/mTOR pathway triggered by the IGF-1R and ErbB3 cell surface receptors. A tetravalent bispecific antibody is a single molecule that has four binding sites, two for each of two different target cell surface receptors. PI3K/AKT/mTOR signaling is often activated in cancers in response to stress induced by chemotherapies or targeted anti-cancer medicines and is believed to play a significant role in promoting tumor cell survival. We are conducting a Phase 1 clinical trial of MM-141 as a monotherapy and in combination with everolimus and docetaxel in patients with solid tumors.

Design and potential advantages of MM-141

We designed MM-141 to suppress the PI3K/AKT/mTOR signaling pathway by reducing the levels of IGF-1R and ErbB3 receptor complexes that trigger the pathway. Based on our preclinical research, we believe that MM-141 offers the following advantages compared to antibodies that solely target IGF-1R or ErbB3:

- MM-141 is a tetravalent antibody that binds to both IGF-1R and ErbB3 with high affinity and avidity.
- MM-141 is designed to block pro-survival signaling of major activators of PI3K/AKT/mTOR, such as heregulin, IGF-1 and IGF-2.
- MM-141 is designed to block mutual compensation in IGF-1R and ErbB3 mediated activation of PI3K/AKT/mTOR by co-inhibiting both targets.
- MM-141 is designed to degrade IGF-1R and ErbB3 containing receptor complexes that are commonly activated in tumors in response to PI3K/AKT/mTOR inhibition by a small molecule or an antibody.
- We do not believe that MM-141 activates the immune system, which minimizes the chance of off-target adverse events.

Clinical development of MM-141

Based on the role of ErbB3 and IGF-1R in tumor growth and survival, we believe that MM-141 is potentially applicable to a broad range of tumors, including lung, prostate, breast, liver and pancreatic cancers. Research suggests that ErbB3 and IGF-1R mediated activation of PI3K/AKT/mTOR is associated with the development of resistance to various anti-cancer therapies. Thus, we believe that MM-141 may be effective in treating solid tumors that are dependent on PI3K/AKT/mTOR and in which this pro-survival pathway is activated as a resistance mechanism to standard of care anti-cancer therapies.

Phase 1 clinical trial of MM-141 in solid tumors

We are conducting an open label, dose escalation Phase 1 clinical trial of MM-141 as a monotherapy and in combination with everolimus and docetaxel in patients with solid tumors. The trial protocol calls for enrollment of between 30 and 120 patients at four sites in the United States and France. The purpose of this trial is to assess the safety of MM-141 and identify the recommended Phase 2 dose.

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Preclinical development of MM-141

We have conducted a comprehensive program of preclinical testing of MM-141, including several *in vitro* analyses and *in vivo* xenograft studies. Key findings from this preclinical program include the following:

- MM-141 blocked the binding of IGF-1, IGF-2 and heregulin to IGF-1R and ErbB3.
- MM-141 induced the degradation of receptor complexes that contain IGF-1R and ErbB3.
- MM-141 suppressed tumor growth in mouse xenograft models of pancreatic cancer, Ewing's sarcoma, prostate cancer, breast cancer and renal cell carcinoma.
- MM-141 overcame acquired ErbB3-mediated resistance to IGF-1R antibody inhibitors.
- MM-141 increased the activity of targeted small molecule inhibitors of the mTOR and MEK enzymes.
- MM-141 increased the activity of docetaxel, gemcitabine and MM-398.

Companion diagnostic development

We are conducting preclinical research on a companion diagnostic for MM-141 that will help to determine which patients will derive benefits from the drug alone or in combination with other therapies, while experiencing a satisfactory safety profile. This research is focused on monitoring the levels of circulating ligands for IGF-1R and ErbB3. In addition, we are studying the roles of activating mutations in the PI3K/AKT/mTOR and other pathways in modulating response to MM-141.

Preclinical Product Candidates

We are developing our preclinical product candidates for a range of solid tumor indications. Our most advanced preclinical candidates are MM-310, a targeted nanotherapeutic, and MM-131, a multispecific antibody.

Therapeutic Design Capabilities

We apply the insights about cell signaling dynamics that we gain from Network Biology across a range of therapeutic technologies to design drug candidates that we believe can be efficiently delivered to the selected molecular target. We believe that the best therapies for the oncology indications that we are pursuing are targeted therapies that, in contrast with conventional chemotherapies, are highly selective for the molecular mechanisms that we are seeking to affect and, as a result, offer the potential for significant efficacy and safety benefits.

Human monoclonal antibodies

Human monoclonal antibodies are a key component of many of our targeted therapies based on their range of favorable attributes, including their significant target specificity and avidity relative to small molecules and their well understood pharmacokinetic properties. We have designed antibodies for use as stand-alone therapeutics and have incorporated antibodies into other therapeutics, such as targeted nanotherapeutics, as targeting or docking agents. We work with several antibody formats, including the following:

- 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.

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Multispecific 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 specifically binds to distinct epitopes on two or more target cell surface proteins or receptors.

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.

Nanotherapeutics

Our nanotherapeutics are lipidic particles carefully constructed to encapsulate active drug payloads. Nanoscale objects typically, though not exclusively, have dimensions on the order of 100 nanometers or smaller. We believe that nanotherapeutics offer the following potentially favorable attributes:

The uniform sizing of our nanotherapeutics is intended to enable targeting and preferential deposition within tumors by taking advantage of the EPR effect.

We formulate our nanotherapeutics 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, and maximizing the amount of active drug that reaches the target.

Encapsulation is designed to protect the active drug payload as it passes through the circulation and organs of the body, such as the liver, preventing premature clearance or metabolism of the active drug, and thereby extend the pharmacokinetic profile and enable more convenient dosing regimens.

We can efficiently create targeted nanotherapeutics using our technical expertise and know-how that enable insertion of targeting agents, such as antibodies, into our nanotherapeutics.

We can customize our nanotherapeutics for use with a variety of drug payloads, including chemotherapies, cytotoxics and nucleic acids, such as siRNA and genes.

Manufacturing

We manufacture drug substance for use in our clinical trials and research and development efforts for all of our therapeutic product candidates using current good manufacturing practices, or cGMP, at our approximately 8,500 square foot multi-product facility located at our corporate headquarters in Cambridge, Massachusetts. We have the capabilities to manufacture antibodies, nanotherapeutics and antibody-targeted nanotherapeutics.

Our manufacturing facility:

is comprised of multiple independent clean rooms;

includes three 1,000 liter single-use bioreactors; and

has capacity to produce approximately 50 kilograms of antibodies per year.

As of January 31, 2013, we employed approximately 54 employees in manufacturing activities.

We believe that our strategic investment in manufacturing capabilities allows us to advance product candidates at a more rapid pace and with more flexibility than a contract manufacturer, produce drug substance in a cost-effective manner while retaining control over the process and prioritize the timing of internal programs.

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Our manufacturing capabilities encompass the full manufacturing process through quality control and quality assurance and are integrated with our project teams from discovery through development. This structure enables us to efficiently transfer research stage lead molecules into manufacturing. We have designed our manufacturing facility and processes to provide maximum flexibility and rapid changeover for the manufacture of different product candidates. We outsource fill-finish, packaging, labeling and shipping.

We manufacture our antibody and nanotherapeutic product candidates using commercially available raw materials and well established manufacturing procedures. We produce antibodies in bioreactors using Chinese hamster ovary cells that have been genetically engineered to secrete our antibody. We then purify the antibodies using industry standard methods, which include affinity chromatography and ultrafiltration operations. We produce nanotherapeutics using high pressure filter extrusion of a mixture of cholesterol and lipids. We then load the nanoliposomes with active pharmaceutical ingredient using a proprietary process.

We have optimized the Phase 2 production process of MM-398 and produced material for our Phase 3 clinical trial at our manufacturing facility. We filed a chemistry manufacturing and controls amendment, or CMC amendment, with the FDA in October 2011 and are currently using the MM-398 product that we manufactured for our Phase 3 clinical trial.

We believe that we can scale our manufacturing processes to support our clinical development programs and the potential commercialization of our product candidates. If any of our product candidates are approved for marketing by the FDA, we intend to oversee the manufacturing of these products, other than MM-121, which Sanofi now manufactures according to the terms of our collaboration agreement.

For our antibody product candidates, we intend to continue to manufacture drug substance for preclinical testing and Phase 1 and Phase 2 clinical development at our current facility. Our long term plan is to establish our own facilities for manufacturing antibody drug substance for Phase 3 clinical development and commercial sale. Pending our establishment of these facilities, we expect to transfer Phase 3 and commercial antibody manufacturing to a contract manufacturing organization. For our nanotherapeutic product candidates, we intend to continue to manufacture drug substance for preclinical testing and all stages of clinical development and initially manufacture drug substance for commercial sale at our current facility.

We are developing and testing diagnostic assays for predictive biomarkers in an internal laboratory under Good Clinical Laboratory Practices. Upon completion of the development of the diagnostic tests, we plan to evaluate external as well as internal options for manufacturing and commercialization of the tests.

We are considering arrangements to use our manufacturing capabilities to manufacture drug product on behalf of third party pharmaceutical companies. We have no current agreements or commitments for any such arrangements.

Sales and Marketing

As our lead product candidates are still in clinical development, we are only in the planning stages of establishing our sales, marketing and product distribution infrastructure. We generally expect to retain commercial rights in the United States and Europe for our oncology product candidates, other than MM-121, for which we receive marketing approvals. We believe that it is possible to access these markets through a focused, specialized field force.

Subject to receiving marketing approvals, we expect to commence commercial activities by building a focused sales and marketing organization for MM-398. This could form the basis of the sales and marketing organization that we will use to sell our other products, subject to receiving marketing

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approval. We believe that such an organization will be able to address the community of oncologists who are the key specialists in treating solid tumors, including the lung, breast, ovarian, pancreatic, colorectal and head and neck cancers for which our product candidates are being developed. Outside the United States and Europe, we expect to enter into distribution and other marketing arrangements with third parties for any of our product candidates that obtain marketing approval.

We also plan to build a marketing and sales management organization to create and implement marketing strategies for any products that we market through our own sales organization and to oversee and support our sales force. The responsibilities of the marketing organization would include developing educational initiatives with respect to approved products and establishing relationships with thought leaders in relevant fields of medicine.

We plan to tightly integrate the marketing of our therapeutics and companion diagnostics. As we expect to pair various types of diagnostics with our therapeutics, it is likely that the sales and marketing tactics and business model employed for our various diagnostics may differ from one another.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our Network Biology technologies, integrated research, clinical and manufacturing capabilities, development experience and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of companion diagnostics in guiding the use of related therapeutics, the level of generic competition and the availability of reimbursement from government and other third party payors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours. In addition, our ability to compete may be affected because in many cases insurers or other third party payors seek to encourage the use of generic products. There are many generic products currently on the market for the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our therapeutic product candidates are approved, we expect that they will be priced at a significant premium over competitive generic products.

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The most common methods of treating patients with cancer are surgery, radiation and drug therapy, including chemotherapy and targeted drug therapy. As discussed under " Cancer Solid Tumor Market," there are a variety of available drug therapies marketed for solid tumors. In many cases, these drugs are administered in combination to enhance efficacy. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis, including the active ingredients in MM-398 and MM-302. Many of these approved drugs are well established therapies and are widely accepted by physicians, patients and third party payors. In general, although there has been considerable progress over the past few decades in the treatment of solid tumors and the currently marketed therapies provide benefits to many patients, these therapies all are limited to some extent in their efficacy and frequency of adverse events, and none of them are successful in treating all patients. As a result, the level of morbidity and mortality from solid tumor cancers remains high.

In addition to the marketed therapies highlighted under " Cancer Solid Tumor Market," there are also a number of products in late stage clinical development to treat solid tumors. These products in development may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies. As a result, they may provide significant competition for any of our product candidates for which we obtain market approval.

Collaboration and License Agreements

We are party to a number of collaboration agreements for the development and commercialization of our product candidates and license agreements under which we license patents, patent applications and other intellectual property. We consider the following collaboration and license agreements to be material to our business.

Sanofi

In September 2009, after MM-121 entered Phase 1 clinical development, we entered into a license and collaboration agreement with Sanofi for the development and commercialization of MM-121. Under the agreement, we granted Sanofi an exclusive, worldwide, royalty-bearing right and license, with the right to grant sublicenses, under our patent rights and know-how to develop and commercialize the monoclonal antibody MM-121 and an MM-121 companion diagnostic. We retained the right, but not the obligation, to participate in the clinical development of MM-121 through Phase 2 proof of concept for each indication and final decision making authority over the conduct of the trials that we conduct, subject to our having the necessary capabilities and resources to conduct those trials and subject to the trials we conduct having been approved by Sanofi as part of the global development plan for MM-121. Sanofi is responsible for using commercially reasonable efforts thereafter to develop, obtain regulatory approvals for and, following regulatory approval, commercialize MM-121 and a companion diagnostic in each of the United States, Europe and Japan. We also retained an option to co-promote MM-121 in the United States.

Under the agreement, Sanofi paid us a non-refundable upfront license fee of $60 million. Sanofi is also responsible for all development and manufacturing costs under the collaboration. In addition, we could receive under the agreement up to an aggregate of $410 million from Sanofi upon the achievement of specified development and regulatory milestones and an additional $60 million based on the achievement of specified sales milestones. We have received $25 million to date based on our achievement of three clinical milestones. Under the agreement, we are entitled to tiered, escalating royalties beginning in the sub-teen double digits based on net sales of MM-121 in the United States and beginning in the high single digits based on net sales of MM-121 outside the United States. In general, Sanofi's obligation to pay us royalties continues on a product-by-product and country-by-country basis until the latest of the expiration of the patent rights covering the product in such country, the expiration of all data and regulatory exclusivity applicable to the product in such country or ten

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years after the first commercial sale of the product in such country. If we co-promote MM-121 in the United States, we will be responsible for paying our sales force costs and a specified percentage of direct medical affairs, marketing and promotion costs for MM-121 in the United States and will be eligible to receive tiered, escalating royalties beginning in the high teens based on net sales of MM-121 in the United States. We are also entitled to an increase in the royalty rate on a product-by-product and country-by-country basis if a diagnostic product is actually used in the treatment of solid tumor indications with a particular therapeutic product.

Under the agreement, we are obligated to pay all licensing costs for specified third party patent rights that we or Sanofi may in the future license for the development and commercialization of MM-121. The third party patent rights for which we are required to pay all licensing costs consist of the patent rights that are the subject of two European Patent Office opposition proceedings and related counterparts worldwide. See Item 3. Legal Proceedings in this Annual Report on Form 10-K for more information. We share the licensing costs for other third party patent rights that we or Sanofi have licensed or may in the future license for the development and commercialization of MM-121 through specified deductions that Sanofi is permitted to take against the royalties Sanofi pays to us. The third party patent rights for which we share the costs with Sanofi include rights that we have licensed from Dyax Corp., or Dyax, the U.S. Public Health Service and Selexis SA, as described in more detail below.

A joint steering committee comprised of an equal number of representatives from each of Sanofi and us is responsible for reviewing and approving the global development plan for MM-121, including all budgets relating to development activities we conduct, and overseeing the parties' development and commercialization activities with respect to MM-121. The joint steering committee also oversees a joint development committee responsible for overseeing the progress of the development program. In general, Sanofi has final decision making authority over matters on which the joint steering committee deadlocks, following escalation to designated executive officer representatives of the parties, with the exception of our retained decision making authority over the conduct of clinical trials that that we conduct in accordance with the global development plan. If necessary and at a time to be mutually agreed by the parties, we and Sanofi have agreed to form a commercialization committee, also to be overseen by the joint steering committee, that will be responsible for overseeing co-promotion activities in the United States and serving as a forum for communication between the parties regarding worldwide commercialization matters for MM-121.

Sanofi has agreed that, subject to limited exceptions, until the second anniversary of the closing of our initial public offering of common stock, or IPO, neither Sanofi nor any of its affiliates will (1) effect or seek, initiate, offer or propose to effect, or cause or participate in any way, advise or assist any other person to effect or seek, initiate, offer or propose to effect or cause or participate in, any acquisition of any of our securities or assets, any tender or exchange offer, merger, consolidation or other business combination involving us, any recapitalization, restructuring, liquidation, dissolution or other extraordinary transaction with respect to us or any solicitation of proxies or consents to vote any of our voting securities; (2) form, join or in any way participate in a group with respect to any of our securities; (3) otherwise act, alone or in concert with others, to seek to control or influence our management, board of directors or policies, except as contemplated by our collaboration agreement; (4) take any action which would reasonably be expected to force us to make a public announcement regarding the foregoing; or (5) enter into any agreements, discussions or arrangements with any third party with respect to any of the foregoing. Notwithstanding these limitations, we granted a waiver allowing Sanofi to purchase up to 6,300,000 shares of our common stock.

If not terminated earlier, the agreement will expire upon expiration of all royalty and other payment obligations of Sanofi under the agreement. Either party may terminate the agreement in the event of an uncured material breach by the other party. Sanofi also may terminate the agreement for its convenience upon 180 days' prior written notice. In addition, we may terminate the agreement if Sanofi challenges or supports any challenge of our licensed patent rights.

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In June 2012, we entered into a right of review agreement with Sanofi pursuant to which, if we determine to enter into negotiations with a third party regarding any license, option, collaboration, joint venture or similar transaction involving any therapeutic or companion diagnostic product candidate in our pipeline, we will notify Sanofi of such opportunity. Following such notice, Sanofi will have a specified period of time to review the opportunity and determine whether to exercise an additional right to exclusively negotiate an agreement with us with respect to such opportunity for a specified period of time. If Sanofi does not exercise such right of negotiation, we may enter into negotiations with third parties with respect to the opportunity, provided that we may only enter into an agreement with a third party with respect to those countries that were initially offered to Sanofi. On the other hand, if Sanofi does exercise such right of negotiation but we and Sanofi do not reach a mutually acceptable agreement during the negotiation period, we may enter into negotiations with third parties with respect to the opportunity, provided that we may not enter into an agreement within a specified period of time following the end of the negotiation period if either (i) the agreement involves countries that were not previously offered to Sanofi or (ii) the terms and conditions of such agreement are materially more favorable to the third party than what was previously offered by Sanofi. If we propose to enter into any third party agreement described in the provisos of the preceding two sentences, we must first offer the same terms and conditions to Sanofi. In addition, if we intend to spin out certain of our research and development activities to a newly established, partially owned subsidiary, we will notify Sanofi prior to the initial fundraising for such spin-out. Following such notice, Sanofi will be entitled to review the proposed investment terms, although the final terms and participants of such investment will be determined solely by the board of directors of the spin-out. The right of review terminates on April 1, 2017.

PharmaEngine

In May 2011, we entered into an assignment, sublicense and collaboration agreement with PharmaEngine. Under the agreement, PharmaEngine assigned to us its rights and obligations under a 2005 agreement with Hermes BioSciences, Inc., or Hermes, to develop and commercialize MM-398 in Europe and certain countries in Asia. Through our acquisition of Hermes in 2009, we hold the rights to MM-398 in North America and the rest of the world. PharmaEngine also granted to us an exclusive right and license, with the right to sublicense, under PharmaEngine technology and rights to develop and commercialize MM-398 worldwide outside of Taiwan. We granted to PharmaEngine a paid-up, royalty free, exclusive right and license under our technology and rights to develop and commercialize MM-398 in Taiwan.

Under the agreement, we have paid PharmaEngine a $10 million upfront license fee and a $5 million milestone payment. In addition, PharmaEngine is eligible to receive up to an aggregate of $205 million from us upon the achievement of specified development, regulatory and annual net sales milestones. Under the agreement, PharmaEngine is entitled to tiered royalties based on net sales of MM-398 in Europe and certain countries in Asia. The royalty rates under the agreement range from high single digits up to the low teens as a percentage of our net sales of MM-398 in these territories. Our obligation to pay royalties to PharmaEngine continues on a country-by-country basis until the later of ten years after the first commercial sale of MM-398 in such country and May 2, 2024. We are responsible for the development and commercialization, and all related costs and expenses, of MM-398 in all countries except Taiwan, where PharmaEngine retains the right to develop and commercialize MM-398 at its expense. Each party has agreed to use commercially reasonable efforts to develop, in accordance with a development plan, and commercialize MM-398 in its respective territory. We also have a diligence obligation to initiate a second Phase 3 clinical trial of MM-398 in a different solid tumor indication within a timeframe specified in the agreement.

Multiple executive committees were formed under the agreement, each comprised of an equal number of representatives from each party. The steering committee is responsible for reviewing and

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approving changes to the development plan, providing overall strategic direction with respect to development of MM-398 under the development plan and overseeing other committees. The steering committee is also responsible for resolving any disputes arising under the agreement at the steering committee or that are referred to it by any of the other committees. If a matter is unresolved by the steering committee, it may be referred for resolution to executive officers from both companies. We have final decision making authority on any such matter not resolved by the executive officers that relates to the worldwide development of MM-398 or commercialization of MM-398 outside of Taiwan. The development committee is responsible for recommending to the steering committee changes to the development plan and overseeing the progress of the development program and monitoring the parties' compliance with their respective obligations under the development plan.

Upon expiration of all royalty and other payment obligations due to PharmaEngine under this agreement on a country-by-country basis, the licenses granted under the agreement will be deemed to be perpetual, fully paid-up and irrevocable with respect to the licensed product in such country. Either party may terminate the agreement in the event of an uncured material breach by the other party. In addition, at any time after May 2013, we may terminate the agreement for convenience upon 90 days' prior written notice. If PharmaEngine terminates this agreement in its entirety or with respect to Europe or the Asian territories because of our material breach, or if we terminate the agreement for convenience with respect to Europe or the Asian territories, then we are required to grant PharmaEngine a license under our technology and rights with respect to MM-398 in Europe or the Asian territories, as applicable, and PharmaEngine is required to pay us single-digit royalties for net sales of MM-398 in such territories.

Dyax

In January 2007, we entered into an amended and restated collaboration agreement with Dyax, which superseded a prior collaboration agreement with Dyax that we entered into in December 2005. Under this collaboration agreement, Dyax uses its proprietary phage display technology to identify antibodies that bind to targets of interest to us as therapeutics or diagnostics. Further, Dyax has granted to us a worldwide, non-exclusive, royalty free right to use and make any and all of the antibodies identified by Dyax for certain research purposes. In order to clinically develop or commercialize any such antibody, however, we must obtain an additional product license from Dyax on a target-by-target basis. We have the option to obtain one or more product licenses on terms set forth in the collaboration agreement, subject to limitations on the availability of each such product license under an agreement between Dyax and Cambridge Antibody Technologies, which has merged with MedImmune, LLC and is now owned by AstraZeneca PLC.

As consideration for the grant of the initial research license, we paid Dyax a research fee based on the total estimated full time equivalent researchers that were required to conduct the research plan and a fee for achieving certain technical milestones. If we elect to obtain a product license with respect to any therapeutic or diagnostic target, we are required to pay to Dyax an additional upfront license fee for the applicable antibody. We also will be required to make additional maximum aggregate development and regulatory milestone payments of $16.2 million for therapeutic products and maximum aggregate regulatory milestone payments of $1.0 million for diagnostic products directed to selected targets. In addition, Dyax is entitled to mid single digit royalties based on net sales of products covered by any product license that we obtain from Dyax. Our obligation to pay royalties to Dyax continues on a product-by-product and country-by-country basis until the later of a specified number of years after the first commercial sale of the product in such country and the expiration of the patent rights covering the product in such country. MM-121 and a component of MM-141 were identified under this agreement, and we have obtained the required target licenses from Dyax by exercising our product license options and paying the applicable license fees. We are obligated to use commercially

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reasonable efforts to develop and commercialize the antibodies for which we obtain a commercial license.

This agreement will remain in effect, unless terminated earlier, for so long as we or any of our affiliates or sublicensees continue to develop or commercialize products that remain royalty-bearing under the agreement. Either party may terminate the agreement in the event of an uncured material breach by the other party. We also may terminate the agreement in its entirety or on a product-by-product basis at any time upon 90 days' prior written notice.

Adimab

In November 2009, we entered into a collaboration agreement with Adimab LLC, or Adimab, to allow us to evaluate the utility of using antibodies identified during the collaboration as therapeutics or diagnostics. Under the agreement, Adimab granted to us a worldwide, non-exclusive, royalty free right to use materials provided by Adimab to perform non-clinical research during the evaluation term. Adimab also granted to us an option to obtain the assignment of specified patent rights claiming the selected antibodies and a license under Adimab's background patent rights and know-how for the development and commercialization of the antibodies.

As partial consideration for the research license grant, we paid Adimab a technology access fee at the time of grant, research fees based on the total estimated full time equivalent researchers that were required to conduct the research plan and a fee for achieving certain technical milestones. We have exercised our assignment and license option by paying Adimab a fee of $1.0 million. In addition, we are required to pay Adimab up to an aggregate of $13.5 million per therapeutic area, for the first four therapeutic areas, upon achievement of specified development and regulatory milestones, of which we have paid $1.5 million with respect to the first therapeutic area, and up to an aggregate of $500,000 per diagnostic product upon the achievement of specified regulatory milestones. In addition, Adimab is entitled to mid single digit royalty payments based on net sales of therapeutic products and diagnostic products arising from the collaboration. Our obligation to pay royalties to Adimab continues on a product-by-product and country-by-country basis until the later of a specified number of years after the first commercial sale of the product in such country and the expiration of the patent rights covering the product in such country, provided that the royalty term will not extend beyond a specified number of years after the first commercial sale of the product in such country. We are obligated to use commercially reasonable efforts to develop and commercialize at least one product that incorporates the antibodies for which we exercised our assignment and license option in each of the United States, Europe and Japan. MM-151 was generated under this agreement.

The term of the agreement expires on a country-by-country basis on the earliest date after which no payments are due to Adimab, unless earlier terminated. Either party may terminate the agreement in the event of an uncured material breach by the other party. In addition, we may terminate the agreement at any time upon 90 days' prior written notice.

University of California

2005 agreement

In March 2005, we entered into a license agreement with The Regents of the University of California, or the Regents. Under the agreement, the Regents granted to us a royalty-bearing right and license in the United States and other countries where the Regents have the right to grant the license under certain patent rights and rights in biological materials to develop and commercialize products for therapeutic or diagnostic use in humans that are covered by the licensed patents. Licensed products under this agreement include MM-111. This license is exclusive with respect to certain patents, including some relevant to MM-111, and non-exclusive with respect to other patents and biological materials. The agreement requires that we diligently pursue the development, manufacture and

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commercialization of licensed products. In addition, we are required to meet specific development, regulatory and commercialization milestones within timeframes specified in the agreement. We have sole responsibility for the development and commercialization of products under the licensed technology. However, the agreement provides that the Regents may require us to sublicense our exclusive rights for the application or use of licensed products covered by any exclusively licensed technology that we are not currently pursuing.

We are required to pay to the Regents an annual license maintenance fee of between $20,000 and $30,000 until the first commercial sale of a licensed product and are responsible for all development costs. In addition, we are required to pay to the Regents up to an aggregate of $725,000 per therapeutic product, other than the second therapeutic product, for which we are responsible for up to an aggregate of $906,250, based on the achievement of specified development and regulatory milestones. The Regents are also entitled to royalties in the low single digits based on net sales of products covered by the licensed technology. A minimum annual royalty is due to the Regents commencing in the earlier of the year of the first commercial sale of a licensed product or 2015. The minimum annual royalty increases from $100,000 in the first year it is payable to $500,000 in the fifth year and thereafter for the life of the patents. If we sublicense the rights granted to us under the licensed technology to a third party, then we are also obligated to pay to the Regents a portion of the sublicensing income related to the licensed technology.

If not terminated earlier, this agreement terminates upon the later of nine years from the market introduction of the last licensed product that contains the licensed biological materials or the expiration of all patent rights licensed under this agreement. At such time, we will have a perpetual, fully paid, world-wide, non-exclusive license. The Regents may terminate the agreement in the event of an uncured material breach by us. We may terminate the agreement on a country-by-country basis at any time upon 60 days' prior written notice.

2000 agreement

In November 2000, we entered into a separate exclusive license agreement with the Regents. Under the agreement, the Regents granted us a royalty-bearing world-wide right and license under certain patent rights for the development and commercialization of products that are covered by the licensed patent rights, including MM-302. The agreement requires that we diligently pursue the development, manufacture and commercialization of licensed products. In addition, we are required to meet specified development, regulatory and commercialization milestones within timeframes specified in the agreement. We have the sole responsibility for the development and commercialization of products under the licensed technology.

We are required to pay to the Regents an annual license maintenance fee of $95,000 until the first commercial sale of a licensed product. We also are responsible for all development costs and have agreed to spend a minimum of $150,000 per year for such costs. In addition, we are responsible for up to an aggregate of $700,000 per product upon the achievement of specified development and regulatory milestones. The Regents are also entitled to royalties in the low single digits based on net sales of products covered by the licensed technology. If we sublicense the rights granted to us under the licensed technology to a third party, then we are also obligated to pay to the Regents a portion of the sublicensing income related to the licensed technology.

If not terminated earlier, this agreement terminates upon the expiration or abandonment of all patents licensed under this agreement. The Regents may terminate the agreement in the event of an uncured material breach by us. We may terminate the agreement on a country-by-country basis at any time upon 60 days' prior written notice.

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U.S. Public Health Service

In February 2008, we entered into a commercial license with the U.S. Public Health Service, a division of the U.S. Department of Health and Human Services, for non-exclusive rights in the United States to patents related to ErbB3 and ErbB3 antibodies associated with MM-121, MM-111 and MM-141. Under the agreement, we may be required to make aggregate development and regulatory milestone payments of up to $6.0 million per therapeutic licensed product and pay low single digit royalties on net sales of licensed products. The term of the agreement extends until the expiration of the licensed patent rights, which is 2016.

Selexis

In June 2008, we entered into a commercial license with Selexis SA for non-exclusive rights to technology for use in the manufacture of certain biologic products, including each of our six most advanced product candidates, other than MM-398. Under this agreement, we are required to make aggregate milestone payments of up to €1.0 million per licensed product and pay royalties of less than one percent on net sales of licensed products. The obligation to pay royalties with respect to each product sold in a country continues until the expiration of the patent rights covering the product in such country.

Intellectual Property

We aggressively strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining patents intended to cover our products and compositions, their methods of use and processes for their manufacture, as well as our diagnostic and drug discovery technologies 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, such as our proprietary network modeling programs and large scale protein and liposome production methods.

Our success will significantly depend on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, 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, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

We seek to obtain domestic and international patent protection, and endeavor to promptly file patent applications for new commercially valuable inventions once the experimental data necessary for an application become available. We generally file international applications under the Patent Cooperation Treaty, or PCT, within one year after the filing of a U.S. provisional application.

As of January 31, 2013, we owned 15 issued U.S. patents and one allowed U.S. patent application, two issued patents in Europe, 14 issued patents and two allowed patent applications in other jurisdictions, as well as 30 pending U.S. provisional and non-provisional patent applications and 175 pending foreign patent applications in Europe and 42 other jurisdictions. As of January 31, 2013, we also co-owned 32 pending foreign patent applications with Sanofi, as well as one U.S. non-provisional and seven foreign patent applications with Silver Creek. As of January 31, 2013, we had licenses to 39 U.S. patents and seven pending U.S. patent applications, as well as numerous foreign counterparts to many of these patents and patent applications. Of these licensed patents and patent applications, we license the majority on an exclusive basis, with the rest licensed non-exclusively to us. The exclusive licenses are, in some cases, limited to certain technical fields, for example for medical and diagnostic purposes.

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The patent portfolios for our six most advanced product candidates as of January 31, 2013 are summarized below.

MM-398

Our MM-398 patent portfolio is wholly owned by us and includes two issued U.S. patents and two pending U.S. patent applications covering the composition of and methods of making and using MM-398, all of which expire or, if issued, will expire in 2025 except for one U.S. patent that expires in 2028. Related international patent applications have issued or been allowed in four countries and are pending in Europe and a number of other countries. These international patents and patent applications, if issued, will expire in 2025. Our MM-398 portfolio further includes one pending U.S. provisional dosage and administration patent application.

MM-121

Our MM-121 patent portfolio is wholly owned by us, with the exception of:

- five PCT method of use applications that are eligible for worldwide filings, along with 27 related pending foreign applications, all of which are co-owned with Sanofi and, if issued, will expire in 2032 and 2033; and

- one family of U.S. patents broadly covering anti-ErbB3 antibodies, the last of which will expire in 2016 that are licensed non-exclusively from the U.S. Public Health Service, a division of the U.S. Department of Health and Human Services.

Our wholly owned MM-121 portfolio includes a U.S. composition of matter patent, an issued foreign patent, two related pending U.S. patent applications and related international patent applications pending in Europe and 24 other jurisdictions that expire or, if issued, will expire in 2028. Pending method of use and diagnostic patents in this portfolio also include one U.S. provisional patent application and three PCT applications that are eligible for worldwide filings that, if issued, will expire in 2032 and 2033, and three U.S. patent applications and related pending foreign applications in Europe and 16 other jurisdictions that, if issued, will expire in 2029.

MM-111

Our MM-111 patent portfolio includes three wholly owned, pending U.S. patent applications covering the composition of, and method of use and diagnostics for, MM-111 that, if issued, will expire in 2029 and 2031. This portfolio also includes four provisional U.S. applications that may be used to establish non-provisional applications that, if issued, will expire in 2033. For three of these four U.S. provisional applications, we intend to submit a single consolidated worldwide filing. This portfolio also includes 22 related patent applications pending in Europe and a number of other jurisdictions that, if issued, will expire between 2028 and 2032.

In addition, this portfolio includes the following patents licensed from the Regents:

- an exclusively licensed family of patents and patent applications that expire or, if issued, will expire in 2023, including three issued U.S. composition of matter patents, a pending U.S. and European divisional application, an issued European composition of matter patent that has been validated in 15 European Patent Organization countries, two issued foreign patents and related applications pending in a number of other countries; and

- a non-exclusively licensed family of patents and a patent application that expire or, if issued, will expire in 2016, including granted U.S. and European composition of matter patents and an application pending in Canada.

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MM-302

Our MM-302 patent portfolio includes one wholly owned PCT dosage and administration patent application eligible for worldwide filings that, if issued, will expire in 2031, and one U.S. provisional combination therapy application that may be used to establish non-provisional applications that, if issued, will expire in 2033. This portfolio also includes the following exclusively licensed issued U.S. patents:

six composition of matter patents that expire between 2014 and 2019; and

one method of use patent that expires in 2019.

In addition, this portfolio includes the following exclusively licensed European patents:

a composition of matter patent that expires in 2019;

a composition of matter and method patent that expires in 2019; and

a composition of matter patent that expires in 2014.

Our licensed MM-302 patent portfolio further includes several foreign composition of matter patents and patent applications that expire or, if issued, will expire between 2014 and 2017.

All of the licensed patents and patent applications related to MM-302 are licensed from the Regents.

MM-151

Our MM-151 patent portfolio is wholly owned, and includes one PCT application covering compositions, methods of use and diagnostics that is eligible for worldwide filings that, if issued, will expire in 2032. This portfolio also consists of one pending U.S. composition of matter and method of use patent application and eight related pending foreign applications that, if issued, will expire in 2031, and one U.S. and related European patent diagnostic patent application that, if issued, will expire in 2032.

MM-141

Our MM-141 patent portfolio is wholly owned, and consists of two pending patent applications. One of these pending applications covers the principle and methods of co-targeting IGF-1R and ErbB3 in human disease and is pending in the US, Europe, Canada, Australia and Japan, and if issued will expire no sooner than 2030. The other pending application is an international application that remains eligible for worldwide filing in all PCT countries and covers compositions, methods of use, disease indications and drug combination regimens related to MM-141, and if issued will expire no sooner than 2032.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug, biological product or medical device approved pursuant to a pre-market approval, or PMA, may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. The length of the patent term extension is related to the length of time the drug is under regulatory review while the patent is in force. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration date set for the patent. Patent extension cannot extend the remaining term of a

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patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be granted an extension and only those claims reading on the approved drug are extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our product candidates receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those products, depending upon the length of the clinical trials for each drug and other factors, including those involved in the filing of a biologics license application, or BLA, or a new drug application, or NDA.

We are currently engaged in two ongoing opposition proceedings to European patents in the European Patent Office to narrow or invalidate the claims of patents owned by third parties. For more information, see Item 3. Legal Proceedings in this Annual Report on Form 10-K. We have obtained favorable interim decisions in both oppositions, which are now under appeal. The ultimate outcome of these oppositions remains uncertain. We are also aware of issued or pending counterparts to some of these European patents in the United States that may be relevant to our development and commercialization of MM-121. In addition, we are aware of issued U.S. patents held by Genentech, Inc., or Genentech, broadly covering methods of producing certain types of recombinant antibodies and related compositions for antibody production that may be relevant to our development and commercialization of MM-121, MM-151and MM-141.

We rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Silver Creek

In August 2010, we acquired 12,000,000 shares of Series A preferred stock of Silver Creek, a newly formed company, in exchange for our grant to Silver Creek of technology licenses. We granted to Silver Creek a royalty free license under certain antibody growth factor patent rights to develop and commercialize products covered by the licensed patent rights. This license is exclusive to Silver Creek for therapeutic or diagnostic use in humans for the promotion of organ regeneration and co-exclusive with us for all other uses. We also granted to Silver Creek royalty free, non-exclusive licenses under certain patent rights and know-how to use certain of our technologies for research and development purposes. Either party may terminate the agreement in the event of an uncured material breach by the other party.

In August and December 2010, Silver Creek issued and sold an aggregate of 4,189,904 additional shares of its Series A preferred stock at a price per share of $1.00 to other investors for an aggregate purchase price of $4,189,904. In addition, on December 21, 2012, Silver Creek entered into a Note Purchase Agreement pursuant to which it issued convertible notes to various lenders, which did not include us, in aggregate principal amounts of $1.6 million on December 21, 2012 and of $280,000 on February 11, 2013. The convertible notes bear interest at 6% and will mature and convert, along with accrued interest, into Silver Creek Series A preferred stock on December 31, 2013. If at any time prior to maturity Silver Creek enters into a qualifying equity financing, defined as a sale or series of related sales of equity securities prior to the maturity date and resulting in at least $4.0 million of gross proceeds, the notes will automatically convert into that financing at a 25% discount. As of January 31,

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2013, we owned approximately 74% of the outstanding capital stock of Silver Creek, making Silver Creek a majority owned subsidiary of ours.

Silver Creek is applying our Network Biology approach to the discovery and development of innovative therapeutics in the field of regenerative medicine. In the future, we may consider forming additional businesses or business units to apply our Network Biology approach to multiple additional disease areas outside the oncology field. We expect to do so in some cases, as with Silver Creek, through the establishment of separately funded companies.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, manufacture, including any manufacturing changes, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, import and export of pharmaceutical products, biological products and medical devices, such as those we are developing.

United States drug and biological product approval process

In the United States, the FDA regulates drugs and biological products under the Federal Food, Drug, and Cosmetic Act, or FDCA, the Public Health Service Act, or PHSA, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of untitled or warning letters, product recalls, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, civil penalties and criminal prosecution.

The process required by the FDA before a drug or biological product may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug or biological product for each indication;
- submission to the FDA of an NDA or BLA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the NDA or BLA.

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We expect that all of our clinical product candidates, other than MM-398, will be subject to review as biological products under BLA standards. We expect that MM-398 will be subject to review as a drug under NDA standards. MM-302 contains both drug and biological components. We believe that this combination product will be subject to review as a biological product, pursuant to a BLA. However, it is possible that the FDA could consider MM-302 subject to review pursuant to an NDA.

Preclinical studies

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as *in vitro* and animal studies to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed protocol for clinical studies, among other things, to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical trials

Clinical trials involve the administration of the investigational new drug to human subjects healthy volunteers or patients under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions. An IRB must operate in compliance with FDA regulations. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their ClinicalTrials.gov website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

Phase 1: The drug or biological product is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, side effects associated with increasing doses, pharmacological action , absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.

Phase 2: The drug or biological product is administered to a limited patient population to identify common adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

Phase 3: The drug or biological product is administered to an expanded patient population in adequate and well-controlled clinical trials, typically at geographically dispersed clinical trial

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sites, to generate sufficient data to statistically confirm the efficacy and safety of the product for approval, to permit the FDA to evaluate the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Disclosure of clinical trial information

Sponsors of clinical trials of FDA regulated products, including drugs, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public on the ClinicalTrials.gov website as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Marketing approval

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's pharmacology chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA or BLA requesting approval to market the product for one or more indications. FDA approval of the NDA or BLA is required before marketing of the product may begin in the United States. Under federal law, the submission of most NDAs and BLAs is additionally subject to a substantial application user fee, currently exceeding $1,958,000, and the sponsor of an approved NDA or BLA is also subject to annual product and establishment user fees, currently exceeding $98,000 per product and $526,000 per establishment. These fees are typically increased annually.

The FDA conducts a preliminary review of all NDAs and BLAs within the first 60 days after receipt before accepting them for filing based on the agency's threshold determination that they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA or BLA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review of NDAs and BLAs. Most such applications for non-priority products are reviewed within ten to twelve months, and most applications for priority review products, that is, drugs and biologics that the FDA determines represent a significant improvement over existing therapy, are reviewed in six to eight months. The review process may be extended by the FDA for three additional months to consider certain late-submitted information or clarification regarding information already provided in the submission. The FDA may also refer applications for novel drugs or biological products or products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

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Before approving an NDA or BLA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. In addition, before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP and integrity of the clinical data submitted.

The testing and approval process requires substantial time, effort and financial resources, and each may take many years to complete. Data obtained from clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all. We may encounter difficulties or unanticipated costs in our efforts to develop our product candidates and secure necessary governmental approvals, which could delay or preclude us from marketing our products.

After the FDA's evaluation of the NDA or BLA and inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the drug or biological product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

Even if the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, some types of changes to the approved product, such as changes in indications, manufacturing changes and labeling, are subject to further testing requirements and FDA review and approval.

Fast track designation

The FDA is required to facilitate the development and expedite the review of drugs and biologics that are intended for the treatment of a serious or life-threatening disease or condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the condition. Under the fast track program, the sponsor of a new drug or biologic candidate may request the FDA to designate the product for a specific indication as a fast track product concurrent with or after the filing of the IND for the product candidate. The FDA must determine if the product candidate qualifies for fast track designation within 60 days after receipt of the sponsor's request.

In addition to other benefits, such as the ability to use surrogate endpoints and have greater interactions with the FDA, the FDA may initiate review of sections of a fast track product's NDA or BLA before the application is complete. This rolling review is available if the applicant provides and the FDA approves a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the NDA or BLA is submitted. In addition, the fast track designation

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may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Priority review

Under FDA policies, a product candidate may be eligible for priority review, or review within a six to eight month time frame from the time a complete application is accepted for filing. Products regulated by the FDA's Center for Drug Evaluation and Research, or CDER, are eligible for priority review if they provide a significant improvement compared to marketed products in the treatment, diagnosis or prevention of a disease. Products regulated by the FDA's Center for Biologics Evaluation and Research are eligible for priority review if they provide a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention of a serious or life-threatening disease. A fast track designated product candidate would ordinarily meet the FDA's criteria for priority review.

Accelerated approval

Under the FDA's accelerated approval regulations, the FDA may approve a drug or biologic for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit. In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

Orphan drugs

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs or biologics intended to treat a rare disease or condition, which is generally defined as a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the generic identity of the drug or biologic and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first NDA or BLA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug or biologic for the same orphan indication, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA or BLA application user fee.

Pediatric information

Under the Pediatric Research Equity Act of 2003, an NDA, BLA or supplement to an NDA or BLA must contain data that are adequate to assess the safety and effectiveness of the drug or biological product for the claimed indications in all relevant pediatric subpopulations, and to support

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dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan drug designation.

The Hatch-Waxman Act

Abbreviated new drug applications

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent whose claims cover the applicant's product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application, or ANDA. Generally, an ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct or submit results of preclinical or clinical tests to prove the safety or effectiveness of their drug product, other than the requirement for bioequivalence testing. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book. Specifically, the applicant must certify that:

the required patent information has not been filed;

the listed patent has expired;

the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or

the listed patent is invalid or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid is called a Paragraph IV certification. If the ANDA applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA also will not be approved until any applicable non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired. Federal law provides a period of five years following approval of a drug containing no previously approved active ingredients during which ANDAs for generic versions of those drugs cannot be received by the FDA unless the submission contains a Paragraph IV challenge to a listed patent, in which case the submission may be made four years following the original product approval. If there is

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no listed patent in the Orange Book, there may not be a Paragraph IV certification, and thus, no ANDA may be filed before the expiration of the exclusivity period. Federal law provides for a period of three years of exclusivity following approval of a listed drug that contains previously approved active ingredients but is approved in a new dosage form, route of administration or combination, or for a new use, the approval of which was required to be supported by new clinical trials conducted by or for the sponsor, during which the FDA cannot grant effective approval of an ANDA based on that listed drug. Under the Best Pharmaceuticals for Children Act, federal law also provides that periods of patent and non-patent marketing exclusivity listed in the Orange Book for a drug may be extended by six months if the NDA sponsor agrees to conduct and report on pediatric studies identified by the FDA in a written request within the statutory timeframes. Applications under the BPCA are treated as priority applications, with all the benefits that designation confers.

Patent term extension

After NDA approval, owners of relevant drug patents may apply for up to a five year patent term extension. The allowable patent term extension is calculated as half of the drug's testing phase, based on the time between IND application and NDA submission, and all of the review phase, based on the time between NDA submission and approval up to a maximum of five years. The time can be shortened if the FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years.

For patents that might expire during the application phase, the patent owner may request an interim patent term extension. An interim patent term extension increases the patent term by one year and may be renewed up to four times. For each interim patent term extension granted, the post-approval patent term extension is reduced by one year. The director of the United States Patent and Trademark Office must determine that approval of the drug covered by the patent for which a patent term extension is being sought is likely. Interim patent term extensions are not available for a drug for which an NDA has not been submitted.

Section 505(b)(2) new drug applications

Most drug products obtain FDA marketing approval pursuant to an NDA or an ANDA. A third alternative is a special type of NDA, commonly referred to as a Section 505(b)(2) NDA, which enables the applicant to rely, in part, on the FDA's previous approval of a similar product, or published literature, in support of its application.

505(b)(2) NDAs often provide an alternate path to FDA approval for new or improved formulations or new uses of previously approved products. Section 505(b)(2) permits the filing of an NDA 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. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. As a result, approval of a 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a

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Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Combination products

A combination product is a product comprised of (i) two or more regulated components (i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic) that are physically, chemically, or otherwise combined or mixed and produced as a single entity; (ii) two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products; (iii) a drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where, upon approval of the proposed product, the labeling of the approved product would need to be changed (e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose); or (iv) any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

The FDA is divided into various branches, or Centers, by product type. Different Centers typically review drug, biologic, or device applications. In order to review an application for a combination product, the FDA must decide which Center should be responsible for the review. FDA regulations require that the FDA determine the combination product's primary mode of action, or PMOA, which is the single mode of a combination product that provides the most important therapeutic action of the combination product. The Center that regulates that portion of the product that generates the PMOA becomes the lead evaluator. If there are two independent modes of action, neither of which is subordinate to the other, the FDA makes a determination as to which Center to assign the product based on consistency with other combination products raising similar types of safety and effectiveness questions or to the Center with the most expertise in evaluating the most significant safety and effectiveness questions raised by the combination product. When evaluating an application, a lead Center may consult other Centers but still retain complete reviewing authority, or it may collaborate with another Center, by which the lead Center assigns review of a specific section of the application to another Center, delegating its review authority for that section. Typically, the FDA requires a single marketing application submitted to the Center selected to be the lead evaluator, although the agency has the discretion to require separate applications to more than one Center. One reason to submit multiple evaluations is if the applicant wishes to receive some benefit that accrues only from approval under a particular type of application, like new drug product exclusivity. If multiple applications are submitted, each application may be evaluated by a different lead Center.

Biosimilars law

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, amended the PHSA to create a new licensure framework for biosimilar products, which could ultimately subject our biological products to competition. Under the BPCIA, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a referenced, branded biologic product. Previously, there had been no licensure pathway for such biosimilar or interchangeable products. For purposes of the BPCIA, a reference product is defined as the single biological product licensed under a full BLA against which a biological product is evaluated in an application submitted under a follow-on BLA. Biosimilarity sufficient to reference a prior FDA-approved product requires that there be no differences in conditions of use, route of administration, dosage form, and strength, and no clinically meaningful differences between the biological product and the reference product in

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terms of safety, purity, and potency. Biosimilarity must be shown through analytical studies, animal studies, and at least one clinical study, absent a waiver by the Secretary of the U.S. Department of Health & Human Services. A biosimilar product may be deemed interchangeable with a prior approved product if it meets the higher hurdle of demonstrating that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. No biosimilar or interchangeable products have been approved under the BPCIA to date. Complexities associated with the larger, and often more complex, structures of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation which are still being evaluated by the FDA.

The BPCIA also created a 12-year period of reference product exclusivity, which can be extended to 12½ years with pediatric exclusivity. The 12-year exclusivity period begins on the date of first licensure of the reference product under the PHSA and during which the licensure of a follow-on application for a biosimilar or interchangeable product cannot be made effective. During the first four years (or four and one-half years with pediatric exclusivity) of the 12-year period, an application for a biosimilar or interchangeable version of the reference product cannot be submitted to the FDA.

The BPCIA includes limits on obtaining 12-year reference product exclusivity for certain changes or modifications to the reference product. A separate 12-year reference product exclusivity period does not apply to:

- a BLA supplement for the product that is the reference product;
- a subsequent BLA filed by the same reference product sponsor or manufacturer (or a licensor, predecessor in interest, or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength; or
- a modification to the structure of the biological product that does not result in a change in safety, purity or potency.

The FDA has not yet issued proposed regulations setting forth its interpretation of the BPCIA's exclusivity provisions and it is unclear when the FDA will do so.

In addition to creating a 12-year period of reference product exclusivity, the BPCIA clarifies the interaction of that exclusivity with orphan drug exclusivity, such that the licensure of a biosimilar or interchangeable version of a reference product that was designated and approved as an orphan drug may only occur after the later of the expiration of any applicable seven-year orphan drug exclusivity or the 12-year reference product exclusivity (or seven and one-half years and 12½ years with pediatric exclusivity).

Like pediatric exclusivity applicable to drug products approved under the FDCA, pediatric exclusivity applicable to biological reference products is subject to an exception. Pediatric exclusivity will not apply to either the 12-year reference product or the seven-year orphan drug exclusivity periods if the FDA determines later than nine months prior to the expiration of such period that the study reports a BLA sponsor submitted in response to a written request for pediatric studies met the terms of that request.

Our investigational biological products, if approved, could be considered reference products entitled to 12-year exclusivity. Even if our products are considered to be reference products eligible for exclusivity, another company could market a competing version of any of our biological products if the FDA approves a full BLA for such product containing the sponsor's own preclinical data and data from

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adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product.

The BPCIA also sets forth a complex mechanism for resolving patent disputes that involves a step-wise exchange of information prior to the initiation of a patent infringement lawsuit against a biosimilar or interchangeable product sponsor. Unlike the Hatch-Waxman Act, the BPCIA provides no automatic stay on approval of a biosimilar or interchangeable product application.

Breakthrough therapy designation

The FDA is also required to expedite the development and review of the application for approval of drugs that are intended to treat a serious or life-threatening disease or condition where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. Under the breakthrough therapy program, the sponsor of a new drug candidate may request that the FDA designate the drug candidate for a specific indication as a breakthrough therapy concurrent with, or after, the filing of the IND for the drug candidate. The FDA must determine if the drug candidate qualifies for breakthrough therapy designation within 60 days of receipt of the sponsor's request.

Overview of FDA regulation of companion diagnostics

We are developing *in vitro* and *in vivo* companion diagnostics for use in selecting the patients that we believe will respond to our cancer therapeutics.

FDA officials have indicated that the agency intends to publish guidance that, when finalized, would address issues critical to developing *in vitro* companion diagnostics, such as biomarker qualification, establishing clinical validity, the use of retrospective data, the appropriate patient population and when the FDA will require that the device and the drug be approved simultaneously. The draft guidance issued in July 2011 states that if safe and effective use of a therapeutic depends on an *in vitro* diagnostic, then the FDA generally will require approval or clearance of the diagnostic at the same time that the FDA approves the therapeutic. Although still in draft, this guidance represents the FDA's current practice. The FDA has yet to issue final guidance, and it is unclear when it will do so, or what the scope would be.

The FDA previously has required *in vitro* companion diagnostics intended to select the patients who will respond to the cancer treatment to obtain PMA, simultaneously with approval of the drug or licensure of the biologic. Based on the draft guidance, and the FDA's past treatment of companion diagnostics, we believe that the FDA will require one or more of our *in vitro* companion diagnostics to obtain PMA for our companion diagnostics to identify patient populations suitable for our cancer therapies, such as the *in vitro* companion diagnostic for MM-121. The review of these *in vitro* companion diagnostics in conjunction with the review of our cancer treatments involves coordination of review by CDER and by the FDA's Center for Devices and Radiological Health Office of In Vitro Diagnostics and Radiological Health.

Our *in vivo* companion diagnostics, which are in the form of imaging agents, are regulated as drugs by CDER and, as such, are generally subject to the regulatory requirements applicable to other new drug candidates.

PMA approval pathway

A medical device, including an *in vitro* diagnostic, or IVD, to be commercially distributed in the United States must receive either 510(k) clearance or PMA approval (or be a Class I exempt device that does not require pre-market review) from the FDA prior to marketing. Devices deemed by the FDA to pose the greatest risk, such as life-sustaining, life supporting or implantable devices, or devices

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deemed not substantially equivalent to a previously 510(k) cleared device or a preamendment class III device for which PMA applications have not been called, are placed in Class III requiring PMA approval. The PMA approval pathway requires proof of the safety and effectiveness of the device to the FDA's satisfaction. The PMA approval pathway generally takes from one to three years or even longer from submission of the application.

A PMA application for an IVD must provide extensive preclinical and clinical trial data. Preclinical data for an IVD includes many different tests, including how reproducible the results are when the same sample is tested multiple times by multiple users at multiple laboratories. The clinical data need to establish that the test is sufficiently safe, effective and reliable in the intended use population. In addition, the FDA must be convinced that a device has clinical utility, meaning that an IVD provides information that is clinically meaningful. A biomarker's clinical significance may be obvious, or the applicant may be able to rely upon published literature or submit data to show clinical utility.

A PMA application also must provide information about the device and its components regarding, among other things, device design, manufacturing and labeling. The sponsor must pay an application fee.

As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with Quality System Regulation, or QSR, requirements, which impose elaborate design control, testing, control, documentation and other quality assurance procedures.

Upon submission, the FDA determines if the PMA application is sufficiently complete to permit a substantive review, and, if so, the FDA accepts the application for filing. The FDA then commences an in-depth review of the PMA application. The entire process typically takes one to three years, but may take longer. The review time is often significantly extended as a result of the FDA asking for more information or clarification of information already provided. The FDA also may respond with a not approvable determination based on deficiencies in the application and require additional clinical trials that are often expensive and time-consuming and can substantially delay approval.

During the review period, an FDA advisory committee, typically a panel of clinicians, likely will be convened to review the application and recommend to the FDA whether, or upon what conditions, the device should be approved. Although the FDA is not bound by the advisory panel decision, the panel's recommendation is important to the FDA's overall decision making process.

If the FDA's evaluation of the PMA application is favorable, the FDA typically issues an approvable letter requiring the applicant's agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the manufacturer. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution. Failure to comply with the conditions of approval can result in material adverse enforcement action, including the loss or withdrawal of the approval.

Even after approval of a PMA, a new PMA or PMA supplement may be required in the event of a modification to the device, its labeling or its manufacturing process. Supplements to a PMA often require the submission of the same type of information required for an original PMA, except that the supplement is generally limited to the information needed to support the proposed change from the product covered by the original PMA.

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Clinical trials

A clinical trial is almost always required to support a PMA application.

All clinical studies of investigational devices must be conducted in compliance with the FDA's requirements. If an investigational device could pose a significant risk to patients pursuant to FDA regulations, the FDA must approve an IDE application prior to initiation of investigational use. IVD trials usually do not require an IDE, as the FDA does not judge them to be a significant risk because the results do not affect the patients in the study. However, for a trial where the IVD result directs the therapeutic care of patients with cancer (companion diagnostics), we believe that the FDA would consider the investigation to present significant risk and require an IDE.

An IDE application must be supported by appropriate data, such as laboratory test results, showing that it is safe to test the device in humans and that the testing protocol is scientifically sound. The FDA typically grants IDE approval for a specified number of patients. A nonsignificant risk device does not require FDA approval of an IDE. Both significant risk and nonsignificant risk investigational devices require approval from IRBs at the study centers where the device will be used.

During the trial, the sponsor must comply with the FDA's IDE requirements for investigator selection, trial monitoring, reporting and record keeping. The investigators must obtain patient informed consent, rigorously follow the investigational plan and study protocol, control the disposition of investigational devices and comply with all reporting and record keeping requirements. Prior to granting PMA approval, the FDA typically inspects the records relating to the conduct of the study and the clinical data supporting the PMA application for compliance with applicable requirements.

Although the QSR does not fully apply to investigational devices, the requirement for controls on design and development does apply. The sponsor also must manufacture the investigational device in conformity with the quality controls described in the IDE application and any conditions of IDE approval that the FDA may impose with respect to manufacturing.

Post-market

After a device is on the market, numerous regulatory requirements apply. These requirements include: the QSR, labeling regulations, the FDA's general prohibition against promoting products for unapproved or "off label" uses, the Medical Device Reporting regulation, which requires that manufacturers report to the FDA if their device may have caused or contributed to a death or serious injury or malfunctioned in a way that would likely cause or contribute to a death or serious injury if it were to recur, and the Reports of Corrections and Removals regulation, which requires manufacturers to report recalls and field actions to the FDA if initiated to reduce a risk to health posed by the device or to remedy a violation of the FDCA.

The FDA enforces these requirements by inspection and market surveillance. If the FDA finds a violation, it can institute a wide variety of enforcement actions, ranging from a public warning letter to more severe sanctions such as: fines, injunctions and civil penalties; recall or seizure of products; operating restrictions, partial suspension or total shutdown of production; refusing requests for PMA approval of new products; withdrawing PMA approvals already granted; and criminal prosecution.

Other regulatory requirements

Any drug or biological products manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval.

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The FDA may impose a number of post-approval requirements as a condition of approval of an NDA or BLA. For example, the FDA may require post-marketing testing, including phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. Regulatory approval of oncology products often requires that patients in clinical trials be followed for long periods to determine the overall survival benefit of the drug or biologic.

In addition, drug and biologic manufacturers and other entities involved in the manufacture and distribution of approved drugs and biological products are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, imposition of post-market studies or clinical trials to assess new safety risks or imposition of distribution or other restrictions under a Risk Evaluation and Mitigation Strategy program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;