INCYTE CORP
Form 10-K
February 17, 2015

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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, 2014

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: 0-27488

INCYTE CORPORATION

(Exact name of registrant as specified in its charter)

Delaware	**94-3136539**
(State of other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)
1801 Augustine Cut-Off Wilmington, DE (Address of principal executives offices)	**19803** (zip code)

(302) 498-6700
(Registrant's telephone number, including area code)

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

Title of each class	**Name of exchange on which registered**
Common Stock, $.001 par value per share	The NASDAQ Stock Market LLC

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

None

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

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

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

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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. (check one)

Large accelerated filer ý	Accelerated filer o	Non-accelerated filer o (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). Yes o No ý

The aggregate market value of Common Stock held by non-affiliates (based on the closing sale price on The NASDAQ Global Select Market on June 30, 2014) was approximately $8.6 billion.

As of February 9, 2015 there were 171,765,591 shares of Common Stock, $.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Items 10 (as to directors and Section 16(a) Beneficial Ownership Reporting Compliance), 11, 12, 13 and 14 of Part III incorporate by reference information from the registrant's proxy statement to be filed with the Securities and Exchange Commission in connection with the solicitation of proxies for the registrant's 2015 Annual Meeting of Stockholders to be held on May 27, 2015.

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Item 1. ***Business***

This report contains forward-looking statements that involve risks and uncertainties. These statements relate to future periods, future events or our future operating or financial plans or performance. Often, these statements include the words "believe," "expect," "target," "anticipate," "intend," "plan," "seek," "estimate," "potential," or words of similar meaning, or future or conditional verbs such as "will," "would," "should," "could," "might," or "may," or the negative of these terms, and other similar expressions. These forward-looking statements include statements as to:

the discovery, development, formulation, manufacturing and commercialization of our compounds, our drug candidates and JAKAFI®/JAKAVI® (ruxolitinib);

conducting clinical trials internally, with collaborators, or with clinical research organizations;

our collaboration and strategic relationship strategy; anticipated benefits and disadvantages of entering into collaboration agreements;

our licensing, investment and commercialization strategies, including our plans to commercialize JAKAFI;

the regulatory approval process, including obtaining U.S. Food and Drug Administration and other international health authorities approval for our products in the United States and abroad;

the safety, effectiveness and potential benefits and indications of our drug candidates and other compounds under development;

the timing and size of our clinical trials; the compounds expected to enter clinical trials; timing of clinical trial results;

our ability to manage expansion of our drug discovery and development operations;

future required expertise relating to clinical trials, manufacturing, sales and marketing;

obtaining and terminating licenses to products, drug candidates or technology, or other intellectual property rights;

the receipt from or payments pursuant to collaboration or license agreements resulting from milestones or royalties;

plans to develop and commercialize products on our own;

plans to use third party manufacturers;

expected expenses and expenditure levels; expected uses of cash; expected revenues and sources of revenues;

expected losses; fluctuation of losses; currency translation impact associated with collaboration royalties;

our profitability; the adequacy of our capital resources to continue operations;

the need to raise additional capital;

the costs associated with resolving matters in litigation;

our expectations regarding competition;

our investments, including anticipated expenditures, losses and expenses;

our patent prosecution and maintenance efforts; and

our indebtedness, and debt service obligations.

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These forward-looking statements reflect our current views with respect to future events, are based on assumptions and are subject to risks and uncertainties. These risks and uncertainties could cause actual results to differ materially from those projected and include, but are not limited to:

our ability to successfully commercialize JAKAFI;

our ability to maintain at anticipated levels, reimbursement for JAKAFI from government health administration authorities, private health insurers and other organizations;

our ability to establish and maintain effective sales, marketing and distribution capabilities;

the risk of reliance on other parties to manufacture JAKAFI, which could result in a short supply of JAKAFI, increased costs, and withdrawal of regulatory approval;

our ability to maintain regulatory approvals to market JAKAFI;

our ability to achieve a significant market share in order to achieve or maintain profitability;

the risk of civil or criminal penalties if we market JAKAFI in a manner that violates health care fraud and abuse and other applicable laws, rules and regulations;

our ability to discover, develop, formulate, manufacture and commercialize our drug candidates;

the risk of unanticipated delays in research and development efforts;

the risk that previous preclinical testing or clinical trial results are not necessarily indicative of future clinical trial results;

risks relating to the conduct of our clinical trials;

changing regulatory requirements;

the risk of adverse safety findings;

the risk that results of our clinical trials do not support submission of a marketing approval application for our drug candidates;

the risk of significant delays or costs in obtaining regulatory approvals;

risks relating to our reliance on third party manufacturers, collaborators, and clinical research organizations;

risks relating to the development of new products and their use by us and our current and potential collaborators;

risks relating to our inability to control the development of out-licensed compounds or drug candidates;

risks relating to our collaborators' ability to develop and commercialize drug candidates;

costs associated with prosecuting, maintaining, defending and enforcing patent claims and other intellectual property rights;

our ability to maintain or obtain adequate product liability and other insurance coverage;

the risk that our drug candidates may not obtain or maintain regulatory approval;

the impact of technological advances and competition;

our ability to compete against third parties with greater resources than ours;

risks relating to changes in pricing and reimbursements in the markets in which we may compete;

competition to develop and commercialize similar drug products;

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our ability to obtain patent protection and freedom to operate for our discoveries and to continue to be effective in expanding our patent coverage;

the impact of changing laws on our patent portfolio;

developments in and expenses relating to litigation;

our ability to in-license drug candidates or other technology;

our substantial leverage;

our ability to obtain additional capital when needed;

fluctuations in net cash provided and used by operating, financing and investing activities;

our history of operating losses; and

the risks set forth under "Risk Factors."

Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by federal securities laws, we undertake no obligation to update any forward-looking statements for any reason, even if new information becomes available or other events occur in the future.

In this report all references to "Incyte," "we," "us," "our" or the "Company" mean Incyte Corporation and our subsidiaries, except where it is made clear that the term means only the parent company.

Incyte and JAKAFI are our registered trademarks. We also refer to trademarks of other corporations and organizations in this Annual Report on Form 10-K.

Overview

Incyte is a biopharmaceutical company focused on the discovery, development and commercialization of proprietary therapeutics to treat serious unmet medical needs, primarily in oncology. JAKAFI (ruxolitinib) is our first product to be approved for sale in the United States. It was approved by the U.S. Food and Drug Administration (FDA) in November 2011 for the treatment of patients with intermediate or high-risk myelofibrosis and in December 2014 for the treatment of patients with polycythemia vera who have had an inadequate response to or are intolerant of hydroxyurea. Myelofibrosis and polycythemia vera are both rare blood cancers.

JAKAFI is marketed in the United States through our own specialty sales force and commercial team. Under our collaboration agreement with Novartis International Pharmaceutical Ltd., Novartis received exclusive development and commercialization rights to ruxolitinib outside of the United States for all hematologic and oncologic indications and sells ruxolitinib outside of the United States under the name JAKAVI.

In 2003, we initiated a research and development program to explore the inhibition of enzymes called janus associated kinases (JAK). The JAK family is composed of four tyrosine kinases JAK1, JAK2, JAK3 and Tyk2 that are involved in the signaling of a number of cytokines and growth factors. JAKs are central to a number of biologic processes, including the formation and development of blood cells and the regulation of immune functions. Dysregulation of the JAK-STAT signaling pathway has been associated with a number of diseases, including myeloproliferative neoplasms, other hematological malignancies, solid tumors, rheumatoid arthritis, psoriasis and other chronic inflammatory diseases. Myeloproliferative neoplasms are a closely related group of blood diseases in which blood cells, specifically platelets, white blood cells, and red blood cells, grow or act abnormally in the bone marrow. These diseases include myelofibrosis (MF), polycythemia vera (PV) and essential thrombocythemia.

We have discovered multiple potent, selective and orally bioavailable JAK inhibitors that are selective for JAK1 or JAK1 and JAK2. JAKAFI is the most advanced compound in our JAK program. It is an

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oral JAK1 and JAK2 inhibitor and was approved by the FDA in November 2011 as a treatment for patients with intermediate or high-risk MF, which includes primary MF, post-polycythemia vera MF and post-essential thrombocythemia MF. We estimate there are between 16,000 and 18,500 patients with MF in the United States. Based on the modern prognostic scoring systems referred to as International Prognostic Scoring System and Dynamic International Prognostic Scoring System, we believe intermediate and high-risk patients represent 80 percent to 90 percent of all patients with MF in the United States and encompass patients over the age of 65, or patients who have or have ever had any of the following: anemia, constitutional symptoms, elevated white blood cell or blast counts, or platelet counts less than 100,000 per microliter of blood.

In December 2014, the FDA approved JAKAFI for the treatment of patients with PV who have had an inadequate response to or are intolerant of hydroxyurea. Current standard treatment for PV is phlebotomy (the removal of blood from the body) plus aspirin. When phlebotomy can no longer control PV, chemotherapy such as hydroxyurea, or interferon, is utilized. Approximately 25,000 patients with PV in the United States are considered uncontrolled because they have an inadequate response to or are intolerant of hydroxyurea, the most commonly used chemotherapeutic agent for the treatment of PV.

JAKAFI was the first FDA-approved JAK inhibitor for any indication and was the first and remains the only product approved by the FDA for use in MF and also now in PV. The FDA has granted JAKAFI orphan drug status for MF, PV and essential thrombocythemia.

In August 2012, the European Commission approved ruxolitinib as JAKAVI for the treatment of disease-related splenomegaly or symptoms in adult patients with primary MF (also known as chronic idiopathic MF), post-polycythemia vera MF or post-essential thrombocythemia MF. In January 2015, the Committee for Medicinal Products for Human Use of the European Medicines Agency adopted a positive opinion for JAKAVI for the treatment of adult patients with polycythemia vera who are resistant to or intolerant of hydroxyurea. We have retained all development and commercialization rights to JAKAFI in the United States and are eligible to receive development and commercial milestones as well as royalties from product sales outside the United States. We hold patents that cover the composition of matter and use of ruxolitinib through late 2027, excluding additional potential patent term extensions. We believe ruxolitinib may have potential as a treatment for other cancers.

Full results from the Phase II proof-of-concept RECAP trial of ruxolitinib in patients with refractory metastatic pancreatic cancer were presented in June 2014 and suggest a demonstrable survival benefit in a pre-specified subgroup of patients with elevated C-reactive protein (CRP). The Company and the FDA have agreed on a Special Protocol Assessment (SPA) for a registration trial for advanced or metastatic pancreatic cancer. Under the SPA, the Phase III JANUS 1 trial can be limited to patients with elevated CRP and there is no requirement to develop a companion diagnostic. The global Phase III program includes a second nearly identical Phase III trial, JANUS 2, and both trials are ongoing. The FDA has granted orphan drug status for ruxolitinib for the treatment of pancreatic cancer.

Elevated CRP has negative prognostic significance in many tumor types, and we believe that JAK inhibition may represent a new treatment approach for other solid tumors. To test this hypothesis, we have initiated three blinded proof-of-concept Phase II trials evaluating ruxolitinib in non-small cell lung cancer, breast cancer and colorectal cancer. The primary endpoint for each trial will be overall survival.

We have a second oral JAK1 and JAK2 inhibitor, baricitinib, which is subject to a collaboration agreement with Eli Lilly and Company in which Lilly received exclusive worldwide development and commercialization rights for the compound for inflammatory and autoimmune diseases. We could receive tiered, double-digit royalty payments on future global sales of products subject to the agreement with rates ranging up to 20 percent if the products are successfully commercialized. This collaboration also contains an option for us to co-develop compounds for any inflammatory and autoimmune disease, whereby we fund 30 percent of development costs from Phase IIb through regulatory approval for that indication in exchange for tiered royalties ranging up to the high twenties on potential future sales. We exercised our co-development option for the development of baricitinib in rheumatoid arthritis in 2010. The Phase III

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program of baricitinib in patients with rheumatoid arthritis is ongoing, and in December 2014, we announced with Lilly that the first of the Phase III trials met the primary endpoint. Baricitinib is also in Phase II trials for patients with moderate-to-severe psoriasis and patients with diabetic nephropathy. We have decided not to exercise our co-development option for psoriasis, and the timeframe for exercising our co-development option for diabetic nephropathy has not yet occurred.

We have a portfolio of wholly-owned JAK1 inhibitors. Our lead JAK1 inhibitor, INCB39110, has completed proof-of-concept studies in patients with psoriasis, rheumatoid arthritis and myelofibrosis. While the results of the psoriasis and rheumatoid arthritis studies were positive, for strategic reasons, we are pursuing oncologic indications with INCB39110. We believe that selective JAK1 inhibition has the potential to minimize the myelosuppression associated with JAK2 inhibition, thus potentially enabling the combination of JAK1 selective inhibitors with myelosuppressive chemotherapy. The clinical program to evaluate INCB39110 in solid tumors includes one ongoing Phase I open-label safety study in combination with gemcitabine and nab-paclitaxel and two blinded proof-of-concept Phase II trials in non-small cell lung cancer. Both trials are now underway, and both trials are designed with overall survival as the primary endpoint. We have another JAK1 inhibitor, INCB52793, which has recently initiated a Phase I/II trial in advanced malignancies.

We have an oral IDO1 inhibitor, epacadostat (previously INCB24360) which belongs to a new class of agents known as immuno-oncology agents. IDO1 is an enzyme whose increased levels in multiple solid tumor types are associated with decreased survival. IDO1 inhibition shifts the immune system from an immunosuppressive state to an activated state, allowing the body to mount a more effective anti-tumor immune response. While preclinical data suggest that IDO1 inhibition can provide anti-tumor effects as monotherapy, based on the significant synergy exhibited in combination with checkpoint inhibitors as well as emerging clinical data, we believe that the optimal development strategy for our IDO1 inhibitor is in combination with other immuno-oncology therapies. During 2014 we signed clinical trial agreements with Merck, Genentech, AstraZeneca and Bristol-Myers Squibb to evaluate epacadostat with their respective PD-1 and PD-L1 agents in Phase I/II trials, and all four of these trials are now in progress. The tumor types under investigation under these agreements include non-small cell lung cancer, metastatic melanoma, head and neck cancer, colorectal cancer, ovarian cancer, diffuse large B-cell lymphoma and pancreatic cancer.

We have recently added two new compounds to our clinical development portfolio. INCB54828 is an FGFR inhibitor that demonstrated potency and selectivity in preclinical studies. The FGFR family of receptor tyrosine kinases can act as oncogenic drivers in a number of liquid and solid tumor types. INCB54329 is a bromodomain (BRD) inhibitor. BRDs are a family of proteins which play important roles in mediating gene transcription, most notably by facilitating the expression of oncogenes such as MYC, one of the most frequently dysregulated oncogenes in all human cancer. We plan to begin clinical trials of INCB54828 and INCB54329 in the first half of this year. We have other orally available small molecule compounds that are in various stages of clinical development, including two PI3K-delta inhibitors, INCB40093 and INCB50465. INCB40093 is being studied as both monotherapy and in combination with our JAK1 inhibitor, INCB39110, in patients with B-lymphoid malignancies.

We have a number of programs in preclinical development, and we intend to continue our investment in drug discovery to expand our pipeline.

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Our current pipeline includes the following compounds:

Target/Drug Compound	Indication	Status
ONCOLOGY		
JAK1 and JAK2		
JAKAFI(1)	Myelofibrosis(11)(12)	FDA Approved Marketed
JAKAFI(1)	Polycythemia Vera(13)	FDA Approved Marketed
ruxolitinib(1)	Pancreatic Cancer	Phase III
ruxolitinib(1)	Breast Cancer	Phase II
ruxolitinib(1)	Non-Small Cell Lung Cancer	Phase II
ruxolitinib(1)	Colorectal Cancer	Phase II
JAK1		
INCB39110	Advanced Malignancies	Phase I/II
INCB39110	Non-Small Cell Lung Cancer	Phase II
INCB39110	Non-Small Cell Lung Cancer	Phase II
INCB52793	Advanced malignancies	Phase I/II
PI3K-delta		
INCB40093	B-lymphoid Malignancies	Phase I/II
INCB50465	Hematology / Oncology	Phase I/II
JAK1+PI3K-delta		
INCB39110+INCB40093	B-lymphoid Malignancies	Phase I/II
IDO1		
epacadostat	Metastatic Melanoma	Phase II
epacadostat(2)	Non-Small Cell Lung Cancer	Phase I/II
epacadostat(3)	Non-Small Cell Lung Cancer	Phase I/II
epacadostat(4)	Multiple tumor types	Phase I/II
epacadostat(5)	Multiple tumor types	Phase I/II
c-MET		
capmatinib(6)	Solid Tumors	Phase I/II
capmatinib(6)	Hepatocellular Carcinoma	Phase II
capmatinib(6)	Non-Small Cell Lung Cancer	Phase II
FGFR		
INCB54828(7)	Solid Tumors	Phase I/II
BRD		
INCB54329(7)	Hematology / Oncology	Phase I/II
INFLAMMATION		
JAK1 and JAK2		
baricitinib(8)	Rheumatoid Arthritis	Phase III
baricitinib(9)	Psoriasis	Phase IIb
baricitinib(10)	Diabetic Nephropathy	Phase II

(1) We licensed rights outside the United States to Novartis and retained U.S. rights.

(2) In combination with Merck's anti-PD-1 immunotherapy, Keytruda (pembrolizumab).

(3) In combination with Genentech's anti-PD-L1 immunotherapy, MPDL3280A.

(4)

In combination with AstraZeneca's anti-PD-L1 immunotherapy, MEDI4736.

(5) In combination with Bristol-Myers-Squibb's anti-PD-1 immunotherapy, Opdivo (nivolumab).

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(6) We licensed worldwide rights to Novartis and retained co-development and co-promotion options.

(7) Clinical trial not yet initiated.

(8) We licensed worldwide rights to Lilly, have elected to co-develop with Lilly, and retained a co-promotion option.

(9) We licensed worldwide rights to Lilly and retained a co-promotion option.

(10) We licensed worldwide rights to Lilly and retained co-development and co-promotion options.

(11) Several clinical trials in patients with myelofibrosis are ongoing, including long-term extension studies, alternative dosing studies, joint global trials with Novartis and trials in patients with low platelet counts.

(12) JAKAFI is approved for treatment of people with intermediate or high-risk myelofibrosis (MF), including primary MF, post polycythemia vera MF, and post essential thrombocythemia MF.

(13) JAKAFI is approved for treatment of people with polycythemia vera (PV) who have had an inadequate response to or are intolerant of hydroxyurea.

JAKAFI

JAKAFI became commercially available in the United States in November 2011 for the treatment of patients with intermediate or high-risk MF and in December 2014 for the treatment of patients with PV who have had an inadequate response to or are intolerant of hydroxyurea, which we refer to as uncontrolled PV. JAKAFI is marketed in the United States through our own specialty sales force and commercial team.

To help ensure that all eligible MF and PV patients have access to JAKAFI, we have established a patient assistance program called IncyteCARES (CARES stands for Connecting to Access, Reimbursement, Education and Support). IncyteCARES helps ensure that any patient with intermediate or high-risk MF or uncontrolled PV who meets certain eligibility criteria and is prescribed JAKAFI has access to the product regardless of ability to pay and has access to ongoing support and educational resources during treatment. In addition, IncyteCARES works closely with payers to help facilitate insurance coverage of JAKAFI.

JAKAFI is distributed primarily through a network of specialty pharmacy providers and group purchasing organizations that allow for efficient delivery of the medication by mail directly to patients or direct delivery to the patient's pharmacy of choice. Our distribution process uses a model that is well-established and familiar to physicians who practice within the oncology field.

To further support appropriate use and future development of JAKAFI, our Medical Affairs department is responsible for providing appropriate scientific and medical education and information to physicians, preparing scientific presentations and publications, and overseeing the process for supporting investigator sponsored trials.

Novartis received approval for JAKAVI in the European Union and Canada in the second half of 2012 for the treatment of disease-related splenomegaly or symptoms in adult patients with primary MF, post-polycythemia vera MF or post-essential thrombocythemia MF. JAKAVI is approved for MF in more than 70 countries with additional worldwide regulatory filings underway for both MF and PV.

Myelofibrosis. Myelofibrosis is a rare, life-threatening condition. MF, considered the most serious of the myeloproliferative neoplasms, can occur either as primary MF, or as secondary MF that develops in some patients who previously had polycythemia vera or essential thrombocythemia.

Most MF patients have enlarged spleens and many suffer from debilitating symptoms, including abdominal discomfort, pruritus (itching), night sweats and cachexia (involuntary weight loss). There were no therapies for MF until the approval of JAKAFI.

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The FDA approval was based on results from two randomized Phase III trials (COMFORT-I and COMFORT-II), which demonstrated that patients treated with JAKAFI experienced significant reductions in splenomegaly (enlarged spleen). COMFORT-I also demonstrated improvements in symptoms. The most common hematologic adverse reactions in both trials were thrombocytopenia and anemia. These events rarely led to discontinuation of JAKAFI treatment. The most common non-hematologic adverse reactions were bruising, dizziness and headache.

In August 2014, the FDA approved supplemental labeling for JAKAFI to include Kaplan-Meier overall survival curves as well as additional safety and dosing information. The overall survival information is based on three-year data from COMFORT-I and II, and shows that at three years the probability of survival for patients treated with JAKAFI in COMFORT-I was 70% and for those patients originally randomized to placebo it was 61%. In COMFORT-II, at three years the probability of survival for patients treated with Jakafi was 79% and for patients originally randomized to best available therapy it was 59%.

Polycythemia Vera. PV is a myeloproliferative neoplasm typically characterized by elevated hematocrit, the volume percentage of red blood cells in whole blood, which can lead to a thickening of the blood and an increased risk of blood clots, as well as an elevated white blood cell and platelet count. When phlebotomy can no longer control PV, chemotherapy such as hydroxyurea, or interferon, is utilized. Approximately 25,000 patients with PV in the United States are considered uncontrolled because they have an inadequate response to or are intolerant of hydroxyurea, the most commonly used chemotherapeutic agent for the treatment of PV.

In December 2014, the FDA approved JAKAFI for the treatment of patients with PV who have had an inadequate response to or are intolerant of hydroxyurea. The approval of JAKAFI for PV was based on data from the pivotal Phase III RESPONSE trial. In this trial, patients treated with JAKAFI demonstrated superior hematocrit control and reductions in spleen volume compared to best available therapy. In addition, a greater proportion of patients treated with JAKAFI achieved complete hematologic remission which was defined as achieving hematocrit control, and lowering platelet and white blood cell counts. In the RESPONSE trial, the most common hematologic adverse reactions (incidence > 20%) were thrombocytopenia and anemia. The most common non-hematologic adverse events (incidence >10%) were headache, abdominal pain, diarrhea, dizziness, fatigue, pruritus, dyspnea and muscle spasms.

Clinical Programs

JAK1/JAK2 Programs for Oncology and Inflammation

Pancreatic Cancer. Pancreatic cancer is a disease in which malignant cells are found in the tissues of the pancreas. Full results from the Phase II proof-of-concept RECAP trial, which compared ruxolitinib in combination with capecitabine versus capecitabine alone in patients with refractory metastatic pancreatic cancer, were presented in June 2014 and suggest a demonstrable survival benefit in a pre-specified subgroup of patients with elevated CRP. In this subgroup, results showed a hazard ratio for overall survival of 0.47, which means the risk of death was reduced by approximately 50 percent for those patients treated with ruxolitinib. The subgroup represented approximately half of the randomized population in this trial.

The Company and the FDA have agreed on an SPA for a registration trial for advanced or metastatic pancreatic cancer. Under the SPA, the Phase III JANUS 1 trial can be limited to patients with elevated CRP and there is no requirement to develop a companion diagnostic. The global Phase III program includes a second nearly identical Phase III trial, JANUS 2. Both JANUS trials are now recruiting patients.

Solid Tumors. Elevated CRP has negative prognostic significance in many tumor types, and we believe that JAK inhibition may represent a new treatment approach for other solid tumors. In the first half of 2014, we initiated three blinded Phase II proof-of-concept trials evaluating ruxolitinib in non-small cell lung cancer, breast cancer and colon cancer. The primary endpoint for each trial is overall survival.

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Rheumatoid Arthritis. Rheumatoid arthritis is an autoimmune disease characterized by aberrant or abnormal immune mechanisms that lead to joint inflammation and swelling and, in some patients, the progressive destruction of joints. Rheumatoid arthritis can also affect connective tissue in the skin and organs of the body.

Current rheumatoid arthritis treatments include the use of non-steroidal anti-inflammatory drugs, disease-modifying anti-rheumatic drugs, such as methotrexate, and the newer biological response modifiers that target pro-inflammatory cytokines, such as tumor necrosis factor, implicated in the pathogenesis of rheumatoid arthritis. None of these approaches to treatment is curative; therefore, there remains an unmet need for new safe and effective treatment options for these patients. Rheumatoid arthritis is estimated to affect about 1 percent of the world population.

We have a second JAK1 and JAK2 inhibitor, baricitinib, which is subject to our collaboration agreement with Lilly. The Phase III program of baricitinib in patients with rheumatoid arthritis began in October 2012 and currently includes four trials that are expected to each recruit between 500 and 1,300 patients. The four trials incorporate all three rheumatoid arthritis populations (methotrexate naïve, biologic naïve, and biologic experienced); use event rates to fully power the baricitinib program for structural comparison and non-inferiority vs. adalimumab; incorporate an MRI sub-study into the methotrexate naïve registration trial; and evaluate patient-reported outcomes. In December 2014, we and Lilly announced that the Phase III RA-BEACON study met the primary endpoint of improved ACR20 response compared to placebo after 12 weeks of treatment. The study included patients with moderately-to-severely active rheumatoid arthritis who previously failed one or more tumor necrosis factor inhibitors and who were taking stable doses of conventional disease-modifying anti-rheumatic drug therapy. We expect to disclose with Lilly results from the remaining three Phase III studies in 2015. We have exercised our co-development option in rheumatoid arthritis to fund 30 percent of development costs from Phase IIb through regulatory approval in exchange for increased tiered royalties ranging up to the high twenties on potential future sales.

Psoriasis. Baricitinib is also being developed in psoriasis. Psoriasis is a skin disease that causes visible scaling and inflammation. Most psoriasis patients have patches of thick, red skin with silvery scales that can occur on the elbows, knees, other parts of the legs, scalp, lower back, face, palms, and soles of the feet. Market research suggests that neither physicians nor patients are satisfied with existing psoriasis treatments primarily because these require constant monitoring to balance safety and efficacy outcomes. There is clear unmet need for a better tolerated and effective treatment. The U.S. psoriasis market consists of approximately six million patients, of which moderate-to-severe patients account for approximately 20 percent of the market.

In December 2011, Lilly initiated a Phase IIb double-blind, placebo-controlled, dose-ranging trial designed to evaluate baricitinib in patients with moderate-to-severe plaque psoriasis. The trial is fully enrolled with approximately 240 patients randomized in several dose groups. The primary objective of this study is to demonstrate that at least one dose group is superior to placebo at week 12 in the treatment of patients with moderate-to-severe psoriasis as measured by the proportion of patients with at least a 75 percent improvement from baseline in Psoriasis Area and Severity Index (PASI) score. We have decided not to exercise our co-development option for this indication, although we retain a co-promotion option.

Diabetic Nephropathy. In August 2012, Lilly initiated a Phase II trial to evaluate baricitinib in patients with diabetic nephropathy. Data suggest that ongoing renal inflammation plays a key role in diabetic nephropathy, and biopsies from the kidneys of early- and late-stage diabetic kidney disease patients suggest that over-activation of the JAK/STAT pathway leads to increased levels of pro-inflammatory cytokines. Therefore, inhibiting cytokine pathways dependent on JAK1 and JAK2 may lead to positive clinical outcomes in diabetic nephropathy.

In this dose-ranging placebo-controlled Phase II trial, the primary endpoint was the change from baseline in the urinary albumin/creatinine ratio at 24 weeks. We retain co-development and co-promotion options for this indication.

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JAK1 Programs for Oncology

We believe that selective JAK1 inhibition has the potential to minimize the myelosuppression associated with JAK2 inhibition, thus potentially enabling the combination of JAK1 selective inhibitors with myelosuppressive chemotherapy. We have a wholly owned portfolio of JAK1 inhibitors, and we are pursuing oncologic indications with our lead JAK1 inhibitor, INCB39110. We have completed a Phase I clinical trial to evaluate the safety and tolerability of INCB39110 in combination with chemotherapy in patients with advanced solid tumors, and have initiated two planned placebo-controlled proof-of-concept Phase II trials of INCB39110 in distinct chemotherapeutic regimens in patients with non-small cell lung cancer. We plan to begin a first line pancreatic cancer study of INCB39110 in combination with gemcitabine and nab-paclitaxel in the second half of 2015.

We have another JAK1 inhibitor, INCB52793, which has recently initiated a Phase I/II trial in advanced malignancies.

IDO1 for Oncology

The enzyme, indoleamine 2, 3-dioxygenase-1, IDO1, is a key regulator of the mechanisms that are responsible for allowing tumors to escape from a patient's immune surveillance. IDO1 expression by tumor cells, or by antigen presenting cells such as macrophages and dendritic cells in tumors, creates an environment in which tumor specific cytotoxic T lymphocytes are rendered functionally inactive or are no longer able to attack a patient's cancer cells. By inhibiting IDO1, it is proposed that this "brake" on the anti-tumor immune response is removed, allowing anti-tumor specific cytotoxic T cells, generated in a patient spontaneously in response to the tumor, or through a therapy designed to stimulate the immune response, to have greater anti-tumor efficacy.

Epacadostat is a novel, potent and selective inhibitor of the enzyme IDO1. We believe that the optimal development strategy for epacadostat is for the compound to be developed in combination with other immuno-oncology agents. We have four clinical trial agreements in place to evaluate the safety and efficacy of epacadostat in combination with four different checkpoint inhibitors: Merck's anti-PD-1 inhibitor Keytruda (pembrolizumab); AstraZeneca's investigational anti-PD-L1 inhibitor, MEDI4736; Bristol-Myers Squibb's anti-PD-1 inhibitor Opdivo (nivolumab); and Genentech's investigational anti-PD-L1 inhibitor, MPDL3280A. These four agreements are non-exclusive and involve multiple tumor types, including non-small cell lung, melanoma, ovarian, colorectal, squamous cell carcinoma of the head and neck, pancreatic and diffuse large B-cell lymphoma, and the Phase I/II trials under these agreements have been initiated.

PI3K-delta Inhibition for Hematology/Oncology

The PI3K-delta pathway mediates oncogenic signaling in B cell malignancies, and we have two PI3K-delta inhibitors in clinical development, INCB40093 and INCB50465. We believe each of these compounds provides an opportunity to differentiate competitor agents on potency, pharmacokinetics and safety, thereby potentially providing more attractive combination opportunities.

INCB50465, a PI3K-delta inhibitor that demonstrated high potency in preclinical studies, has now entered Phase I development as monotherapy, and INCB40093, our first PI3K-delta inhibitor, is advancing in both monotherapy and combination (with our JAK1 selective inhibitor INCB39110) proof-of-concept trials in B-cell malignancies. In-house preclinical studies have demonstrated that the JAK1 and PI3K-delta signaling pathways play inter-related functions in maintaining the growth and survival of B-lymphoid cells, and the data suggest that concurrent inhibition of the two pathways may achieve synergistic cellular efficacy.

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c-MET for Solid Tumors

c-MET is a clinically validated receptor kinase cancer target. Abnormal c-MET activation in cancer correlates with poor prognosis. Dysregulation of the c-MET pathway triggers tumor growth, formation of new blood vessels that supply the tumor with nutrients, and causes cancer to spread to other organs. Dysregulation of the c-MET pathway is seen in many types of cancers, including kidney, liver, stomach, breast and brain.

Several small molecule c-MET kinase inhibitors have demonstrated clinical efficacy in a number of cancers; however, these molecules have limited potency and are relatively non-selective, which could lead to off-target toxicities. We believe our lead c-MET inhibitor, capmatinib, which is licensed to Novartis, has the requisite properties to overcome these limitations, including greater selectivity, improved potency and more effective inhibition of c-MET. Under our agreement, Novartis received worldwide exclusive development and commercialization rights to capmatinib and certain back-up compounds in all indications. Capmatinib is being evaluated in hepatocellular carcinoma, non-small cell lung cancer, and other solid tumors and may have potential utility as a combination agent.

Early Stage Clinical / Discovery

We have recently added two new compounds to our clinical development portfolio. INCB54828 is an FGFR inhibitor that demonstrated potency and selectivity in preclinical studies. The FGFR family of receptor tyrosine kinases can act as oncogenic drivers in a number of liquid and solid tumor types. We plan to begin clinical trials of INCB54828 in the first half of 2015. INCB54329 is a BRD inhibitor. BRDs are a family of proteins which play important roles in mediating gene transcription, most notably by facilitating the expression of oncogenes such as MYC, one of the most frequently dysregulated oncogenes in all human cancer. We plan to begin clinical trials of INCB54329 in the first half of 2015.

We have a number of other early programs at various stages of preclinical and clinical testing. We intend to describe these programs once we have obtained clinical proof-of-concept and established that a compound within a specific program warrants further development.

License Agreements

Novartis

In November 2009, we entered into a Collaboration and License Agreement with Novartis. Under the terms of the agreement, Novartis received exclusive development and commercialization rights outside of the United States to ruxolitinib and certain back-up compounds for hematologic and oncology indications, including all hematological malignancies, solid tumors and myeloproliferative diseases. We retained exclusive development and commercialization rights to JAKAFI (ruxolitinib) in the United States and in certain other indications. Novartis also received worldwide exclusive development and commercialization rights to our c-MET inhibitor compound capmatinib and certain back-up compounds in all indications. We retained options to co-develop and to co-promote capmatinib in the United States.

Under this agreement, we received an upfront payment and immediate milestone payment totaling $210 million and were initially eligible to receive additional payments of up to approximately $1.2 billion if defined development and commercialization milestones are achieved. We are also eligible to receive tiered, double-digit royalties ranging from the upper-teens to the mid-twenties on future ruxolitinib net sales outside of the United States. In addition, Novartis has received reimbursement and pricing approval for ruxolitinib in a specified number of countries, and we are now obligated to pay to Novartis tiered royalties in the low single digits on future ruxolitinib net sales within the United States. Each company is responsible for costs relating to the development and commercialization of ruxolitinib in its respective territories, with costs of collaborative studies shared equally. Novartis is now responsible for all costs relating to the development and commercialization of capmatinib.

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The Novartis agreement will continue on a program-by-program basis until Novartis has no royalty payment obligations with respect to such program or, if earlier, the termination of the agreement or any program in accordance with the terms of the agreement. Royalties are payable by Novartis on a product-by-product and country-by-country basis until the latest to occur of (1) the expiration of the last valid claim of the licensed patent rights covering the licensed product in the relevant country, (2) the expiration of regulatory exclusivity for the licensed product in such country and (3) a specified period from first commercial sale in such country of the licensed product by Novartis or its affiliates or sublicensees. The agreement may be terminated in its entirety or on a program-by-program basis by Novartis for convenience. The agreement may also be terminated by either party under certain other circumstances, including material breach.

Lilly

In December 2009, we entered into a License, Development and Commercialization Agreement with Lilly. Under the terms of the agreement, Lilly received exclusive worldwide development and commercialization rights to baricitinib and certain back-up compounds for inflammatory and autoimmune diseases. We received an initial payment of $90 million, and were initially eligible to receive additional payments of up to $665 million based on the achievement of defined development, regulatory and commercialization milestones. We also could receive tiered, double-digit royalty payments on future global net sales with rates ranging up to 20% if the product is successfully commercialized.

We retained options to co-develop our JAK1/JAK2 inhibitors with Lilly on a compound-by-compound and indication-by-indication basis. Lilly is responsible for all costs relating to the development and commercialization of the compounds unless we elect to co-develop an