Incyte Announces FDA Approval of Zynyz™ (retifanlimab-dlwr) for the Treatment of Metastatic or Recurrent Locally Advanced Merkel Cell Carcinoma (MCC)

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—First regulatory approval for Incyte PD-1 inhibitor based on the results of the POD1UM-201 trial

—Zynyz is also being studied in additional tumor types and in combination with other Incyte pipeline compounds

WILMINGTON, Del.--(BUSINESS WIRE)--Mar. 22, 2023-- Incyte (Nasdaq:INCY) today announced that the U.S. Food and Drug Administration (FDA) has approved Zynyz ™ (retifanlimab-dlwr), a humanized monoclonal antibody targeting programmed death receptor-1 (PD-1), for the treatment of adults with metastatic or recurrent locally advanced Merkel cell carcinoma (MCC). The Biologics License Application (BLA) for Zynyz for this indication has been approved under accelerated approval by the U.S. FDA based on tumor response rate and duration of response (DOR). Continued approval of Zynyz for this indication may be contingent on verification and description of clinical benefit in confirmatory trials.

MCC is a rare and aggressive type of skin cancer that frequently appears as a single, painless, reddish-purple skin nodule on the head, neck and arms in skin exposed to sunlight[1]. MCC tends to grow quickly and has a high rate of metastatic disease, leading to a poor prognosis[2,3]. The estimated five-year overall survival (OS) rate is 14% in patients with MCC who present with distant metastatic disease[3]. MCC impacts less than 1 per 100,000 people in the U.S., but incidence rates are rapidly rising, especially in adults over the age of 65[4,5].

“More than a third of patients with MCC present with regional or distant metastases, which are associated with high rates of mortality,” said Dr. Shailender Bhatia, University of Washington and Fred Hutchinson Cancer Center. “The approval of Zynyz offers healthcare providers another first-line treatment option against MCC that can result in durable responses in patients with metastatic disease, and I look forward to having Zynyz in our treatment portfolio for these difficult-to-treat patients.”

The FDA approval was based on data from the POD1UM-201 trial, an open-label, multiregional, single-arm study that evaluated Zynyz in adults with metastatic or recurrent locally advanced MCC who had not received prior systemic therapy for their advanced disease. Among chemotherapy-naïve patients (n=65), Zynyz monotherapy resulted in an objective response rate (ORR) of 52% (95% confidence interval [CI]: 40-65) as determined by independent central review (ICR) using RECIST v1.1. Complete response was seen in 12 patients (18%), and 22 patients (34%) showed partial response. Among the responding patients, the duration of response (DOR) ranged from 1.1 to 24.9+ months, and 76% (26/34) experienced a DOR of six months or longer, and 62% (21/34) experienced a DOR of 12 months or longer by landmark analysis.

Serious adverse reactions occurred in 22% of patients receiving Zynyz. The most frequent serious adverse reactions (≥ 2% of patients) were fatigue, arrhythmia and pneumonitis. Permanent discontinuation of Zynyz due to an adverse reaction occurred in 11% of patients. The most common (≥10%) adverse reactions that occurred in patients receiving Zynyz were fatigue, musculoskeletal pain, pruritus, diarrhea, rash, pyrexia and nausea.

“Zynyz offers patients and healthcare professionals an additional first-line anti-PD-1 option for patients with metastatic or recurrent locally advanced MCC, which can be a challenging and aggressive disease to treat,” said Hervé Hoppenot, Chief Executive Officer, Incyte. “Incyte is grateful to the investigators and patients around the world who participated in the POD1UM-201 trial. We continue to study the potential of Zynyz in additional tumor types and in combination with other Incyte pipeline compounds.”

Incyte is committed to supporting patients and removing barriers to access medicines. Eligible patients in the U.S. who are prescribed Zynyz have access to IncyteCARES (Connecting to Access, Reimbursement, Education and Support), a comprehensive program offering personalized patient support, including financial assistance and ongoing education and additional resources. More information about IncyteCARES is available by visiting www.incytecares.com or calling 1-855-452-5234.

About POD1UM

The POD1UM (PD1 Clinical Program in Multiple Malignancies) clinical trial program for retifanlimab includes POD1UM-201 and several other Phase 1, 2 and 3 studies for patients with solid tumors, including registration-directed POD1UM trials evaluating retifanlimab as a monotherapy for patients with microsatellite instability-high endometrial cancer and squamous cell carcinoma of the anal canal (SCAC); and in combination with platinum-based chemotherapy for patients with non-small cell lung cancer and SCAC.

About POD1UM-201

POD1UM-201 (NCT03599713) is an open label, multiregional, single arm study evaluating retifanlimab in patients with metastatic or recurrent locally advanced Merkel cell carcinoma (MCC) who had not received prior systemic therapy for their advanced disease.

Patients received Zynyz 500 mg intravenously every four weeks until disease progression, unacceptable toxicity, for up to 24 months. Tumor response assessments were performed every eight weeks for the first year of therapy and 12 weeks thereafter.

The primary endpoint was objective response rate (ORR) as determined by independent central radiographic review using RECIST v1.1. Secondary endpoints included duration of response (DOR), disease control rate (DCR), progression-free survival (PFS) and overall survival (OS); safety and pharmacokinetics.

For more information about the study, please visit: https://clinicaltrials.gov/ct2/show/NCT03599713.

About Zynyz™ (retifanlimab-dlwr)

Zynyz (retifanlimab-dlwr), is an intravenous PD-1 inhibitor indicated in the U.S. for the treatment of adult patients with metastatic or recurrent locally

advanced Merkel cell carcinoma (MCC). This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Zynyz is marketed by Incyte in the U.S. In 2017, Incyte entered into an exclusive collaboration and license agreement with MacroGenics, Inc. for global rights to retifanlimab.

Zynyz is a trademark of Incyte.

Important Safety Information

What is the most important information I should know about ZYNYZ?

ZYNYZ is a medicine that may treat a certain type of skin cancer by working with your immune system. ZYNYZ can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. You can have more than one of these problems at the same time. These problems may happen anytime during treatment or even after your treatment has ended.

Call or see your healthcare provider right away if you develop any new or worsening signs or symptoms, including:

Lung problems: cough, shortness of breath, chest pain

Intestinal problems: diarrhea (loose stools) or more frequent bowel movements than usual; stools that are black, tarry, sticky, or have blood or mucus; severe stomach-area (abdomen) pain or tenderness

Liver problems: yellowing of your skin or the whites of your eyes; severe nausea or vomiting; pain on the right side of your stomach area (abdomen); dark urine (tea colored); bleeding or bruising more easily than normal

Hormone gland problems: headaches that will not go away or unusual headaches; eye sensitivity to light; eye problems; rapid heartbeat; increased sweating; extreme tiredness; weight gain or weight loss; feeling more hungry or thirsty than usual; urinating more often than usual; hair loss; feeling cold; constipation; your voice gets deeper; dizziness or fainting; changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness

Kidney problems: decrease in your amount of urine, blood in your urine, swelling of your ankles, loss of appetite

Skin problems: rash; itching; skin blistering or peeling; painful sores or ulcers in your mouth or nose, throat, or genital area; fever or flu-like symptoms; swollen lymph nodes

Problems can also happen in other organs and tissues. These are not all of the signs and symptoms of immune system problems that can happen with ZYNYZ. Call or see your healthcare provider right away for any new or worsening signs or symptoms, which may include:

- chest pain, irregular heartbeat, shortness of breath, or swelling of ankles
- confusion, sleepiness, memory problems, changes in mood or behavior, stiff neck, balance problems, tingling or numbness of the arms or legs
- double vision, blurry vision, sensitivity to light, eye pain, changes in eyesight
- persistent or severe muscle pain or weakness, muscle cramps
- low red blood cells, bruising

Infusion reactions that can sometimes be severe. Signs and symptoms of infusion reactions may include: chills or shaking, itching or rash, flushing, shortness of breath or wheezing, dizziness, feel like passing out, fever, back or neck pain

Rejection of a transplanted organ. Your healthcare provider should tell you what signs and symptoms you should report and monitor you, depending on the type of organ transplant that you have had.

Complications, including graft-versus-host disease, in people who have received a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic). These complications can be serious and can lead to death. These complications may happen if you underwent transplantation either before or after being treated with ZYNYZ. Your healthcare provider will monitor you for these complications.

Getting medical treatment right away may help keep these problems from becoming more serious. Your healthcare provider will check you for these problems during your treatment with ZYNYZ. Your healthcare provider may treat you with corticosteroid or hormone replacement medicines. Your healthcare provider may also need to delay or completely stop treatment with ZYNYZ if you have severe side effects.

Before you receive ZYNYZ, tell your healthcare provider about all of your medical conditions, including if you:

- have immune system problems such as Crohn’s disease, ulcerative colitis, or lupus
- have received an organ transplant
- have received or plan to receive a stem cell transplant that uses donor stem cells (allogeneic)
- have received radiation treatment to your chest area
- have a condition that affects your nervous system, such as myasthenia gravis or Guillain-Barré syndrome
- are pregnant or plan to become pregnant. ZYNYZ can harm your unborn baby.
  Females who are able to become pregnant:
  — Your healthcare provider should do a pregnancy test before you start treatment with ZYNYZ.
  — You should use an effective method of birth control during your treatment and for 4 months after your last dose of ZYNYZ. Talk to your healthcare provider about birth control methods that you can use during this time.
  — Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with

ZYNYZ.

- are breastfeeding or plan to breastfeed. It is not known if ZYNYZ passes into your breast milk. Do not breastfeed during treatment and for 4 months after your last dose of ZYNYZ.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

The most common side effects of ZYNYZ include tiredness, muscle and bone pain, itching, diarrhea, rash, fever, nausea

These are not all the possible side effects of ZYNYZ. Call your doctor for medical advice about side effects.

General information about the safe and effective use of ZYNYZ.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. If you would like more information about ZYNYZ, talk with your healthcare provider. You can ask your healthcare provider for information about ZYNYZ that is written for health professionals.

You may report side effects to the FDA at (800) FDA-1088 or http://www.fda.gov/medwatch. You may also report side effects to Incyte Corporation at 1-855-463-3463.

Please see the full Prescribing Information for ZYNYZ for additional Important Safety Information.

About Incyte

Incyte is a Wilmington, Delaware-based, global biopharmaceutical company focused on finding solutions for serious unmet medical needs through the discovery, development and commercialization of proprietary therapeutics. For additional information on Incyte, please visit Incyte.com and follow @Incyte.

Forward-Looking Statements

Except for the historical information set forth herein, the matters set forth in this press release, including statements regarding whether and when Zynyz might provide a successful treatment option for patients with MCC and Incyte's POD1UM clinical program generally, contain predictions, estimates and other forward-looking statements.

These forward-looking statements are based on Incyte's current expectations and subject to risks and uncertainties that may cause actual results to differ materially, including unanticipated developments in and risks related to: unanticipated delays; further research and development and the results of clinical trials possibly being unsuccessful or insufficient to meet applicable regulatory standards or warrant continued development; the ability to enroll sufficient numbers of subjects in clinical trials; the effects of the COVID-19 pandemic and measures to address the pandemic on Incyte and its partners' clinical trials, supply chain, other third-party providers and development and discovery operations; determinations made by the U.S. FDA and other regulatory authorities outside of the United States; the efficacy or safety of Incyte and its partners' products; the acceptance of Incyte and its partners' products in the marketplace; market competition; sales, marketing, manufacturing and distribution requirements; and other risks detailed from time to time in Incyte's reports filed with the Securities and Exchange Commission, including its annual report for the year ended December 31, 2022. Incyte disclaims any intent or obligation to update these forward-looking statements.

[1] Müller-Richter UDA, et al. Merkel Cell Carcinoma of the Head and Neck: Recommendations for Diagnostics and Treatment. *Ann Surg Oncol.* 2017;24:3430–3437.

[2] Paulson KG, Bhatia S., et al. Advances in Immunotherapy for Metastatic Merkel Cell Carcinoma: A Clinician's Guide. *JNCCN*. 2018;16(6):782-790.

[3] Harms KL, et al. Analysis of Prognostic Factors from 9387 Merkel Cell Carcinoma Cases Forms the Basis for the New 8th Edition AJCC Staging System. *Ann Surg Oncol.* 2016;23:3564-3571.

[4] Jacobs D, et al. Assessment of Age, Period, and Birth Cohort Effects and Trends in Merkel Cell Carcinoma Incidence in the United States. *JAMA Dermatol.* 2021;157:59–65.

[5] Paulson KG, et al. Merkel cell carcinoma: Current US incidence and projected increases based on changing demographics. *J Am Acad Dermatol.* 2018;78:457–463.e2

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