Incyte Announces Positive Results from Phase 3 Trial Evaluating Retifanlimab (Zynyz®) in Combination with Platinum-Based Chemotherapy in Patients with Non-Small Cell Lung Cancer

December 7, 2024

—Phase 3 POD1UM-304 trial met primary endpoint of overall survival (OS) and all secondary endpoints in patients with previously untreated metastatic non-small cell lung cancer (NSCLC)

—Data presented at the European Society for Medical Oncology (ESMO) Asia Congress 2024 support the planned 2025 filing of a supplemental Biologics License Application (sBLA) in the U.S. for retifanlimab in NSCLC

WILMINGTON, Del.--(BUSINESS WIRE)--Dec. 7, 2024-- Incyte (Nasdaq:INCY) today announced results from the Phase 3 POD1UM-304 trial of retifanlimab (Zynyz®), a humanized monoclonal antibody targeting programmed death receptor-1 (PD-1), in combination with platinum-based chemotherapy for the treatment of adults with previously untreated non-squamous and squamous metastatic non-small cell lung cancer (NSCLC) not harboring a driver mutation. These data were featured today in a mini oral presentation at the European Society for Medical Oncology (ESMO) Asia Congress 2024, held in Singapore and virtually.

The POD1UM-304 trial results show a clinically meaningful and statistically significant improvement over chemotherapy alone. Patients in the retifanlimab and chemotherapy combination treatment group achieved a median overall survival (OS) of 18.1 months compared to 13.4 months in the placebo and chemotherapy combination group (Hazard Ratio [HR]: 0.75; 95% Confidence Interval [CI] (0.60, 0.93); *P*=0.0042).

“The positive POD1UM-304 trial results provide additional proof of retifanlimab’s safety and efficacy profile in solid tumors,” said Pablo J. Cagnoni, M.D., President and Head of Research and Development, Incyte. “We look forward to leveraging these results to advance our pipeline, particularly in hard-to-treat cancers like NSCLC, and to submitting a supplemental Biologic License Application for this indication to the U.S. Food and Drug Administration next year.”

The trial also met secondary endpoints, including:

- Patients who received retifanlimab in combination with chemotherapy had a 2-month improvement in median progression-free survival (PFS) compared to the placebo and chemotherapy combination group (7.7 vs 5.5 months; [HR: 0.64; 95% CI (0.52, 0.79); *P*<0.0001]).
- Overall response rate (ORR) and duration of response (DOR) by Blinded Independent Central Review (BICR) each showed improvement in the retifanlimab and chemotherapy combination treatment group versus the placebo and chemotherapy combination group (ORR of 52% [95% CI (47, 57) vs. 39% (95% CI 32, 46), respectively; *P*=0.0012]; DOR of 12.7 months [95% CI (9.4, 15.2) vs. 6.1 months and [95% CI (4.2, 8.3), respectively]).

Retifanlimab was generally well-tolerated and no new safety issues were identified. The most common treatment-emergent adverse events (TEAEs), in >10% of patients in the retifanlimab and chemotherapy combination treatment group, were anemia (62.7%), decreased appetite (22.6%) and decreased neutrophil count (22.1%). Chemotherapy administration was not compromised by the addition of retifanlimab.

“Lung cancer is the leading cause of cancer deaths globally, with the high majority of cases being NSCLC,” said Shun Lu, M.D., Ph.D., Shanghai Chest Hospital. “I am encouraged by the observed safety and efficacy profile of retifanlimab when added to platinum-based chemotherapy in this patient population and believe the positive results from the POD1UM-304 trial support retifanlimab in combination with chemotherapy as an additional treatment option for previously untreated metastatic NSCLC.”

About Non-Small Cell Lung Cancer

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, accounting for approximately 85% of all lung cancer cases worldwide.[1] It is characterized by the uncontrolled growth of malignant cells in the lungs and is often diagnosed at an advanced stage, making it a leading cause of cancer-related mortality globally.[1, 2, 3]

About POD1UM

The POD1UM (PD1 Clinical Program in Multiple Malignancies) clinical trial program for retifanlimab includes POD1UM-304 in non-small cell lung cancer (NSCLC) and POD1UM-303 in squamous cell anal carcinoma (SCAC), as well as other Phase 1 and 2 studies for patients with solid tumors, including registration-directed trials evaluating retifanlimab as a monotherapy for patients with Merkel cell carcinoma and microsatellite instability-high endometrial cancer.

About POD1UM-304

POD1UM-304 is a Phase 3, global, multicenter, randomized, double-blind study evaluating platinum-based chemotherapy with retifanlimab or placebo in patients with first-line, metastatic squamous or non-squamous NSCLC.

During the study, patients were randomized to receive retifanlimab or placebo intravenously in combination with pemetrexed and carboplatin/cisplatin for non-squamous NSCLC, and with paclitaxel and carboplatin for squamous NSCLC. The primary endpoint is overall survival (OS), and secondary endpoints include progression-free survival (PFS), overall response rate (ORR) and duration of response (DOR) as assessed by blinded independent central review (BICR). After verified progressive disease by BICR, patients assigned to the placebo and chemotherapy combination group had the option to cross over to open-label retifanlimab monotherapy.

For more information about the study, please visit https://clinicaltrials.gov/study/NCT04205812.

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.

In Europe, Zynyz is approved as a monotherapy for the first-line treatment of adult patients with metastatic or recurrent locally advanced MCC not amenable to curative surgery or radiation therapy.

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 registered 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

A global biopharmaceutical company on a mission to *Solve On.*, Incyte follows the science to find solutions for patients with unmet medical needs. Through the discovery, development and commercialization of proprietary therapeutics, Incyte has established a portfolio of first-in-class medicines for patients and a strong pipeline of products in Oncology and Inflammation & Autoimmunity. Headquartered in Wilmington, Delaware, Incyte has operations in North America, Europe and Asia.

For additional information on Incyte, please visit Incyte.com or follow us on social media: LinkedIn, X, Instagram, Facebook, YouTube.

Incyte Forward-looking Statements

Except for the historical information set forth herein, the matters set forth in this press release, including statements regarding the presentation of data from Incyte's Phase 3 POD1UM-304 trial of retifanlimab (Zynyz), the potential presented by retifanlimab, whether or when retifanlimab, alone or in combination, will be approved or commercially available for use in humans anywhere in the world outside of the already approved indications in specific regions, and Incyte's goal of improving the lives of patients, contain predictions, estimates, and other forward-looking statements.

These forward-looking statements are based on our current expectations and are 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 and the ability to enroll subjects in accordance with planned schedules; determinations made by the FDA and regulatory agencies outside of the United States; the efficacy or safety of our products; the acceptance of our products in the marketplace; market competition; unexpected variations in the demand for our products and the products of our collaboration partners; the effects of announced or unexpected price regulation or limitations on reimbursement or coverage for our products; sales, marketing, manufacturing, and distribution requirements, including our ability to successfully commercialize and build commercial infrastructure for newly approved products and any additional new products that become approved; and other risks detailed from time to time in our reports filed with the U.S. Securities and Exchange Commission, including our annual report on Form 10-K and our quarterly report on Form 10-Q for the quarter ended September 30, 2024. We disclaim any intent or obligation to update these forward-looking statements.

[1] Duma N, et al. Mayo Clin Proc. 2019;94:1623-1640.

[2] Yang SR, et al. Front Oncol. 2022;12.

[3] Alexander M, et al. *Lung*. 2020;198:897-907.

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