Incyte's Retifanlimab (Zynyz®) Extends Progression-Free Survival in Patients with Squamous Cell Anal Carcinoma (SCAC); Data Featured at ESMO 2024 Presidential Symposium

September 14, 2024

- Phase 3 POD1UM-303/InterAACT2 trial met primary endpoint of progression-free survival and demonstrated improvement across secondary endpoints in patients with squamous cell anal carcinoma (SCAC) taking retifanlimab in combination with platinum-based chemotherapy (carboplatin-paclitaxel)

- Late-breaking data presented at the European Society for Medical Oncology (ESMO) Congress 2024 support the planned U.S. filing of a supplemental Biologics License Application (sBLA) for retifanlimab in SCAC by year-end 2024

- Incyte to host an in-person analyst and investor event to review key data at ESMO on Saturday, September 14, 2024 from 1:00-2:30 p.m. ET (7:00-8:30 p.m. CEST)

WILMINGTON, Del.--(BUSINESS WIRE)--Sep. 14, 2024-- Incyte (Nasdaq:INCY) today announced results from the Phase 3 POD1UM-303/InterAACT2 trial of retifanlimab (Zynyz®), a humanized monoclonal antibody targeting programmed death receptor-1 (PD-1), in combination with platinum-based chemotherapy (carboplatin–paclitaxel) for the treatment of adults with inoperable locally recurrent or metastatic squamous cell anal carcinoma (SCAC). These data were featured today in a Presidential Symposium (LBA 2) at the European Society for Medical Oncology (ESMO) Congress 2024, held in Barcelona and virtually.

The POD1UM-303/InterAACT2 trial results build on previously announced topline results, showing that the study met its primary endpoint by demonstrating a statistically significant and clinically meaningful improvement in progression-free survival (PFS) in patients with SCAC not previously treated with systemic therapy, as assessed by blinded independent central review (BICR) using RECIST v1.1. Adding retifanlimab to standard of care chemotherapy resulted in a clinically meaningful 37% reduction in the risk of progression or death (Hazard Ratio [HR]: 0.63; 95% Confidence Interval [CI] (0.47, 0.84); *P*=0.0006). Patients in the retifanlimab and chemotherapy combination group achieved a median PFS of 9.3 months compared to 7.4 months for patients in the placebo combination group.

"The POD1UM-303/InterAACT2 trial is the first and largest Phase 3 trial evaluating a checkpoint inhibitor for the treatment of patients with squamous cell anal carcinoma, a disease with significant medical need. The positive efficacy and safety data presented today at ESMO illustrate the potential of retifanlimab in combination with carboplatin and paclitaxel to become a new standard-of-care treatment for patients with advanced SCAC," said Pablo J. Cagnoni, M.D., President and Head of Research and Development, Incyte. "We look forward to working with regulatory authorities to progress the supplemental Biologics License Application (sBLA) for retifanlimab and potentially bring the first-ever PD-1 or PD-L1 antibody to patients with SCAC."

The trial also showed improvement in key secondary endpoints, including:

- In an interim analysis for overall survival (OS), patients that received retifanlimab in combination with chemotherapy achieved an approximately 6-month improvement in median OS versus the placebo combination group, with a strong trend toward statistical significance (median OS 29.2 months vs. 23 months [HR: 0.70; 95% CI (0.49, 1.01); *P*=0.0273]; OS follow-up is ongoing).
- Overall response rate (ORR) and duration of response (DOR) by BICR each showed improvement in the retifanlimab and chemotherapy combination group versus the placebo combination group (ORR of 56% vs. 44% [95% CI (48, 64) and (36, 52), respectively; nominal *P*=0.0129]; DOR of 14 months vs. 7 months [95% CI (8.6, 22.2) and (5.6, 9.3), respectively]).

Retifanlimab was generally well-tolerated, and safety was consistent with other chemotherapy plus checkpoint inhibitor regimens. The most common treatment-emergent adverse events (TEAEs) in the retifanlimab and chemotherapy combination group were anemia (66.2%), nausea (56.5%) and alopecia (51.3%).

"Advanced SCAC is an often-neglected rare condition that, despite its increasing incidence and the often poor prognosis, has had the same standard-of-care treatment for decades with very few trials," said Sheela Rao, M.D., Consultant Medical Oncologist, The Royal Marsden National Health Service Foundation Trust. "I believe the positive results from the POD1UM-303/InterAACT2 trial may provide a long-awaited, new treatment option with retifanlimab in addition to platinum-based chemotherapy for adults with inoperable locally recurrent or metastatic SCAC."

About Squamous Cell Anal Carcinoma (SCAC)

Squamous cell anal carcinoma (SCAC) is an orphan disease for which the incidence is increasing approximately 3% per year, largely due to endemic human papillomavirus (HPV).[1,2,3,4] Human immunodeficiency virus (HIV) is an important amplifier of SCAC, as people with HIV are 25 to 35 times more likely to develop SCAC.[5,6] Patients with unresectable metastatic SCAC have poor 5-year survival, and there are currently no FDA-approved treatments for patients with advanced disease.[7]

About POD1UM

The POD1UM (PD1 Clinical Program in Multiple Malignancies) clinical trial program for retifanlimab includes POD1UM-303 and several other Phase 1, 2 and 3 studies for patients with solid tumors, including registration-directed trials evaluating retifanlimab as a monotherapy for patients with microsatellite instability-high endometrial cancer; and in combination with platinum-based chemotherapy for patients with non-small cell lung cancer.

About POD1UM-303/InterAACT 2

POD1UM-303/InterAACT2 (NCT04472429) is a Phase 3, randomized, multicenter, double-blind, placebo-controlled study evaluating retifanlimab or placebo in combination with platinum-based chemotherapy (carboplatin and paclitaxel) in adult patients with inoperable locally recurrent or metastatic SCAC who have not been previously treated with systemic chemotherapy.

During the blinded portion of the study, patients, including those with well-controlled HIV infection, were randomized 1:1 to receive retifanlimab 500 mg intravenously or placebo during each 28-day cycle for up to 6 months in combination with standard therapy of carboplatin and paclitaxel followed by monotherapy for up to 1-year total treatment. Crossover to active therapy retifanlimab was allowed for patients assigned to placebo upon verification of progression by blinded independent central review (BICR).

The primary endpoint is progression-free survival (PFS) as determined by BICR using RECIST v1.1. The key secondary endpoint includes overall survival (OS). Secondary objectives include objective response rate (ORR), duration of response (DOR), disease control rate (DCR) by BICR, safety and pharmacokinetics.

For more information about the study, please visit https://clinicaltrials.gov/study/NCT04472429.

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 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 retifanlimab, the POD1UM-303 clinical trial, the potential for retifanlimab to become an approved treatment option for SCAC, Incyte's plans to share data with the scientific community and Incyte's expectations with respect to filing an sBLA or otherwise engaging with regulators, 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; 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 on Form-10K and its report on Form 10-Q for the quarter ended June 30, 2024. Incyte disclaims any intent or obligation to update these forward-looking statements.

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[5] Wang C-CJ, et al. Surg Oncol Clin N Am. 2017;26:17-31.
[6] NCCN Clinical Practice Guidelines in Oncology: Cancer in People with HIV. Version 1.2021. 2021.
[7] Eng C, et al. Oncotarget 2014;5:11133-11142.

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