Phase 3 Data for Incyte's Retifanlimab (Zynyz®) in Patients with Squamous Cell Carcinoma of the Anal Canal (SCAC) Published in The Lancet

June 12, 2025

- *POD1UM-303/InterAACT 2 is the first and largest global Phase 3 trial evaluating a PD-1 inhibitor in combination with chemotherapy for the treatment of patients with advanced SCAC not previously treated with systemic chemotherapy*
- *The trial met its primary endpoint; treatment with retifanlimab in combination with platinum-based chemotherapy (carboplatin-paclitaxel) resulted in clinically meaningful improvements in progression-free survival and overall survival*
- *In May 2025, the U.S. Food and Drug Administration (FDA) approved Zynyz® (retifanlimab-dlwr) in combination with carboplatin and paclitaxel and as a single agent for the treatment of advanced SCAC; submissions to other global regulatory agencies are also under review*

WILMINGTON, Del.--(BUSINESS WIRE)--Jun. 12, 2025-- Incyte (Nasdaq:INCY) today announced that primary results from the Phase 3 POD1UM-303/InterAACT 2 trial of retifanlimab (Zynyz®), a humanized monoclonal antibody targeting programmed death receptor-1 (PD-1), in combination with carboplatin and paclitaxel (platinum-based chemotherapy) in adult patients with inoperable locally recurrent or metastatic squamous cell carcinoma of the anal cancer (SCAC) who have not been previously treated with systemic chemotherapy, were published in *The Lancet*.[1]

"The publication of the POD1UM-303/InterAACT 2 trial in *The Lancet* is a testament to the strength of the data generated for retifanlimab in patients with inoperable locally recurrent or metastatic SCAC, a disease which until recently had seen limited innovation for decades," said Steven Stein, M.D., Chief Medical Officer, Incyte. "SCAC can be a devastating disease, and patients often have a poor prognosis. These data supported the U.S. Food and Drug Administration (FDA) approval of Zynyz® (retifanlimab-dlwr) in May 2025, providing U.S. patients the first and only first-line treatment for inoperable locally recurrent or metastatic SCAC."

The POD1UM-303/InterAACT2 trial results, which were also featured at a Presidential Symposium on Practice-Changing Trials at the European Society for Medical Oncology (ESMO) in 2024, showed that the study met its primary endpoint by demonstrating a statistically significant improvement in progression-free survival (PFS) in patients with inoperable locally recurrent or metastatic SCAC not previously treated with systemic chemotherapy, as assessed by blinded independent central review (BICR) using RECIST v1.1.[2] Adding retifanlimab to carboplatin and paclitaxel 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).[2] 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.[2]

New data published today in *The Lancet* show that in patients treated with retifanlimab plus chemotherapy:[1]

- A consistent benefit in PFS in favor of retifanlimab plus chemotherapy was observed for all pre-defined subgroups with sufficient patients for comparison.
- A clinically meaningful 6-month difference in overall survival (OS) was observed at the interim analysis (29.2 months in the retifanlimab plus carboplatin and paclitaxel group vs 23.0 months in the placebo plus carboplatin and paclitaxel group). Interim OS results were not statistically significant, and patients continue to be followed for the final key secondary OS analysis.
- The overall response rate (ORR) to treatment was improved by the addition of retifanlimab to the chemotherapy (55.8% in the retifanlimab plus carboplatin and paclitaxel group vs 44.2% in the placebo plus carboplatin and paclitaxel group) and the median duration of response was approximately doubled (14 months in the retifanlimab plus carboplatin and paclitaxel group vs 7.2 months in the placebo plus carboplatin and paclitaxel group) when compared to placebo.

As reported in *The Lancet,* no new safety signals were observed in POD1UM-303/InterAACT2, and safety was consistent with chemotherapy plus checkpoint inhibitor regimens. Serious and Grade 3 or worse adverse events were more frequent in the retifanlimab plus carboplatin and paclitaxel group compared with placebo plus carboplatin and paclitaxel group (47.4% vs 38.8% and 83.1% vs 75.0%, respectively). The most common Grade ≥3 adverse events were neutropenia (35.1% for retifanlimab plus carboplatin and paclitaxel vs 29.6% for placebo plus carboplatin and paclitaxel) and anemia (19.5% vs 20.4%). Despite the higher rate of serious, Grade 3 or worse, and fatal adverse events with retifanlimab plus carboplatin and paclitaxel than placebo plus carboplatin–paclitaxel, these toxicities were manageable with standard measures and carboplatin and paclitaxel delivery was not compromised.

The publication, entitled "Retifanlimab with carboplatin and paclitaxel for locally recurrent or metastatic squamous cell carcinoma of the anal canal (POD1UM-303/InterAACT-2): a global, phase 3 randomised controlled trial," can be found online here.

"The incidence of SCAC is increasing by approximately 3% annually, driven mainly by endemic human papillomavirus (HPV infection). With no approved treatments available for advanced cases until recently, it is crucial to develop effective therapies for this orphan disease," said Sheela Rao, M.D., Consultant Medical Oncologist, The Royal Marsden National Health Service Foundation Trust.

In May 2025, the FDA approved Zynyz® (retifanlimab-dlwr) in combination with carboplatin and paclitaxel (platinum-based chemotherapy) for the first-line treatment of adult patients with inoperable locally recurrent or metastatic SCAC. In addition, the FDA granted approval for Zynyz as a single agent for the treatment of adult patients with locally recurrent or with metastatic SCAC with disease progression on or intolerance to platinum-based chemotherapy. Incyte has also submitted a Type II variation Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for retifanlimab in advanced SCAC and in March 2025 submitted and received acceptance of a Japanese New Drug Application (J-NDA) by the Pharmaceuticals and Medical Devices Agency (PMDA) for retifanlimab in advanced SCAC.

About Squamous Cell Carcinoma of the Anal Canal (SCAC)

SCAC is the most common type of anal cancer, making up 85% of cases.[3] It is a rare disease for which the incidence is increasing approximately 3% per year.[4] About 90% of cases are associated with human papillomavirus (HPV) infection—the number one risk factor for anal cancer.[5] HIV is an important amplifier of anal cancer, as people with HIV are 25 to 35 times more likely to develop it.[6,7] Anal cancer shares many of the same symptoms as non-cancerous conditions, such as hemorrhoids—including pain, itching, a lump or mass and changes in bowel movements—and as a result can go undetected leading to the majority of patients presenting with locally advanced disease.[8,9] More information about SCAC is available by visiting www.analcancer.com.

About POD1UM

The POD1UM (PD1 Clinical Program in Multiple Malignancies) clinical trial program for retifanlimab includes POD1UM-303, POD1UM-202 and several other Phase 1, 2 and 3 studies for patients with solid tumors, including a registration-directed trial evaluating retifanlimab in combination with platinum-based chemotherapy for patients with non-small cell lung cancer.

About POD1UM-303/InterAACT 2

POD1UM-303/InterAACT 2 (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 retifanlimab or placebo monotherapy for up to 1-year total treatment in the absence of disease progression or unacceptable toxicity. Crossover to retifanlimab monotherapy was allowed for patients assigned to placebo upon verification of progression by blinded independent central review (BICR).

The primary endpoint was progression-free survival (PFS) as determined by BICR using RECIST v1.1. The key secondary endpoint was overall survival (OS). Other secondary endpoints 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 a humanized monoclonal antibody targeting programmed death receptor-1 (PD-1), indicated in combination with carboplatin and paclitaxel (platinum-based chemotherapy) for the first-line treatment of adult patients with inoperable locally recurrent or metastatic squamous cell carcinoma of the anal canal (SCAC) and as a single agent for the treatment of adult patients with locally recurrent or metastatic SCAC with disease progression or intolerance to platinum-based chemotherapy in the U.S.

Zynyz is also indicated for the treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma (MCC) in the U.S. 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 United States. 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 certain types of cancers 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 doctor 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 doctor 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 or tissue. Your doctor should tell you what signs and symptoms you should report and monitor you, depending on the type of organ or tissue 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 doctor will monitor you for these complications.

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

Before you receive Zynyz, tell your doctor 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 or tissue transplant, including corneal 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 doctor should do a pregnancy test before you start treatment.
- You should use an effective method of birth control during your treatment and for 4 months after your last dose. Talk to your doctor about birth control methods that you can use during this time.
- Tell your doctor right away if you become pregnant or think you may be pregnant during treatment.
- 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

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

The most common side effects of Zynyz when given with the chemotherapy medicines carboplatin and paclitaxel in people with SCAC include tiredness, numbness, pain, tingling, or burning in your hands or feet; nausea; hair loss; diarrhea; muscle and bone pain; constipation; bleeding; rash; vomiting; decreased appetite; itching; stomach-area pain.

The most common side effects of Zynyz when used alone in people with SCAC include tiredness, muscle and bone pain, diarrhea, infection, rectal or genital-area pain, bleeding, urinary tract infection (UTI), rash, nausea, loss of appetite, constipation, stomach-area pain, shortness of breath, fever, vomiting, cough, itching, low levels of thyroid hormone, headache, decreased weight.

The most common side effects of Zynyz when used alone in people with MCC 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. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Incyte Corporation at 1-855-463-3463.

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 doctor. You can ask your doctor for information about **Zynyz** that is written for health professionals.

Please see the full Prescribing Information, including the Medication Guide, for Zynyz.

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

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 whether and when Zynyz might provide a successful treatment option for patients with SCAC, contain predictions, estimates and other forward-looking statements.

These forward-looking statements are based on Incyte's 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; determinations made by FDA or other regulatory authorities; Incyte's dependence on its relationships with its collaboration partners; the efficacy or safety of Incyte's products and the products of Incyte's collaboration partners; the acceptance of Incyte's products and the products of Incyte's collaboration partners 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 and its quarterly report on Form 10-Q for the quarter ended March 31, 2025. Incyte disclaims any intent or obligation to update these forward-looking statements.

---

[1] Rao S, et al. Retifanlimab with carboplatin and paclitaxel for locally recurrent or metastatic squamous cell carcinoma of the anal canal (POD1UM-303/InterAACT-2): a global, phase 3 randomised controlled trial. *The Lancet*. 2025;405(10495):2144-52.

[2] Lu S, et al. POD1UM-304: Phase 3 Study of Retifanlimab Plus Platinum-Based Chemotherapy as First-Line Therapy for Nonsquamous or Squamous Metastatic Non–Small Cell Lung Cancer. European Society of Medical Oncology (ESMO) Asia 2024.

[3] Symer MM, Yeo HL. F1000Research. 2018;7:F1000 Faculty Rev-1572.

[4] National Cancer Institute. Anal Cancer Incidence and Deaths Are Rising in the United States. https://www.cancer.gov/news-events/cancer-currents-blog/2019/anal-cancer-incidence-mortality-rise. Accessed April 16, 2025.

[5] U.S. Centers for Disease Control and Prevention. Cancers Linked With HPV Each Year. https://www.cdc.gov/cancer/hpv/cases.html. Accessed April 16, 2025.

[6] Wang C-CJ, et al. *Surg Oncol Clin N Am*. 2017;26:17-31.

[7] NCCN Clinical Practice Guidelines in Oncology: Cancer in People with HIV. Version 1.2021. 2021.

[8] Anal Cancer Foundation. Anal Cancer: Signs, Symptoms, Causes & Treatment. https://www.analcancerfoundation.org/what-is-anal-cancer/. Accessed April 16, 2025.

[9] Rao S, et al. *Ann Oncol*. 2020;31(4):S1170-S1171.

View source version on businesswire.com: https://www.businesswire.com/news/home/20250612476128/en/

Media
media@incyte.com

Investors
ir@incyte.com

Source: Incyte