Incyte Announces FDA Approval of Zynyz® (retifanlimab-dlwr) Making it the First and Only Approved First-Line Treatment for Advanced Anal Cancer Patients in the United States

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- *Zynyz® (retifanlimab-dlwr), a PD-1 inhibitor, is now approved for the treatment of advanced squamous cell carcinoma of the anal canal (SCAC) in combination with chemotherapy and as a monotherapy*
- *Patients with SCAC treated with Zynyz achieved a statistically significant improvement in progression-free survival and improvement in overall survival*

WILMINGTON, Del.--(BUSINESS WIRE)--May 15, 2025-- 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), 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). 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.

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Zynyz logo

"The FDA approval of Zynyz marks a pivotal moment, bringing effective combination and monotherapy treatment options to patients with advanced anal cancer after decades of limited innovation," said Hervé Hoppenot, Chief Executive Officer, Incyte. "At Incyte, we focus our efforts where we can make the biggest impact for patients. I am proud of our scientists and development teams for their perseverance in delivering the first approved PD-1 inhibitor to U.S. patients with SCAC."

The Priority Review and FDA approval of the supplemental Biologics License Application (sBLA) for Zynyz was based on data from two trials: the Phase 3 POD1UM-303/InterAACT2 trial evaluating Zynyz in combination with platinum-based chemotherapy (carboplatin-paclitaxel) in adult patients with metastatic or inoperable locally recurrent SCAC not previously treated with systemic chemotherapy, and the Phase 2 POD1UM-202 trial evaluating Zynyz monotherapy in previously treated patients with locally advanced or metastatic SCAC who have progressed on or were intolerant of platinum-based chemotherapy.

Results from POD1UM-303/InterAACT2, featured at a Presidential Symposium on Practice-Changing Trials at the European Society for Medical Oncology (ESMO) in 2024, showed a clinically meaningful and statistically significant 37% reduction in the risk of progression or death (*P*=0.0006). Patients in the Zynyz and chemotherapy combination group achieved a median progression-free survival (PFS) of 9.3 months compared to 7.4 months for patients in the placebo combination group. Additionally, a 6.2-month improvement in median overall survival (OS) was observed (*P*=0.0273) at an interim analysis; OS follow-up is ongoing. No new safety signals were observed. Serious adverse reactions occurred in 47% of patients receiving Zynyz in combination with chemotherapy. The most frequent serious adverse reactions (≥ 2% of patients) were sepsis (3.2%), pulmonary embolism (3.2%), diarrhea (2.6%) and vomiting (2.6%).

"Patients with inoperable locally recurrent or metastatic anal cancer have historically faced poor five-year survival rates and limited treatment options.[1] The POD1UM data highlight the potential of Zynyz to be a meaningful new option, and notably demonstrate that the addition of Zynyz to platinum-based chemotherapy significantly improves progression-free survival," said Marwan Fakih, M.D., Professor, Medical Oncology & Therapeutics Research, Associate Director, Clinical Sciences, Medical Director, Briskin Center for Clinical Research, Division Chief, GI Medical Oncology, Co-Director, Gastrointestinal Cancer Program, City of Hope. "This approval marks an important advancement as it makes a new treatment approach available for this challenging cancer."

The Zynyz monotherapy approval is based on results from the POD1UM-202 study which demonstrated that treatment with Zynyz monotherapy produced an objective response rate (ORR) of 14% and disease control rate of 49%. Zynyz demonstrated a safety profile as expected of a PD-1 inhibitor with no loss of human immunodeficiency virus (HIV) infection control.[2] Serious adverse reactions occurred in 40% of patients receiving Zynyz. The most frequent serious adverse reactions (≥ 2% of patients) were non-urinary tract infection, perineal pain, abdominal pain, anemia, hemorrhage, diarrhea, pyrexia, urinary tract infection, musculoskeletal pain and dyspnea.

“Patients with anal cancer often face a troubling lack of public awareness and understanding when it comes to risk factors, symptoms and their overall cancer journey,” said David Winterflood, Chief Executive Officer of the Anal Cancer Foundation. “The approval of Zynyz marks a step forward for advanced SCAC treatment, brings attention to a long-overlooked condition with limited treatment options and offers patients whose anal cancer has returned or spread an option to treat their disease.”

In addition to the sBLA in the U.S., Incyte submitted a Type II variation Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for retifanlimab in advanced SCAC and a Japanese New Drug Application (J-NDA) which was accepted by the Pharmaceuticals and Medical Devices Agency (PMDA) for retifanlimab in advanced SCAC.

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, Monday through Friday, from 8 a.m. to 8 p.m. ET.

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.[2,8] 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 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] Eng C, et al. *Oncotarget*. 2014;5:11133-11142.

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

[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.

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