Mirum Pharmaceuticals and Incyte Announce Positive Pivotal Phase 2 Results from PROGRESS Study of Zilurgisertib in Fibrodysplasia Ossificans Progressiva

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- Cohort 1 results presented at ENDO 2026 demonstrate meaningful reductions in total heterotopic ossification (HO) lesion volume, new HO lesions and flare activity in adolescents and adults with FOP
- U.S. Food and Drug Administration (FDA) accepted the New Drug Application (NDA) for zilurgisertib in FOP under Priority Review

FOSTER CITY, Calif. & WILMINGTON, Del.--(BUSINESS WIRE)--Mirum Pharmaceuticals, Inc. (Nasdaq:MIRM) and Incyte (Nasdaq:INCY) today announced pivotal Phase 2 results from Cohort 1 of the PROGRESS study evaluating zilurgisertib, an investigational oral activin receptor-like kinase 2 (ALK2) inhibitor, in adolescents and adults (≥12 years of age) with fibrodysplasia ossificans progressiva (FOP). Results were shared in a late-breaking rapid-fire presentation at ENDO 2026, the Endocrine Society's annual meeting.

Results from Cohort 1 of the PROGRESS study demonstrated a consistent treatment effect across measures of disease activity and durability through Week 48. During the open-label extension, no new HO lesions were observed among patients who continued to receive zilurgisertib or among placebo-treated patients who crossed over to active treatment at Week 24.

"The findings presented at ENDO represent an important milestone for the zilurgisertib program and further strengthen the growing body of clinical evidence supporting its potential as a treatment for FOP," said Steven Stein, M.D., Executive Vice President, Chief Medical Officer and Head of Late-Stage Development at Incyte.

"People living with FOP and their families urgently need additional treatment options," said Joanne Quan, M.D., Chief Medical Officer at Mirum Pharmaceuticals. "These results reinforce our confidence in the potential of zilurgisertib and our commitment to working with Incyte to bring this important program forward as we prepare for potential commercialization and support the FOP community."

Cohort 1 of the PROGRESS study evaluated zilurgisertib 100 mg once-daily in 63 adolescents and adults (≥12 years of age) with FOP. Patients were randomized 1:1 to receive zilurgisertib (n=32) or placebo (n=31) during a 24-week, placebo-controlled, double-blind period, followed by an open-label extension period. Baseline demographics and disease characteristics were generally balanced between treatment groups, with a mean age of approximately 21 years and evidence of recent disease activity prior to enrollment. A total of 61 patients had 48-week whole-body CT scan data available at the time of the open-label extension analysis.

Key efficacy findings included:

- Fewer patients receiving zilurgisertib developed new HO lesions at Week 24, with an 81% reduction versus placebo (p=0.0986).
- >99% reduction in total volume of new HO lesions in patients receiving zilurgisertib versus placebo at Week 24 (nominal p-value<0.0001).
- Reduction in total HO lesion volume compared with an increase observed in placebo-treated patients at Week 24 (nominal p-value=0.004).
- Among patients receiving zilurgisertib, no new HO lesions were observed and total HO lesion volume continued to decrease from Week 24 to Week 48.
- Among patients who crossed over from placebo to zilurgisertib, no new HO lesions were observed and total HO lesion volume decreased from Week 24 to Week 48.

Key Efficacy Findings (Week 24 Placebo-Controlled Period and Week 48 Crossover)

Endpoint	**Zilurgisertib (ZGB) (n=32) Week 24**	**Placebo (n=31) Week 24**	**Key Finding**	**Open-Label Extension Week 48**
Number (%) of patients who developed new HO lesions *P-value*	1 (3.1)	5 (16.7)	81% reduction vs placebo *0.0986*	No patients with new HO lesions observed at Week 48 (n=61)
Mean (SD) total number of new HO lesions	0.06 (0.35)	0.23 (0.63)	Fewer new lesions vs placebo	No new lesions observed (n=61)
Mean (SD) new lesion volume, cm³ *P-value*	0.003 (0.02)	6.57 (20.70)	>99% lower volume of new lesions vs placebo *<0.0001**	No new lesions observed (n=61)

Mean (SD) change in total lesion volume, cm³ *P-value*	-3.24 (19.86)	24.64 (51.94)	Reduction vs increase on placebo *0.004**	Continued reduction from Week 24 • -6.37 (19.43) ZGB (n=32) • -5.32 (20.91) crossover (n=29)
Mean (SD) new flares (annualized)	2.34 (6.06)	4.55 (7.71)	Lower flare activity vs placebo	Low flare activity maintained • 1.01 (3.26) ZGB (n=32) • 1.22 (2.54) crossover (n=30)

**Nominal P-value*

Zilurgisertib was generally well-tolerated during the 24-week placebo-controlled period of the study. Data showed:

- Most adverse events were mild or moderate in severity.
- No adverse events led to treatment discontinuation or dose reduction.
- Serious adverse events and Grade ≥3 adverse events occurred at low rates in both treatment groups.
- The most commonly reported adverse events among patients receiving zilurgisertib were FOP flare-up or aching/pain due to FOP (25%), headache (21.9%), upper respiratory tract infection (21.9%), arthralgia (18.8%), epistaxis (12.5%), and nausea (12.5%).

The full abstract is available on the Endocrine Society's ENDO 2026 website. Detailed analyses are also posted on the Publications & Presentations section of Mirum's website.

The U.S. Food and Drug Administration (FDA) has accepted the New Drug Application (NDA) for zilurgisertib for the treatment of FOP in patients 12 years of age and older and granted Priority Review. The Prescription Drug User Fee Act (PDUFA) target action date for zilurgisertib is September 26, 2026.

About Zilurgisertib

Zilurgisertib is an investigational, oral, small molecule, activin receptor-like kinase 2 (ALK2) inhibitor in development for the treatment of Fibrodysplasia Ossificans Progressiva (FOP). Zilurgisertib is designed to inhibit the ALK2 receptor, which is abnormally active in most patients with FOP and leads to bone formation in soft tissues, a process known as heterotopic ossification (HO). FOP is an ultra-rare genetic disease that affects approximately 300 patients in the U.S. and 900 worldwide, with diagnosis typically occurring in early childhood. Zilurgisertib was evaluated in the PROGRESS pivotal Phase 2 study, which formed the basis of a new drug application (NDA). The FDA has accepted the NDA for zilurgisertib in FOP under Priority Review with a Prescription Drug User Fee Act (PDUFA) date of September 26, 2026.

Mirum Pharmaceuticals, Inc. licensed zilurgisertib from Incyte for worldwide development and commercialization.

About the PROGRESS Study

PROGRESS is a global, randomized, double-blind, placebo-controlled Phase 2 study evaluating the efficacy and safety of zilurgisertib in patients with fibrodysplasia ossificans progressiva (FOP). PROGRESS Cohort 1 enrolled patients 12 years of age and older who were randomized 1:1 to receive zilurgisertib 100 mg once daily or placebo during a 24-week double-blind treatment period, followed by an open-label extension. Additional PROGRESS cohorts will evaluate the efficacy and safety of zilurgisertib in patients ages 6 to <12 years of age (Cohort 2) and in patients ages 2 to <12 years of age (Cohort 3).

The primary endpoint of the study is the proportion of Cohort 1 patients with new heterotopic ossification (HO) lesions at Week 24 as assessed by whole-body CT scan data. Key secondary endpoints include the number and total volume of new HO lesions, changes in total HO lesion volume and flare activity through Week 24.

About Mirum Pharmaceuticals

Mirum Pharmaceuticals (NASDAQ: MIRM) is a leading rare disease company with a global footprint of approved products and a broad pipeline of investigational medicines. Purpose-built to bring forward breakthrough medicines for people with overlooked conditions, Mirum focuses on rare liver and rare genetic diseases, where it has built deep expertise and strong connections to patient communities. The company's commercial portfolio includes LIVMARLI® (maralixibat) for Alagille syndrome (ALGS) and progressive familial intrahepatic cholestasis (PFIC), CHOLBAM® (cholic acid) for bile-acid synthesis disorders, and CTEXLI® (chenodiol) for cerebrotendinous xanthomatosis (CTX).

Mirum's clinical-stage pipeline includes volixibat, an IBAT inhibitor in late-stage development for primary sclerosing cholangitis (PSC) and primary biliary cholangitis (PBC), brelovitug, a fully human monoclonal antibody in late-stage development for chronic hepatitis delta virus (HDV), zilurgisertib, an ALK2 inhibitor under regulatory review with the FDA for fibrodysplasia ossificans progressiva (FOP), and MRM-3379, a PDE4D inhibitor being evaluated for Fragile X syndrome (FXS).

Mirum's success is driven by a team dedicated to advancing high impact medicines through strategic development, disciplined execution and purposeful collaboration across the rare disease ecosystem. Learn more at www.mirumpharma.com and follow Mirum on Facebook, LinkedIn, Instagram and X.

About Incyte®

Incyte is redefining what's possible in biopharmaceutical innovation. Through deep scientific expertise and a relentless focus on patients, we have built an established portfolio of first-in-class medicines and an extensive portfolio of next-generation medicines across our key franchises: Hematology, Oncology and Inflammation & Autoimmunity.

To learn more, visit Incyte.com and Investor.Incyte.com. Follow us on social media: LinkedIn, X and Instagram.

Mirum Forward-Looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements include statements regarding, among other things, the Company's planned participation at a scientific congress, Mirum's continued advancement of zilurgisertib with Incyte, the likelihood of a FDA approval pathway for zilurgisertib and the potential benefit of zilurgisertib in real world settings versus scientific presentations of data. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Words such as "expected," "will," "could," "would," "guidance," "potential," "continue" and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon Mirum's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation, risks and uncertainties associated with Mirum's business in general, the impact of geopolitical and macroeconomic events, and the other risks described in Mirum's Annual Report for the year ended December 31, 2025, filed with the Securities and Exchange Commission on February 25, 2026, and subsequent filings with the Securities and Exchange Commission, which are available at www.sec.gov. All forward-looking statements contained in this press release speak only as of the date on which they were made and are based on management's assumptions and estimates as of such date. Mirum undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made, except as required by law.

Incyte Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws, including statements regarding the presentation of data from the PROGRESS study; the potential for zilurgisertib to become a treatment option for people living with FOP; expectations regarding ongoing and future clinical trials for zilurgisertib, including the timing of such trials; and Incyte's aspirations and goals as set forth under the heading "About Incyte."

Actual results may differ materially from those indicated in the forward-looking statements as a result of various important factors, including the sufficiency of clinical trial data 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; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials and marketing approval; the efficacy or safety of Incyte's and its partners' products; the ability of Incyte and its partners to achieve commercial success for their marketed products and product candidates, if approved; Incyte's and its partners' ability to obtain and maintain protection of intellectual property for their products and technology; Incyte's reliance on third parties and partners; the acceptance of Incyte's and its partners' products in the marketplace; market competition, sales, marketing, manufacturing and distribution requirements; greater than expected expenses, including expenses relating to litigation or strategic activities; and those risks and uncertainties discussed in greater detail in Incyte's reports filed with the U.S. Securities and Exchange Commission, including its annual report on Form 10-K for the year ended December 31, 2025, and its quarterly report on Form 10-Q for the quarter ended March 31, 2026. Incyte disclaims any intent or obligation to update these forward-looking statements.

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