News Release

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Late-Breaking Phase 2 Data for Investigational Oral Factor XIa Inhibitor Milvexian Suggest Favorable Antithrombotic Profile Across a Wide Range of Doses

Milvexian demonstrated efficacy and no increase in bleeding across doses with no major bleeds in the milvexian arms, when compared with enoxaparin, for postoperative venous thromboembolism (VTE) prevention in patients undergoing elective total knee replacement (TKR) surgery

AXIOMATIC-TKR is the first of two studies to read out from the Phase 2 milvexian program, which together will inform the design and dose regimens of the Phase 3 program

Data simultaneously published in The New England Journal of Medicine and presented at the American Heart Association Scientific Sessions 2021

Milvexian is being developed by The Bristol Myers Squibb-Janssen Collaboration

RARITAN, NJ, November 15, 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson in collaboration with Bristol Myers Squibb today announced results from the Phase 2 AXIOMATIC-TKR study, which showed investigational oral

milvexian reduced the risk of postoperative venous thromboembolism (VTE) in a dose dependent manner without increasing the risk of bleeding compared with enoxaparin in patients undergoing total knee replacement (TKR) surgery. These data were presented today at a Late-Breaking Science session at the American Heart Association (AHA) Scientific Sessions 2021 and simultaneously published in *The New England Journal of Medicine* (NEJM).

"This study establishes proof-of-principle for milvexian as a differentiated antithrombotic agent," said Jeffrey Weitz, M.D., Professor of Medicine & Biochemistry and Biomedical Sciences at McMaster University and Executive Director of the Thrombosis and Atherosclerosis Research Institute.[i] "Furthermore, the consistently low rates of bleeding across a 16-fold range of milvexian doses suggest that it has a wide therapeutic window, which opens the opportunity to explore milvexian across a broad range of patients including those for whom factor Xa inhibitors are underutilized or not indicated."

The trial met both of its pre-specified proof-of-principle requirements: the dose response for efficacy with twice-daily milvexian was significant ($p<0.001$), and the 12% rate of VTE with combined twice-daily doses of milvexian was significantly lower ($p<0.0001$) than the prespecified benchmark rate of 30%.

At daily doses of at least 100 mg, the rates of VTE with milvexian were significantly lower than with enoxaparin ($p\leq0.014$).

	Milvexian Twice Daily				**Milvexian Once Daily**			**Enoxaparin Once Daily**
	25 mg	**50 mg**	**100 mg**	**200 mg**	**25 mg**	**50 mg**	**200 mg**	**40 mg**
No. of patients evaluated	129	124	134	131	28	127	123	252
Venous thromboembolism*	21%	11%	9%	8%	25%	24%	7%	21%
No. of patients evaluated†	148	148	149	148	33	150	147	296
Any bleeding	1%	5%	5%	3%	0	5%	6%	4%
Major or clinically relevant nonmajor bleeding	0	1%	1%	1%	0	1%	1%	2%
Major bleeding	0	0	0	0	0	0	0	0.3%

*Primary efficacy outcome defined as the composite of asymptomatic deep-vein thrombosis (detected by mandatory unilateral venography performed 10 to 14 days after surgery), confirmed symptomatic venous thromboembolism (symptomatic deep-vein thrombosis of the leg or nonfatal pulmonary embolism), or death.
† Safety outcomes were assessed in the safety population, which consisted of all patients who received at least one dose of trial medication.

There were no major bleeds with milvexian and one with enoxaparin. The rates of major plus clinically relevant nonmajor bleeds (CRNM) with milvexian and enoxaparin were 0.8% and 1.4%, respectively. Across a 16-fold range of doses, milvexian demonstrated a low risk of major plus CRNM bleeding with no major bleeds and no dose-response on this composite outcome.

"These promising Phase 2 data support a profile that is consistent with better efficacy and safety than enoxaparin and reinforce our confidence in milvexian," said James List, M.D., Ph.D., Global Therapeutic Area Head, Cardiovascular, Metabolism, & Retina, Janssen Research & Development, LLC. "We're optimistic about the milvexian program and its potential impact for patients."

The TKR study is the first of two studies to read out from the Phase 2 milvexian program. Results from the ongoing Phase 2 study of milvexian for secondary stroke prevention (AXIOMATIC-SSP) are expected in the first half of 2022. Janssen and Bristol Myers Squibb thank the patients and investigators involved in this clinical trial.

About AXIOMATIC-TKR

AXIOMATIC-TKR is a Phase 2, randomized, open-label, parallel-group, dose-ranging multicenter study that evaluated the efficacy and safety of milvexian, an oral factor XIa (FXIa) inhibitor, versus subcutaneous enoxaparin in patients undergoing elective TKR surgery. The primary efficacy outcome was the incidence of total VTE up to 14 days. The principal safety outcome was any bleeding, defined as the composite of major, clinically relevant nonmajor and minimal bleeding.

A total of 1,242 patients were randomized to receive one of seven regimens of oral milvexian given twice or once-daily or to receive 40 mg of subcutaneous enoxaparin once-daily. The assignment to milvexian or enoxaparin was open label, but the milvexian dose assignment was blinded. Treatment was given for 10-14 days. More information can be found on www.clinicaltrials.gov (NCT03891524).

About Milvexian*

Milvexian is a potential first-in-class oral factor XIa (FXIa) inhibitor (anti-thrombotic) for the prevention and treatment of major thrombotic conditions. Phase 2 TKR data, complementing human genetic, epidemiologic, and preclinical evidence, now provide further support for the hypothesis that inhibiting FXIa can reduce the risk of vascular events without increasing the risk of bleeding. The milvexian Phase 2 clinical trial program consists of two Phase 2 studies: AXIOMATIC-TKR (NCT03891524) evaluating milvexian in TKR surgery and AXIOMATIC-SSP (NCT03766581) evaluating milvexian for secondary stroke prevention (SSP).

*Milvexian is an investigational agent and has not been approved for use in any country, for any indication.

About The Bristol Myers Squibb-Janssen Collaboration

Bristol Myers Squibb and Janssen Pharmaceuticals, Inc., two leaders in thrombosis treatment and care, are collaborating to develop and commercialize milvexian, a potentially first-in-class oral factor XIa (FXIa) inhibitor, with the goal of improving upon the benefit-risk profile of existing anticoagulants. With extensive expertise and unparalleled leadership in cardiovascular treatments spanning decades, Bristol Myers Squibb and Janssen share a long-standing commitment to improving treatment options for patients with life-threatening cardiovascular conditions.

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology and Pulmonary Hypertension.

Learn more at https://www.janssen.com/. Follow us at @JanssenGlobal. Janssen Research & Development, LLC is one of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding milvexian. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC, any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 3, 2021, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

[i] Dr. Weitz is affiliated with McMaster University, and was provided payment for his participation in the Phase 2 AXIOMATIC-TKR clinical trial.