News Release

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Late-Breaking Data at ACC.21 Show XARELTO® (rivaroxaban) Plus Aspirin Significantly Reduced Total Ischemic Events in Peripheral Artery Disease (PAD) Patients After Lower-Extremity Revascularization

Phase 3 VOYAGER PAD is the first investigational study in 20 years to highlight the benefit of long-term treatment in these high-risk patients

Data add to growing body of evidence on the role of dual pathway inhibition in targeting both thrombin generation and platelets

RARITAN, N.J., May 16, 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson today presented new data from the Phase 3 VOYAGER PAD study which showed XARELTO® (rivaroxaban) (2.5 mg twice daily) in combination with aspirin (100 mg once daily) consistently reduced severe vascular events in patients with peripheral artery disease (PAD) after lower-extremity revascularization (LER) compared to aspirin alone regardless of whether it was the first, second, third, or subsequent event. The primary results of VOYAGER PAD showed that XARELTO® plus aspirin reduced first events by 15 percent among patients with PAD after LER. This

analysis showed a very high burden of subsequent events and a consistent 14 percent reduction in both primary endpoint events and total vascular events over a median of 2.5 years. These data were presented as a late-breaking presentation during the virtual American College of Cardiology's 70th Annual Scientific Session (ACC.21) and simultaneously published in the *Journal of the American College of Cardiology*.

PAD is a chronic circulatory condition which causes blood vessels to narrow, thereby reducing blood flow to the limbs, most often the legs.[1] An estimated 20 million Americans are living with PAD, but only 8.5 million are currently diagnosed.[2] While usually starting as asymptomatic, PAD symptoms can progress to severe and require revascularization to avoid amputation.

"Even years after revascularization, patients with PAD continue to have a markedly high-risk for future thrombotic events due to excessive thrombin generation and platelet aggregation," said Marc P. Bonaca*, M.D., Department of Medicine, Division of Cardiovascular Medicine, University of Colorado Anschutz Medical Campus, Aurora, Colorado. "This analysis from VOYAGER PAD looked beyond the first event and found subsequent thrombotic event reduction with rivaroxaban plus aspirin, underscoring the importance of long-term prevention in these high-risk patients."

CLICK TO TWEET: Late-breaking data at #ACC21 offer insights on long-term prevention of future thrombotic events in patients with #PAD after lower-extremity revascularization. Full @JanssenUS press release here: https://bit.ly/33sm1yt

In addition to evaluating the time to first event, this sub-analysis from VOYAGER PAD also evaluated thrombotic events that occurred after the first event. Specifically, it showed XARELTO® plus aspirin significantly reduced total primary endpoint events (acute limb ischemia, major amputation for vascular causes, non-fatal myocardial infarction, non-fatal ischemic stroke, or death from vascular causes) compared to aspirin alone (Hazard Ratio (HR)=0.86, 95% Confidence Internal (CI) 0.75 to 0.98; p=0.02). The XARELTO® plus aspirin regimen also significantly reduced total vascular

events (all primary endpoints plus subsequent peripheral revascularizations of both index and contralateral leg and venous thromboembolic events) compared to aspirin alone (HR 0.86, 95% CI 0.79 to 0.95; p=0.003). No significant increase in Thrombolysis in Myocardial Infarction (TIMI) major bleeding was observed in the VOYAGER PAD study in patients treated with XARELTO® plus aspirin compared to aspirin alone (2.65% vs. 1.87% respectively; HR=1.43, 95% CI, 0.97–2.10; p=0.07).

"The VOYAGER PAD trial is the first and only study of antithrombotic therapy in the past 20 years to demonstrate a significant benefit in patients with peripheral artery disease after lower-extremity revascularization," said James List, M.D., Ph.D., Global Therapeutic Area Head, Cardiovascular & Metabolism, Janssen Research & Development, LLC. "With these new data, we now have a full picture of evidence demonstrating the potential of XARELTO® in treating patients through various stages of peripheral artery disease - chronic, symptomatic, those requiring revascularization and beyond."

On October 26, 2020, Janssen announced the submission of a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration to expand the use of XARELTO® in patients with PAD to include reducing the risk of major thrombotic vascular events, such as heart attack and amputation, in symptomatic patients after recent LER. XARELTO® is currently approved in combination with aspirin to reduce the risk of major cardiovascular (CV) events (CV death, myocardial infarction and stroke) in patients with chronic coronary artery disease (CAD) or PAD.

About VOYAGER PAD

The Phase 3 VOYAGER PAD study included 6,564 patients from 542 sites across 34 countries worldwide. Patients were randomized in a 1:1 ratio and received either XARELTO® (2.5 mg twice daily) plus aspirin (100 mg once daily) (n=3,286) or aspirin alone (100 mg once daily) (n=3,278). Patients were stratified by revascularization procedure type (endovascular vs. surgical) and use of clopidogrel, which was administered at the treating physician's discretion. Patients were followed for a median of 28 months.

The primary efficacy endpoint was a composite of major adverse limb and cardiovascular (CV) events, including acute limb ischemia, major amputation for vascular causes, heart attack (myocardial infarction), ischemic stroke, or death from CV causes. Additional prespecified categories of vascular events included subsequent peripheral revascularizations of both index and contralateral leg and venous thromboembolic events. The principal safety endpoint was major bleeding according to the TIMI classification.

IMPORTANT SAFETY INFORMATION

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT XARELTO®?

XARELTO® may cause serious side effects, including:

- **Increased risk of blood clots if you stop taking XARELTO®.** People with atrial fibrillation (an irregular heart beat) that is not caused by a heart valve problem (nonvalvular) are at an increased risk of forming a blood clot in the heart, which can travel to the brain, causing a stroke, or to other parts of the body. XARELTO® lowers your chance of having a stroke by helping to prevent clots from forming. If you stop taking XARELTO®, you may have increased risk of forming a clot in your blood.

Do not stop taking XARELTO® without talking to the doctor who prescribes it for you. Stopping XARELTO® increases your risk of having a stroke. If you have to stop taking XARELTO®, your doctor may prescribe another blood thinner medicine to prevent a blood clot from forming.

- **Increased risk of bleeding.** XARELTO® can cause bleeding which can be serious, and may lead to death. This is because XARELTO® is a blood thinner medicine (anticoagulant) that lowers blood clotting. During treatment with XARELTO® you are likely to bruise more easily, and it may take longer for bleeding to stop. You may be at higher risk of bleeding if you take XARELTO® and have certain other medical problems.

You may have a higher risk of bleeding if you take XARELTO® and take other medicines that increase your risk of bleeding, including:

- Aspirin or aspirin-containing products
- Long-term (chronic) use of non-steroidal anti-inflammatory drugs (NSAIDs)
- Warfarin sodium (Coumadin®, Jantoven®)
- Any medicine that contains heparin

- Clopidogrel (Plavix®)
- Selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs)
- Other medicines to prevent or treat blood clots

Tell your doctor if you take any of these medicines. Ask your doctor or pharmacist if you are not sure if your medicine is one listed above.

Call your doctor or get medical help right away if you develop any of these signs or symptoms of bleeding:

- Unexpected bleeding or bleeding that lasts a long time, such as:
  - Nosebleeds that happen often
  - Unusual bleeding from gums
  - Menstrual bleeding that is heavier than normal, or vaginal bleeding
- Bleeding that is severe or you cannot control
- Red, pink, or brown urine
- Bright red or black stools (looks like tar)
- Cough up blood or blood clots
- Vomit blood or your vomit looks like "coffee grounds"
- Headaches, feeling dizzy or weak
- Pain, swelling, or new drainage at wound sites

- **Spinal or epidural blood clots (hematoma).** People who take a blood thinner medicine (anticoagulant) like XARELTO®, and have medicine injected into their spinal and epidural area, or have a spinal puncture, have a risk of forming a blood clot that can cause long-term or permanent loss of the ability to move (paralysis). Your risk of developing a spinal or epidural blood clot is higher if:
  - A thin tube called an epidural catheter is placed in your back to give you certain medicine
  - You take NSAIDs or a medicine to prevent blood from clotting
  - You have a history of difficult or repeated epidural or spinal punctures
  - You have a history of problems with your spine or have had surgery on your spine

If you take XARELTO® and receive spinal anesthesia or have a spinal puncture, your doctor should watch you closely for symptoms of spinal or epidural blood clots. Tell your doctor right away if you have back pain, tingling, numbness, muscle weakness (especially in your legs and feet), or loss of control of the bowels or bladder (incontinence).

XARELTO® is not for use in people with artificial heart valves.

XARELTO® is not for use in people with antiphospholipid syndrome (APS), especially with positive triple antibody testing.

Do not take XARELTO® if you:

- Currently have certain types of abnormal bleeding. Talk to your doctor before taking XARELTO® if you currently have unusual bleeding.
- Are allergic to rivaroxaban or any of the ingredients of XARELTO®.

Before taking XARELTO®, tell your doctor about all your medical conditions, including if you:

- Have ever had bleeding problems
- Have liver or kidney problems
- Have antiphospholipid syndrome (APS)
- Are pregnant or plan to become pregnant. It is not known if XARELTO® will harm your unborn baby.
    - Tell your doctor right away if you become pregnant during treatment with XARELTO®. Taking XARELTO® while you are pregnant may increase the risk of bleeding in you or in your unborn baby.
    - If you take XARELTO® during pregnancy, tell your doctor right away if you have any signs or symptoms of bleeding or blood loss. **See "What is the most important information I should know about XARELTO®?" for signs and symptoms of bleeding.**
- Are breastfeeding or plan to breastfeed. XARELTO® may pass into your breast milk. Talk to your doctor about the best way to feed your baby during treatment with XARELTO®.

Tell all of your doctors and dentists that you are taking XARELTO®. They should talk to the doctor who prescribed XARELTO® for you before you have any surgery, medical or dental procedure.

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

Some of your other medicines may affect the way XARELTO® works, causing side effects. Certain medicines may increase your risk of bleeding. **See "What is the most important information I should know about XARELTO®?"**

HOW SHOULD I TAKE XARELTO®?

- Take XARELTO® exactly as prescribed by your doctor.
- **Do not change your dose or stop taking XARELTO® unless your doctor tells you to.** Your doctor may change your dose if needed.
- Your doctor will decide how long you should take XARELTO®.
- XARELTO® may need to be stopped for one or more days before any surgery or medical or dental procedure. Your doctor will tell you when to stop taking XARELTO® and when to start taking XARELTO® again after your surgery or procedure.
- If you need to stop taking XARELTO® for any reason, talk to the doctor who prescribed XARELTO® to you to find out when you should stop taking it. Do not

stop taking XARELTO® without first talking to the doctor who prescribes it to you.

- If you have difficulty swallowing XARELTO® tablets whole, talk to your doctor about other ways to take XARELTO®.
- Do not run out of XARELTO®. Refill your prescription of XARELTO® before you run out. When leaving the hospital following a hip or knee replacement, be sure that you will have XARELTO® available to avoid missing any doses.
- If you take too much XARELTO®, go to the nearest hospital emergency room or call your doctor right away.

If you take XARELTO® for:

- **Atrial Fibrillation that is not caused by a heart valve problem:**
  - Take XARELTO® **1 time a day with your evening meal.**
  - If you miss a dose of XARELTO®, take it as soon as you remember on the same day. Take your next dose at your regularly scheduled time.
- **Blood clots in the veins of your legs or lungs:**
  - Take XARELTO® **1 or 2 times a day** as prescribed by your doctor.
  - For the **10-mg dose**, XARELTO® **may be taken with or without food.**
  - For the **15-mg and 20-mg doses**, take XARELTO® **with food at the same time each day.**
  - If you miss a dose:
    - **If you take the 15-mg dose of XARELTO® 2 times a day (a total of 30 mg of XARELTO® in 1 day):** Take XARELTO® as soon as you remember on the same day. You may take 2 doses at the same time to make up for the missed dose. Take your next dose at your regularly scheduled time.
    - **If you take XARELTO® 1 time a day:** Take XARELTO® as soon as you remember on the same day. Take your next dose at your regularly scheduled time.
- **Hip or knee replacement surgery:**
  - Take XARELTO® 1 time a day with or without food.
  - If you miss a dose of XARELTO®, take it as soon as you remember on the same day. Take your next dose at your regularly scheduled time.
- **Blood clots in people hospitalized for an acute illness:**
  - Take XARELTO® 1 time a day, with or without food, while you are in the hospital and after you are discharged as prescribed by your doctor.
  - If you miss a dose of XARELTO®, take it as soon as you remember on the same day. Take your next dose at your regularly scheduled time.

- **Reducing the risk of serious heart problems, heart attack and stroke in coronary artery disease or peripheral artery disease:**
  - Take XARELTO® 2.5 mg 2 times a day with or without food.
  - If you miss a dose of XARELTO®, take your next dose at your regularly scheduled time.
  - Take aspirin 75 to 100 mg once daily as instructed by your doctor.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF XARELTO®?

XARELTO® may cause serious side effects:

- See **"What is the most important information I should know about XARELTO®?"**

The most common side effect of XARELTO® was bleeding.

Call your doctor for medical advice about side effects. **You may report side effects to the FDA at 1-800-FDA-1088.** You may also report side effects to Janssen Pharmaceuticals, Inc., at 1-800-JANSSEN (1-800-526-7736).

Please read full Prescribing Information, including Boxed Warnings, and Medication Guide for XARELTO®.

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Janssen and Bayer together are developing rivaroxaban. For more information about XARELTO®, visit www.xarelto.com.

About Janssen Cardiovascular & Metabolism

In Cardiovascular & Metabolism (CVM), we take on the most pervasive diseases that burden hundreds of millions of people and healthcare systems around the world. As part of this long-standing commitment and propelled by our successes in treating type 2 diabetes and thrombosis, we advance highly differentiated therapies that prevent and treat life-threatening cardiovascular, metabolic and retinal diseases. Uncovering new therapies that can improve the quality of life for this large segment of the population is an important endeavor – one which Janssen CVM will continue to lead in the years to come. Our mission is global, local and personal. Together, we can reshape the future of cardiovascular, metabolic and retinal disease prevention and treatment. Please visit www.janssen.com/cardiovascular-and-metabolism.

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 www.janssen.com. Follow us at www.twitter.com/JanssenUS and www.twitter.com/JanssenGlobal. Janssen Research & Development, LLC, is part 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 rivaroxaban. 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.

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1. American Heart Association. About Peripheral Artery Disease (PAD). Retrieved April 29, 2021 from https://www.heart.org/en/health-topics/peripheral-artery-disease/about-peripheral-artery-disease-pad
2. American Heart Association. Peripheral Artery Disease (PAD) Resources For Patients and Providers. Retrieved April 29, 2021 from https://www.heart.org/en/health-topics/peripheral-artery-disease/pad-resources

*CPC Clinical Research was provided a grant for their participation in the Phase 3 VOYAGER PAD clinical trial.