Media Contacts:
Leal Morehouse
Phone: (617) 487-3060
Lmorehou@its.jnj.com

Joy-Lee Pasqualoni
Phone: (917) 547-8078
Lpasqua7@its.jnj.com

Investor Relations:
Raychel Kruper
investor.relations@its.jnj.com

New VOYAGER PAD Analyses Reinforce Benefit of XARELTO® (rivaroxaban) Plus Aspirin Across High-Risk and Complex Patient Populations with Peripheral Artery Disease (PAD)

Data presentations at AHA 2023 Meeting reinforce treatment with XARELTO® plus aspirin consistently reduces major cardiovascular events (MACE) as well as major adverse limb events (MALE) in complex patients with PAD

Janssen continues commitment to supporting PAD patients with ongoing research to help understand this undertreated and underdiagnosed disease[1]

TITUSVILLE, NJ, November 14, 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced data from two new analyses from the Phase 3 VOYAGER PAD clinical trial reinforcing the benefit of XARELTO® (rivaroxaban [2.5 mg twice daily plus aspirin 100 mg once daily]) over standard of care (aspirin alone). Data from the two analyses demonstrate the role of XARELTO® in treating both high-risk and fragile patients and those with and without comorbid coronary artery diseases (CAD). Results were presented at the American Heart Association's (AHA) 2023 Scientific Sessions, hosted in Philadelphia, Pennsylvania, November 11-13, 2023.

"These analyses reinforce the consistency of the favorable benefit-risk profile of XARELTO® plus aspirin for patients with vascular disease, regardless of comorbidity. For example, patients categorized as 'fragile' are often undertreated due to concerns about benefit-risk, particularly with antithrombotic treatments," said Marc P. Bonaca*, M.D., Department of Medicine, Division of Cardiovascular Medicine, University of Colorado Anschutz Medical Campus, Aurora, Colorado. "We hope the ongoing wealth of data coming from VOYAGER PAD presented at AHA offers clinicians the information they need to support shared decision-making in prescribing XARELTO® plus aspirin as the standard of care for their PAD patients, including those who are high-risk or complex."

Impact of XARELTO® plus Aspirin on Total Vascular Events in Fragile Patients with PAD

Fragile patients with PAD can be at a heightened risk for MALE, defined as a composite of acute limb ischemia (ALI) and major amputation. In this analysis, fragile patients are defined as age greater than 75 years, or weight less than 50 kg or baseline eGFR less than 50 mL/min/1.73^2. XARELTO® plus aspirin (2.5 mg twice daily plus aspirin 100 mg once daily) was shown to be effective in reducing the occurrence of MALE in both fragile and non-fragile patients, compared to placebo (aspirin alone). In fragile patients treated with XARELTO® plus aspirin, 6.2% of patients experienced a MALE compared to 10.3% of patients treated with placebo. In non-fragile patients, 7.9% of patients treated with XARELTO® plus aspirin experienced a MALE compared to 9.7% of patients treated with placebo.

XARELTO® plus aspirin also reduced the occurrence of total vascular events in fragile patients over time, with an absolute rate of 82.1 events per 100 patients at three years compared to 99.3 events per 100 patients in those treated with placebo at three years. A similar benefit was also seen in non-fragile patients, with a rate of 70.4 events per 100 patients at three years in those treated with XARELTO® plus aspirin compared to 81.6 events per 100 patients in those treated with placebo at three years. Importantly, thrombolysis in myocardial infarction (TIMI) major

bleeding was consistent in both the fragile and non-fragile treatment groups. XARELTO® plus aspirin demonstrated a consistent, numerical increase in TIMI major bleeding for both the fragile (HR 1.66; 95% CI 0.87-3.19) and the non-fragile (HR 1.37; 95% CI 0.83-2.24, p-interaction 0.65) patients.

Role of XARELTO® Plus Aspirin on Myocardial Infarction in Patients with PAD with and without Concomitant CAD Following Lower Extremity Revascularization (LER)

Following LER, patients with PAD are four times more likely to experience acute limb ischemia, or a rapid decrease in lower limb blood flow, which is often associated with long hospitalizations and high incidences of amputation, disability, and death unless appropriate treatment is given.[2] Patients with PAD are also at a heightened risk of MACE, defined as myocardial infarction (MI), ischemic stroke, or cardiovascular death. In this analysis, 14.1% of patients with PAD and CAD treated with XARELTO® plus aspirin experienced a MACE versus 17.6% of patients treated with placebo (aspirin alone). In patients with PAD only, 11% of patients treated with XARELTO® plus aspirin experienced a MACE versus 9.8% of patients treated with placebo. Overall, XARELTO® plus aspirin showed a consistent benefit in reducing MACE in patients with and without CAD.

In this analysis, patients with CAD (HR 2.23; CI 1.10-4.53) and patients without CAD (HR 1.15; CI 0.72-1.84) had higher rates of TIMI major bleeding with XARELTO® plus aspirin compared to placebo plus aspirin. The rates of intracerebral hemorrhage (ICH) and fatal bleeding were similar across both patient groups. Overall, the safety of XARELTO® plus aspirin in patients with PAD was consistent regardless of CAD with no significant interactions.

"At Janssen, we work tirelessly to bring the latest research and clinical practice insights to healthcare providers and their patients to help improve cardiovascular care for all," said Avery Ince, M.D., Ph.D., Vice President, Medical Affairs, Cardiovascular & Metabolism, Janssen Scientific Affairs, LLC. "These new findings

continue to support the use of XARELTO® with its positive benefit-risk profile in many types of patients, including those who are high-risk and considered harder to treat."

In August 2021, the U.S. Food and Drug Administration (FDA) approved an expanded PAD indication for XARELTO® (2.5 mg twice daily plus aspirin 75 - 100 mg once daily) to include patients following a recent LER due to symptomatic PAD. XARELTO® acts on a dual pathway inhibition (DPI) approach to target both clotting mechanisms, thrombin and platelet activation.

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 the XARELTO® (rivaroxaban [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 VOYAGER PAD study met its primary efficacy and principal safety endpoints, demonstrating the XARELTO® plus aspirin was superior to aspirin alone in reducing the risk of major adverse limb and cardiovascular events (composite outcome of acute limb ischemia, major amputation for vascular causes, myocardial infarction, ischemic stroke, or cardiovascular death) by 15 percent in patients with symptomatic PAD after lower-extremity revascularization. The benefit of adding XARELTO® to aspirin was apparent early, was consistent among major subgroups and continued to accrue over time. There was no significant increase in thrombolysis in myocardial infarction (TIMI) major bleeding observed in patients treated with the XARELTO® plus aspirin compared to aspirin alone (Kaplan-Meier estimate at three years 2.65% vs. 1.87%, respectively).

About XARELTO® (rivaroxaban)

XARELTO® is a prescription medicine used to:

- reduce the risk of stroke and blood clots in adults who have a medical condition called atrial fibrillation that is not caused by a heart valve problem. With atrial fibrillation, part of the heart does not beat the way it should. This can lead to the formation of blood clots, which can travel to the brain, causing a stroke, or to other parts of the body
- treat blood clots in the veins of your legs (deep vein thrombosis or DVT) or lungs (pulmonary embolism or PE)
- reduce the risk of blood clots from happening again in adults who continue to be at risk for DVT or PE after receiving treatment for blood clots for at least 6 months
- help prevent a blood clot in the legs and lungs of adults who have just had hip or knee replacement surgery
- help prevent blood clots in certain adults hospitalized for an acute illness and after discharge, who are at risk of getting blood clots because of the loss of or decreased ability to move around (mobility) and other risks for getting blood clots, and who do not have a high risk of bleeding

XARELTO® is used with low dose aspirin to:

- reduce the risk of serious heart problems, heart attack and stroke in adults with coronary artery disease (a condition where the blood supply to the heart is reduced or blocked)
- reduce the risk of a sudden decrease in blood flow to the legs, major amputation, serious heart problems or stroke in adults with peripheral artery disease (a condition where the blood flow to the legs is reduced) and includes adults who have recently had a procedure to improve blood flow to the legs

XARELTO® is used in children to:

- treat blood clots or reduce the risk of blood clots from happening again in children from birth to less than 18 years, after receiving at least 5 days of treatment with injectable or intravenous medicines used to treat blood clots
- help prevent blood clots in children 2 years and older with congenital heart disease after the Fontan procedure

XARELTO® was not studied and is not recommended in children less than 6 months of age who:

- were less than 37 weeks of growth (gestation) at birth
- had less than 10 days of oral feeding, **or**
- had a body weight of less than 5.7 pounds (2.6 kg)

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 or your child 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 or your child:

- 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 or your child:

- 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.
    - Females who are able to become pregnant: Talk with your doctor about pregnancy planning during treatment with XARELTO®. Talk with your doctor about your risk for severe uterine bleeding if you are treated with blood thinner medicines, including XARELTO®.
    - 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 or your child 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 or your child 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:**
  - 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.

- **Reducing the risk of a sudden decrease in blood flow to the legs, major amputation, serious heart problems or stroke in people with peripheral artery disease, including those who have recently had a procedure to improve blood flow to the legs:**
  - 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.

For children who take XARELTO®:

- The dose of XARELTO® depends on your child's body weight and will be calculated by your child's doctor. Your child's doctor will tell you if XARELTO® can be given to your child with or without food.
- The adult caregiver should give the dose.
- If your child is taking the tablet, the tablet should be taken whole and should not be split in an attempt to provide a lower dose of XARELTO®.
- If your child is taking the oral suspension, use the syringes provided in the original carton. The suspension will be prepared by the pharmacy. See the **Instructions for Use** included in the carton on how to properly give a dose of XARELTO® oral suspension to your child.
- Do not switch between the XARELTO® oral suspension or tablet without first talking to your doctor.
- If your child vomits or spits up:
  - right after or within 30 minutes of taking the oral suspension, give a new full dose.
  - more than 30 minutes after taking the oral suspension, do not give the dose again. Give the next dose at the regularly scheduled time.
  - if vomiting or spitting up persists, contact your child's doctor right away.
- If your child misses a dose:
  - If your child is taking XARELTO® 1 time a day, give the dose as soon as you remember on the same day. If this is not possible, skip this dose and give the next dose at the regularly scheduled time.
  - If your child is taking XARELTO® 2 times a day, give the missed morning dose as soon as you remember. You may give the missed morning dose together with the evening dose. However, a missed evening dose can only be taken in the same evening.
  - If your child is taking XARELTO® 3 times a day, skip the missed dose and give the next dose at the regularly scheduled time.

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® in adults was bleeding.

The most common side effects of XARELTO® in children include:

- bleeding
- vomiting
- cough
- inflamed stomach and gut

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®.

Trademarks are those of their respective owners. Janssen and Bayer together are developing rivaroxaban.

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: Oncology, Immunology, Neuroscience, Cardiovascular, Pulmonary Hypertension and Retina.

Learn more at www.janssen.com. Follow us at @JNJInnovMed and @JanssenUS

Janssen Scientific Affairs, LLC, is a Johnson & Johnson company.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of 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 Scientific Affairs, LLC 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 1, 2023, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other 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 Janssen Scientific Affairs, LLC nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

References

1. Afzal N, Sohn S, Scott CG, Liu H, Kullo IJ, Arruda-Olson AM. Surveillance of Peripheral Arterial Disease Cases Using Natural Language Processing of Clinical Notes. *AMIA Jt Summits Transl Sci Proc*. 2017;2017:28-36. Accessed October 20, 2023. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5543345/#r2-2609862.
2. Beckman, JA, Schneider PA, Conte MS. Advances in revascularization for peripheral artery disease: revascularization in PAD. *Circ Res.* 2021;128.12: 1885-1912. Accessed October 27, 2023. https://www.ahajournals.org/doi/full/10.1161/CIRCRESAHA.121.318261

###

*Dr. Marc Bonaca is the lead study author of the VOYAGER PAD analysis entitled "Impact of Low-dose Rivaroxaban plus Aspirin on Total Vascular Events in Fragile Patients with Peripheral Artery Disease: Insights from VOYAGER PAD" and "Impact of Low-dose Rivaroxaban plus Aspirin on Myocardial Infarction in Patients with Peripheral Artery Disease with and without Concomitant Coronary Artery Disease: Insights from VOYAGER PAD," and was provided payment for his participation in the study; he has not been compensated for contributing to this press release.

