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Media contact:
Leal Morehouse
lmorehou@its.jnj.com
617-487-3060

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

Findings Presented at ACC.24 Showed XARELTO® (rivaroxaban) Reduced the Risk of Clinically Significant Bleeding and Net Adverse Clinical Events or Rehospitalization

New exploratory analysis demonstrates consistent results of XARELTO® in treating elderly and non-elderly patients with nonvalvular atrial fibrillation undergoing percutaneous coronary intervention

XARELTO® is one of the most studied oral anticoagulants, and has been prescribed to more than 10 million patients in the United States

NEW BRUNSWICK, NJ (April 8, 2024) – Johnson & Johnson announced today a new analysis of data from the PIONEER AF-PCI clinical trial demonstrating that XARELTO® (rivaroxaban) was associated with a reduced risk of clinically significant bleeding (CSB), and net adverse clinical events (NACE; a composite of clinically significant bleeding [CSB] or major adverse cardiovascular event [MACE]) or rehospitalization compared to warfarin among both elderly and non-elderly patients with nonvalvular atrial fibrillation (AF) undergoing percutaneous coronary intervention (PCI), a nonsurgical procedure designed to relieve narrowing or occlusion of the coronary artery.[1,2] These data were featured in an oral presentation yesterday at the American College of Cardiology 73rd Annual Scientific Session & Expo (ACC.24) in Atlanta, Georgia (Abstract #906-04).

“Despite advances in cardiovascular care, patients with nonvalvular AF continue to be at risk of potentially life-threatening cardiovascular events, especially older patients considered difficult to treat due to multiple factors, including age and co-morbidities,” said C. Michael Gibson*, M.D., CEO, of the nonprofit Baim Institute and professor of Medicine, Harvard Medical School. “A significant challenge in managing nonvalvular AF in older individuals undergoing PCI is determining a treatment that balances the prevention of stroke with the risk for bleeding. Results from the PIONEER AF-PCI trial reinforce the need to continue to research this complex and fragile elderly patient population.”

The PIONEER AF-PCI exploratory trial enrolled 2,124 patients with nonvalvular AF undergoing PCI, of whom 729 (34.3%) were elderly.[1,3] Patients were randomized to either rivaroxaban- or warfarin-based antithrombotic regimens.[1,3] The data analysis demonstrated a reduced rate of CSB among both elderly (≥75 years) and non-elderly (<75) patients with nonvalvular AF undergoing PCI treated with XARELTO® compared to warfarin.[1] Elderly patients treated with XARELTO® had a lower rate of CSB at 12 months compared to those treated with warfarin (21.3% vs 31.4%; hazard ratio [HR], 0.64; 95% confidence interval [CI], 0.46-0.88; P=0.005; number needed to treat [NNT]=10).[1] The reduction in CSB was consistent among non-elderly patients treated with XARELTO® compared to warfarin (15.3% vs 24.6%; HR, 0.58; 95% CI, 0.45-0.75; P<0.001; NNT=11; interaction P=0.676).[1]

The analysis also showed XARELTO® treatment was associated with a lower risk of NACE or rehospitalization in both elderly (HR, 0.77; 95% CI, 0.62-0.96) and non-elderly patients (HR, 0.69; 95% CI, 0.58-0.82; interaction P=0.435), primarily driven by a lower risk of CSB.[1] In addition, the rates of major bleeding were lower in patients treated with XARELTO® compared to warfarin in both elderly (3.7% vs 5.2%; HR, 0.71; 95% CI, 0.33-1.55) and non-elderly (1.1% vs 2.5%; HR, 0.45; 95% CI, 0.18-1.10) patients.[1] Patients treated with XARELTO® also experienced lower rates of minor bleeding compared to warfarin in both elderly (1.4% vs 3.8%; HR, 0.36; 95% CI, 0.12-1.07) and non-elderly (1.0% vs 1.4%; HR, 0.67; 95% CI, 0.23-1.92) patients.[1]

“At Johnson & Johnson, we are committed to driving innovation that can improve outcomes for all patients,” said Avery Ince, M.D., Ph.D., Vice President, Medical Affairs, Cardiovascular & Metabolism, Johnson & Johnson. “With this new exploratory analysis at ACC.24, we’re pleased to bring the latest research to healthcare providers that adds to the growing body of clinical evidence in older adults.”

About PIONEER AF-PCI

PIONEER AF-PCI was an international, multi-center, randomized, open-label clinical trial evaluating the safety of rivaroxaban compared to warfarin for the treatment of patients at least 18 years of age with paroxysmal, persistent, or permanent nonvalvular AF who had undergone PCI with stent placement. In the trial, 2,124 participants with nonvalvular atrial fibrillation who had undergone PCI with stenting received, in a 1:1:1 ratio, low-dose rivaroxaban (15 mg once daily) plus a $P2Y_{12}$

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inhibitor for 12 months (group 1), low-dose rivaroxaban (2.5 mg twice daily) plus DAPT for 1, 6, or 12 months (group 2), or standard therapy with a dose-adjusted vitamin K antagonist (once daily) plus DAPT for 1, 6, or 12 months (group 3).

The primary safety endpoint was the occurrence of clinically significant bleeding, a composite of major bleeding or minor bleeding according to Thrombolysis in Myocardial Infarction (TIMI) criteria or bleeding requiring medical attention during the treatment period (which was defined as the time from the first administration of a trial drug to 2 days after the trial drugs were discontinued, through 12 months of therapy). Secondary endpoints included the incidence of each component of the primary safety endpoint, as well as the following efficacy endpoints: the occurrence of a major adverse cardiovascular event (a composite of death from cardiovascular causes, myocardial infarction, or stroke), each component of the major adverse cardiovascular event endpoint, and stent thrombosis.[3]

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

FDA approved dosing for patients with nonvalvular AF is 20 mg once daily with an evening meal in patients with CrCl >50 mL/min. For patients with moderate to severe renal impairment (CrCl ≤50 mL/min), the FDA approved dosing is 15 mg once daily with an evening meal.

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®)

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- 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.

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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.

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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:

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- **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®.

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- 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®.

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About Johnson & Johnson

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow, and profoundly impact health for humanity.

Learn more at https://www.jnj.com/ or at www.janssen.com/johnson-johnson-innovative-medicine. Follow us at @JanssenUS and @JNJInnovMed.

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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 Research & Development, LLC, Janssen Biotech, Inc., Janssen Pharmaceuticals, Inc. 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 December 31, 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 Research & Development, LLC, Janssen Biotech, Inc., Janssen Pharmaceuticals, Inc. nor Johnson & Johnson undertake to update any forward-looking statement as a result of new information or future events or developments.

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1 Chi G, Allaham L, Molina AC, et. al. Effect of Rivaroxaban on Bleeding or Ischemic Event and Rehospitalization Among Elderly or Non-Elderly Patients with Atrial Fibrillation Undergoing Percutaneous Coronary Intervention: Insights from the PIONEER AF-PCI Trial. American College of Cardiology 2024 Scientific Session. April 2024. Abstract 906-04. Accessed February 15, 2024. Available at: https://www.abstractsonline.com/pp8/#!/10973/presentation/12157.

2 Ahmad M, Mehta P, Reddivari AKR, at al. National Library of Medicine. Percutaneous Coronary Intervention. StatPearls Publishing. 2023 Jun. Accessed February 15, 2024. Available at: https://www.ncbi.nlm.nih.gov/books/NBK556123/.

3 Gibson CM, Mehran R, Bode C, et al. Prevention of bleeding in patients with atrial fibrillation undergoing PCI. *N Engl J Med*. 2016;375(25):2423-2434. doi: 10.1056/NEJMoa1611594.

**Dr. C. Michael Gibson is author of the PIONEER AF-PCI analysis titled, "Effect of Rivaroxaban on Bleeding or Ischemic Event and Rehospitalization Among Elderly or Non-Elderly Patients with Atrial Fibrillation Undergoing Percutaneous Coronary Intervention: Insights from the PIONEER AF-PCI Trial," and was provided payment for his participation in the study; he has not been compensated for contributing to this press release.*