U.S. FDA Grants Priority Review of XARELTO® (rivaroxaban) sNDA for a 10 mg Dose to Reduce the Risk of Recurrent Venous Thromboembolism (VTE)

*XARELTO® is the only NOAC to show superiority over aspirin with comparable rates of major bleeding in reducing the risk of recurrent VTEs after initial treatment*

*Approval of 10 mg dose would provide physicians another option to customize patient treatment plans*

RARITAN, NJ (June 28, 2017) – Janssen Research & Development, LLC announced today the U.S. Food and Drug Administration (FDA) accepted for Priority Review a supplemental New Drug Application (sNDA) for XARELTO® (rivaroxaban) to include a 10 mg once-daily dose for reducing the risk of VTE after at least six months of standard anticoagulant therapy. This application is based on data from EINSTEIN CHOICE, which is the only study to find a non-vitamin K antagonist oral anticoagulant (NOAC), specifically two doses of XARELTO® (10 mg and 20 mg), to be superior to aspirin in reducing the risk of recurrent VTE, with comparable rates of major bleeding.

VTE includes deep vein thrombosis (DVT), a blood clot in a deep vein (often in the legs), and pulmonary embolism (PE), a clot that travels to the lung. Once anticoagulant therapy is...
stopped, up to 10 percent of people will experience a recurrence during the first year and up to 20 percent within three years.\textsuperscript{\textit{i}}

"The FDA's acceptance of our sNDA for priority review marks another important step toward a potential shift in how people with VTE are managed over time," said Paul Burton, MD, PhD, FACC, Vice President, Medical Affairs, Janssen. "We are pleased the FDA sees the urgency in offering the choice of a 10 mg dose of XARELTO\textsuperscript{\textregistered} or the currently approved 20 mg dose. This will broaden the physician’s ability to customize treatment plans based on the needs of each patient."

The FDA grants Priority Review to medicines that may offer significant improvements in the treatment, diagnosis or prevention of a serious condition. This designation shortens the review period to six months compared to 10 months for Standard Review. This accelerated review advances the FDA’s Prescription Drug User Fee Act (PDUFA) target date to October 28, 2017.

Data from the EINSTEIN CHOICE study support this sNDA. This phase 3, global, randomized, double-blind, superiority study met its primary efficacy endpoint, finding both XARELTO\textsuperscript{\textregistered} doses (10 mg and 20 mg) to be superior to aspirin in reducing the risk of recurrent VTE following at least a 6 months of standard anticoagulation therapy. Specifically, XARELTO\textsuperscript{\textregistered} 10 mg reduced the risk of recurrent VTE by 74 percent and XARELTO\textsuperscript{\textregistered} 20 mg by 66 percent. All three treatment groups had low rates of major bleeding.\textsuperscript{\textit{iii}}

XARELTO\textsuperscript{\textregistered} currently has six indications approved by the FDA, including the treatment of VTE (15 mg twice daily for the first 21 days followed by 20 mg once daily for the remainder of treatment), and reduction in the risk of recurrent VTE (20 mg once daily).

**About EINSTEIN CHOICE**

Patients enrolled in EINSTEIN CHOICE had confirmed DVT or PE and were treated initially with standard anticoagulant therapy for six to 12 months. During EINSTEIN CHOICE, patients received either XARELTO\textsuperscript{\textregistered} 10 mg, XARELTO\textsuperscript{\textregistered} 20 mg or aspirin 100 mg once daily for up to an additional 12 months of extended treatment. A total of 3,365 patients from 31 countries were included in the study analysis. People who required extended anticoagulation at therapeutic doses were not included, as the objective of the study was to investigate
those patients for whom the treating physician was uncertain about the need for continuing anticoagulant therapy.

Results were presented during a Joint American College of Cardiology/Journal of the American Medical Association Late-Breaking Clinical Trials session at the American College of Cardiology’s 66th Annual Scientific Session (ACC.17) in March and simultaneously published in The New England Journal of Medicine.

About EXPLORER
EINSTEIN CHOICE is part of the EXPLORER clinical research program for XARELTO®. Unmatched by any oral anticoagulant in the NOAC class in its size, scope and ambition, EXPLORER seeks to generate important clinical evidence on the safety and efficacy of XARELTO® and its potential role in addressing additional critical medical needs. More than 275,000 people will have participated in the program by the time of its completion. EXPLORER includes 10 indication-seeking and label expansion studies beyond the six approved indications for XARELTO® in the United States, with the potential to reach more than 40 million people at risk for blood clots in the years to come.

WHAT IS XARELTO®?
XARELTO® is a prescription medicine used to reduce the risk of stroke and blood clots in people with atrial fibrillation, not caused by a heart valve problem. For patients currently well managed on warfarin, there is limited information on how XARELTO® and warfarin compare in reducing the risk of stroke.

XARELTO® is also a prescription medicine used to treat deep vein thrombosis and pulmonary embolism, and to help reduce the risk of these conditions occurring again.

XARELTO® is also a prescription medicine used to reduce the risk of forming a blood clot in the legs and lungs of people who have just had knee or hip replacement surgery.

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

- For people taking XARELTO® for atrial fibrillation:

  People with atrial fibrillation (an irregular heart beat) 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.

- **XARELTO® can cause bleeding**, which can be serious, and rarely may lead to death. This is because XARELTO® is a blood thinner medicine that reduces blood clotting. While you take XARELTO® you are likely to bruise more easily and it may take longer for bleeding to stop.

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
- 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 that 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 patients with artificial heart valves.**

**WHO SHOULD NOT TAKE XARELTO®?**
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®.

**WHAT SHOULD I TELL MY DOCTOR BEFORE OR WHILE TAKING XARELTO®?**
Before taking XARELTO®, tell your doctor if you:
- Have ever had bleeding problems
- Have liver or kidney problems
- Have any other medical condition
- 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 while taking XARELTO®. If you take XARELTO® during pregnancy, tell your doctor right away if you have bleeding or symptoms of blood loss.
- Are breastfeeding or plan to breastfeed. It is not known if XARELTO® passes into your breast milk. You and your doctor should decide if you will take XARELTO® or breastfeed.

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 nonprescription medicines, vitamins, and herbal supplements. Some of your other medicines may affect the way XARELTO® works. Certain medicines may increase your risk of bleeding. **See “What is the most important information I should know about XARELTO®?”**

Especially tell your doctor if you take:
- Ketoconazole (Nizoral®)
- Itraconazole (Onmel™, Sporanox®)
- Ritonavir (Norvir®)
- Lopinavir/ritonavir (Kaletra®)
- Indinavir (Crixivan®)
- Carbamazepine (Carbatrol®, Equetro®, Tegretol®, Tegretol®-XR, Teril™, Epitol®)
- Phenytoin (Dilantin-125®, Dilantin®)
- Phenobarbital (Solfoton™)
- Rifampin (Rifater®, Rifamate®, Rimactane®, Rifadin®)
- St. John’s wort (Hypericum perforatum)

Ask your doctor if you are not sure if your medicine is one listed above. Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

**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 will tell you how much XARELTO® to take and when to take it.
• Your doctor may change your dose if needed.

If you take XARELTO® for:
  • **Atrial Fibrillation**: 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® once or twice a day as prescribed by your doctor.
    - Take XARELTO® with food at the same time each day.
    - If you miss a dose of XARELTO®:
      - **and take XARELTO® 2 times a 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.
      - **and 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.

• If you have difficulty swallowing the tablet whole, talk to your doctor about other ways to take XARELTO®.
• Your doctor will decide how long you should take XARELTO®. Do not stop taking XARELTO® without talking to your doctor first.
• Your doctor may stop XARELTO® for a short time before any surgery, medical or dental procedure. Your doctor will tell you when to start taking XARELTO® again after your surgery or procedure.
• Do not run out of XARELTO®. Refill your prescription for XARELTO® before you run out. When leaving the hospital following a hip or knee replacement, be sure that you 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.

**WHAT ARE THE POSSIBLE SIDE EFFECTS OF XARELTO®?**

*Please see “What is the most important information I should know about XARELTO®?”*

Tell your doctor if you have any side effect that bothers you or that does not go away.

Call your doctor for medical advice about side effects. You are also encouraged to report side effects to the FDA: visit [http://www.fda.gov/medwatch](http://www.fda.gov/medwatch) or call 1-800-FDA-1088. You may also report side effects to Janssen Pharmaceuticals, Inc., at 1-800-JANSSEN (1-800-526-7736).
Please click here for full Prescribing Information, including Boxed Warnings, and Medication Guide.

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Janssen Research & Development, LLC and Bayer AG together are developing rivaroxaban. For more information about XARELTO®, visit www.xarelto.com.

About the Janssen Pharmaceutical Companies

At the Janssen Pharmaceutical Companies of Johnson & Johnson, we are working to create a world without disease. Transforming lives by finding new and better ways to prevent, intercept, treat and cure disease inspires us. We bring together the best minds and pursue the most promising science. We are Janssen. We collaborate with the world for the health of everyone in it. Learn more at www.janssen.com. Follow us at @JanssenUS.

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, including the potential availability of an additional dosing option for XARELTO® (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 inherent in product research and development, including uncertainty of clinical success and obtaining regulatory approvals; competition, including technological advances, new products and patents attained by competitors; challenges to patents; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and description 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, 2017, including under “Item 1A. Risk Factors”, its most recently filed Quarterly Report on Form 10-Q, including in the section captioned "Cautionary Note Regarding Forward-Looking Statements,” 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 or Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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