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Two New Real-World Studies Confirm Positive Efficacy and Safety Profile of XARELTO® (rivaroxaban) in Treating and Preventing Blood Clots

TITUSVILLE, NJ (October 23, 2016) – Janssen Pharmaceuticals, Inc. (Janssen) and its development partner, Bayer, today announced results of two new real-world studies confirming the positive benefit-risk profile of XARELTO® (rivaroxaban) in treating venous thromboembolism (VTE), or blood clots, and reducing the risk of recurrence.

One study showed that people with VTE taking XARELTO® for longer than three months had a lower risk of VTE recurrence, without an increase in major bleeding, compared to those taking the medicine for only three months. The second was the first readout from Janssen's Post-Marketing Safety Surveillance (PMSS) study in VTE, which showed the rates and patterns of major bleeding in people taking XARELTO® for VTE in routine clinical practice were consistent with those reported in clinical trials. Results of both studies were presented at the American College of Chest Physicians (CHEST) Annual Meeting 2016.

VTE is a collective term encompassing deep vein thrombosis (DVT), a blood clot in a deep vein (usually the leg), and pulmonary embolism (PE), when a clot travels to the lung. VTE affects more than 900,000 Americans each year, and one-third of these occurrences will be fatal. Once a person experiences VTE, they are at increased risk of it occurring again.

Real-World Study Confirms Benefit of Extended Use of XARELTO® in VTE

In nearly 5,000 people who were diagnosed with their first VTE, researchers examined the long-term safety and effectiveness of XARELTO® and found those who continued taking XARELTO® for up to one year had significantly lower rates of VTE recurrence at all measured time points, without an increased risk of major bleeding, compared to those who discontinued XARELTO® after three months. Specifically:

- At three months, recurrent VTE occurred in 0.57 percent of people in the continued cohort* and 1.19 percent in the discontinued cohort** ($p<0.05$). Major bleeding occurred in 0.51 percent and 0.72 percent, respectively ($p>0.05$).
- At six months, recurrent VTE occurred in 1.07 percent of people in the continued cohort and 2.10 percent in the discontinued cohort ($p<0.05$). Major bleeding occurred in 0.79 percent and 0.72 percent, respectively ($p>0.05$).
- At 12 months, recurrent VTE occurred in 1.45 percent of people in the continued cohort and 2.60 percent in the discontinued cohort ($p<0.05$). Major bleeding occurred in 1.06 percent and 1.13 percent, respectively ($p>0.05$).

Clinical guidelines recommend people diagnosed with VTE be treated with an anticoagulant, such as rivaroxaban, for a minimum of three months when they are at the highest risk of experiencing a recurrence. However, the risk still remains after treatment ends and up to 10 percent of people will have a recurrent event within the first year.[1]

"This study in a broad real-world setting affirms the ACCP guidelines for the extended treatment of an unprovoked VTE," said Dr. Scott Kaatz, lead study investigator and hospitalist, Henry Ford Hospital. "Extended treatment with rivaroxaban showed a decrease in recurrent VTE without an increase in major bleeding and is consistent with a previous clinical trial."

This study builds on findings from the Phase 3 EINSTEIN clinical program, which was used by regulatory authorities worldwide to approve XARELTO® for the treatment of DVT and PE and reduction in the risk of recurrence of DVT and PE. The EINSTEIN-Extension study found continuing treatment with XARELTO® for an additional six to 12 months beyond the initial treatment period resulted in significantly fewer VTE recurrences (1.3 percent) versus placebo (7.1 percent), $p<0.001$. There was no difference in major bleeding between the two groups.

Study Confirms Safety Profile of XARELTO® in VTE

Also presented were the first results from Janssen's ongoing PMSS VTE study, which follows people with DVT and PE in the U.S. taking XARELTO®. Like Janssen's PMSS study in non-valvular atrial fibrillation (NVAF), this retrospective, observational study evaluates major bleeding in these patients in a real-world, post-approval setting, using electronic health records from the U.S. Department of Defense (DoD) database.

The first data cut of 9,638 people with VTE (5,426 with DVT; 4,212 with PE) showed:

- Of the 9,638 people taking XARELTO®, 130 (1.3 percent) experienced a major bleeding event, translating into an incidence rate of 2.47 per 100 person-years[2], primarily in gastrointestinal sites.
- With DVT, major bleeding events in PMSS were observed in 74 people with DVT (1.4 percent), translating into an incidence rate of 2.74 per 100 person-years.
- With PE, major bleeding events in PMSS were observed in 56 people with PE (1.3 percent), translating into an incidence rate of 2.18 per 100 person-years.
- People who experienced major bleeding were typically older, female and had more comorbidities; fatal outcomes were rare.

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*Continued cohort defined as patients with VTE who continued XARELTO® treatment for more than three months and up to one year.

**Discontinued cohort defined as patients with VTE who were treated with XARELTO® for three months and stopped treatment at that time.

[1] Bauersachs R et al. Oral Rivaroxaban for Symptomatic Venous Thromboembolism. *N Engl J Med* 2010;363(26):2500.

[2] Incidence rate was calculated using a person-time approach: the total number of people experiencing major bleeding divided by the number of years of all people receiving XARELTO® (expressed in 100-year increments).

"Post-marketing research is invaluable to physicians who are continually looking to understand how a medicine is performing in real-world settings in order to make informed treatment decisions for their patients," said PMSS study investigator W. Frank Peacock, MD, FACEP, Associate Chair and Research Director, Emergency Medicine, Baylor College of Medicine. "We have been closely examining the use of rivaroxaban in daily clinical practice for more than three years in people with non-valvular atrial fibrillation, and are pleased to expand our work to those with VTE."

The PMSS study in VTE was designed by Janssen in conjunction with the DoD and Health ResearchTx LLC (HRTX), and in agreement with the U.S. Food and Drug Administration (FDA), to proactively ascertain, analyze and report potential side effects with XARELTO® use, including major bleeding events, associated risk factors and bleeding-related clinical outcomes in people with VTE taking XARELTO®. PMSS is a retrospective study with no comparator arm.

Commitment to Real-World Research and Patient Access
To date, more than 91,000 people have been enrolled in real-world studies for XARELTO® across all six approved indications in the U.S., including DVT, PE and NVAF, and the number is growing. Real-world studies are part of the EXPLORER clinical research program for XARELTO®, which also seeks to evaluate the potential role of the medicine in addressing additional critical medical needs. A collaborative research effort between Janssen and Bayer, EXPLORER is a blend of completed and ongoing studies and registries, including six additional indication-seeking programs underway in the United States. More than 275,000 people will have participated by the time of its completion.

"These results add to a rapidly growing body of real-world research for XARELTO®, and specifically in the case of VTE, reaffirm the results observed in our landmark EINSTEIN clinical trial program," said Paul Burton, MD, PhD, FACC, Vice President, Medical Affairs, Janssen. "Beyond our clinical work, we are also committed to making XARELTO® affordable and accessible for the patients who need it."

XARELTO® leads the non-vitamin K antagonist oral anticoagulant (NOAC) class by having the strongest affordability and access position in the U.S. For qualifying people with commercial insurance using the Janssen CarePath savings card, XARELTO® has no cost.[3] For people with Medicare and commercial insurance, XARELTO® is broadly reimbursed, with more than 95 percent of commercial patients and people on Medicare Part D covered at the lowest branded co-pay. XARELTO® is also now preferred by CVS Caremark and has the lowest average out-of-pocket cost of any NOAC available in the U.S. today with more than 20 million prescriptions written for XARELTO® in the U.S. since its launch.

There are limitations associated with real-world research, which may include data entry error or incompleteness, differing behaviors in clinical vs. real-world settings, and limited generalizability to all hospitals.

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.

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[3] Subject to a maximum annual program benefit of $3,400.

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* 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. Trademarks are those of their respective owners.

Janssen and Bayer 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 on Twitter 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 extended rivaroxaban treatment for VTE and accessibility 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 Pharmaceuticals, Inc. 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 3, 2016, including in Exhibit 99 thereto, 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.