NEWS RELEASE

Real-World Data Confirms Safety and Efficacy Profile of XARELTO®, With Shorter Hospital Stays, for the Treatment of Deep Vein Thrombosis

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XALIA is First Prospective Study to Confirm Benefit of a Non-Vitamin K Antagonist Oral Anticoagulant (NOAC) for Treating Deep Vein Thrombosis in Routine Clinical Practice, Adds to More than 91,000 Patients Enrolled in Real-World Studies

Orlando, FL (December 7, 2015) - Janssen Pharmaceuticals, Inc. (Janssen) and its development partner, Bayer HealthCare, today announced the results from their real-world study XALIA showing that, in people with deep vein thrombosis (DVT), the rates of major bleeding and recurrent blood clots for XARELTO® (rivaroxaban) in routine clinical practice were generally consistent with those observed in Phase 3 research. Patients taking XARELTO® also had shorter length of hospital stays than those given standard anticoagulation. The prospective study was presented at the 2015 American Society of Hematology (ASH) Annual Meeting and simultaneously published in **Lancet Hematology**.

"On average, every 37 seconds someone in the Western world dies from a venous blood clot, so it is important we understand the effectiveness and safety of available treatment options for these potentially life-threatening blood clots," said XALIA principal investigator Professor Alexander G. G. Turpie, McMaster University and Hamilton Health Sciences, Hamilton, Ontario, Canada. "The real-world insights from XALIA confirm the positive benefit-risk profile of rivaroxaban for the treatment of deep vein thrombosis that was observed in the Phase 3 EINSTEIN-DVT study, signalling that the medicine is performing as expected in patients that physicians typically see in everyday clinical practice."

XALIA - which included approximately 5,000 patients from 21 countries[1] - evaluated the safety and effectiveness of XARELTO®, taken once daily, for the treatment of DVT in routine clinical practice as compared to standard anticoagulation. The primary outcome was the incidence of adverse events (major bleeding, recurrent blood clots and all-cause mortality). Healthcare resource utilization, including length of stay, also was evaluated. A propensity score analysis was completed to address differences in baseline characteristics and help correct any selection bias. Methodological and other differences between the studies limit the ability to directly compare results of XALIA to the pivotal Phase 3 **EINSTEIN-DVT study**, which was used by regulatory authorities worldwide to approve XARELTO®.

Key XALIA findings (from the propensity score analysis) included:

- Major bleeding occurred in 0.8 percent of patients receiving XARELTO® and 2.1 percent of those receiving standard anticoagulation (HR 0.77; CI 0.40-1.50; p=0.44). There were no fatal bleeding events in the XARELTO® group; two fatal bleeding events occurred in the standard anticoagulation group. In EINSTEIN-DVT, major bleeding occurred in 0.8 percent of patients taking XARELTO® and there was one fatal bleeding event.
- Recurrent blood clots occurred in 1.4 percent of patients receiving XARELTO® and 2.3 percent of those receiving standard anticoagulation (HR 0.91; CI 0.54-1.54; p=0.72). In EINSTEIN-DVT, recurrent blood clots occurred in 2.1 percent of patients taking XARELTO®.
- All-cause mortality occurred in 0.4 percent of patients taking XARELTO® and 3.4 percent of those taking standard anticoagulation (HR 0.51; CI 0.24-1.07; p=0.07). In EINSTEIN-DVT, all-cause mortality occurred in 2.2 percent of patients taking XARELTO®.

As hospitalization for blood clots remains a major healthcare cost, the study also examined hospital admissions and found them to be shorter in duration for patients treated with XARELTO® compared to those receiving standard anticoagulation. Specifically, the mean length of hospital stay was 5.0 days for patients treated with XARELTO® and 7.7 days for those treated with standard anticoagulation (geometric means ratio 0.66; CI 0.61-0.72).

About XALIA

Sponsored by Janssen and Bayer HealthCare, XALIA (XA inhibition with rivaroxaban for Long-term and Initial Anticoagulation in venous thromboembolism) was a Phase 4, prospective, non-interventional, observational study of patients with DVT, or DVT with concomitant pulmonary embolism (PE), treated with XARELTO® or standard anticoagulation. Standard anticoagulation was considered initial treatment with heparin, low-molecular-weight heparin (LMWH) or fondaparinux, typically overlapping with and followed by warfarin.

A total of 5,142 patients, age 18 or older, were enrolled, and of these, 4,768 were included in the primary analysis. For the propensity score analysis, which was pre-specified in the protocol, 4,515 patients were included (2,505 in the XARELTO® group and 2,010 in the standard anticoagulation group). Patients were enrolled between June 2012

and March 2014, and followed for at least 12 months. The study was requested by the European Medicines Agency (EMA), with the protocol developed with and approved by the EMA.

Commitment to Real-World Research

Janssen and Bayer HealthCare initiated XALIA to evaluate the real-world performance of XARELTO® in patients with DVT. To date, more than 91,000 patients have been enrolled in real-world studies for XARELTO® across all six approved indications, including DVT, PE and non-valvular atrial fibrillation (NVAF), and the number is growing. These 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 HealthCare, EXPLORER is a blend of completed and ongoing studies and registries, including six additional indication-seeking programs. More than 275,000 patients will have participated by the time of its completion.

"Real-world research helps to build the bridge between clinical trials and clinical practice, and as the first NOAC approved for the treatment of DVT four years ago, we have been able to closely monitor and understand how our medicine performs both in the initial and long-term treatment of this life-threatening condition," said Hayes Dansky, MD, Therapeutic Area Leader, Cardiovascular, Janssen. "XARELTO® has the most published data in the Factor Xa class examining critical aspects of treatment in the real-world setting, including safety, efficacy and adherence - and to build on this research, we are initiating a new study to evaluate the real-world safety of our medicine in patients with DVT and PE treated in the U.S."

Part of the EXPLORER research program, the new study, called PMSS (Post-Marketing Safety Surveillance), will follow DVT and PE patients in the U.S. taking XARELTO®. Like Janssen's PMSS study in NVAF patients, this new retrospective, observational study will evaluate major bleeding in these patients in a real-world, post-approval setting, using electronic healthcare records from the U.S. Department of Defense (DoD) database.

About XARELTO® (rivaroxaban)

XARELTO® works by blocking the blood clotting Factor Xa. XARELTO® does not require routine blood monitoring. XARELTO® has a broad indication profile and is approved for six indications that include:

To reduce the risk of strokes and blood clots in patients 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.
To treat patients with deep vein thrombosis (DVT).
To treat patients with pulmonary embolism (PE).
To reduce the risk of recurrence of DVT or PE following an initial six-month treatment for acute venous thromboembolism.

To reduce the risk of blood clots in the legs and lungs of patients who have just had knee replacement surgery.
To reduce the risk of blood clots in the legs and lungs of patients who have just had 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®)
- 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&#8482, Sporanox®)
- Ritonavir (Norvir®)
- Lopinavir/ritonavir (Kaletra®)
- Indinavir (Crixivan®)
- Carbamazepine (Carbatrol®, Equetro®, Tegretol®, Tegretol®-XR, Teril&#8482, Epitol®)
- Phenytoin (Dilantin-125®, Dilantin®)
- Phenobarbital (Solfoton&#8482)
- 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®?" above.

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.

Janssen and Bayer HealthCare together are developing rivaroxaban.

For more information about XARELTO®, visit **www.xarelto.com**. The XARELTO® CarePath™ Support Program is a resource designed for healthcare providers, patients and caregivers. Visit **www.xareltocarepath.com** or call 1-888-XARELTO to learn more about the XARELTO® CarePath™ resources focused on access, education and adherence.

About Janssen

At Janssen, we are dedicated to addressing and solving some of the most important unmet medical needs of our time in oncology, immunology, neuroscience, infectious diseases and vaccines, and cardiovascular and metabolic diseases. Driven by our commitment to patients, we develop innovative products, services and healthcare solutions to help people throughout the world. Janssen Pharmaceuticals, Inc. is one of the Janssen Pharmaceutical Companies of Johnson & Johnson. Please visit **www.Janssen.com** for more information.

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[1] XALIA was conducted in Austria, Belgium, Canada, Czech Republic, Denmark, France, Germany, Greece, Hungary, Israel, Italy, Moldova, The Netherlands, Norway, Portugal, Slovenia, Spain, Sweden, Switzerland, Ukraine and United Kingdom.

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