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Janssen Leverages Wearable Technology to Reimagine Clinical Trial Design

CHIEF-HF is the first-ever completely decentralized, mobile, indication-seeking study assessing effectiveness of INVOKANA® (canagliflozin) in adults with heart failure (HF), with or without type 2 diabetes (T2D)

Company tests innovative trial design with potential to bring medicines to patients faster and more cost-effectively

Titusville, N.J., November 16, 2019 — The Janssen Pharmaceutical Companies of Johnson & Johnson announced today the launch of the next evolution of digital clinical trial design with CHIEF-HF, the first-ever completely decentralized, mobile, indication-seeking clinical study. To accelerate the study and fast-track results, all contact with participants will be done virtually, with no in-person clinical visits required. Drawing on previous experience, the Company is utilizing smart technology and wearable devices to more quickly and efficiently gather and analyze real-world evidence to assess the effectiveness of canagliflozin in adults with heart failure (HF), with or without type 2 diabetes (T2D). Through a collaboration with

global research organization PRA Health Sciences and their innovative mobile clinical trial platform, CHIEF-HF (**C**anagliflozin: Impact on **H**ealth Status, Qual**i**ty of Life and **F**unctional Status in **H**eart **F**ailure), will examine the use of canagliflozin compared to placebo on quality of life improvement scales, in participants with either preserved or reduced ejection fraction heart failure.

CLICK TO TWEET: Learn how Janssen is bringing together digital & health care: innovative new trial will assess quality of life and track physical activity of people with heart failure with or without type 2 diabetes using smartphones and wearable technology #HF https://ctt.ec/245Qy+

"Traditional clinical trials are undeniably essential in medical research but are often long and costly. Through the CHIEF-HF study, we are exploring how we can harness technology that consumers already have at their fingertips, including smartphones and wearable devices, to change this paradigm," said Paul Stoffels, M.D., Vice Chairman of the Executive Committee and Chief Scientific Officer, Johnson & Johnson. "Through this virtual trial approach, we hope to make clinical studies more inclusive, faster and more cost-effective, so that we can deliver innovative solutions to the people who need them."

The CHIEF-HF study continues Janssen's efforts to rethink traditional healthcare models and evolve them to be more patient-centric and cost-effective through technology. Janssen's first digital trial, mSToPs (**m**Health **S**creening **To P**revent **s**trokes), laid the foundation for the HEARTLINE™ multi-year research study that was announced earlier this year. Additionally, Joanne Waldstreicher, M.D., Chief Medical Officer, Johnson & Johnson, shared insights from trials, such as mSToPs, in a recently-published white paper in *Circulation* that examines how claims, electronic health records, and mobile and wearable devices can be applied to clinical trials.

"Our mission at Janssen is to bring transformational innovation to improve the lives of patients around the world. The CHIEF-HF study embodies that mission by combining new cutting-edge ways of doing clinical research, in a group of patients with a high unmet medical need, testing a well-studied medicine – canagliflozin," said Paul Burton, M.D., Ph.D., FACC, Vice President, Medical Affairs, Internal

Medicine, Janssen Scientific Affairs, LLC. "Additionally, CHIEF-HF is focused on the patient experience, returning their own data to them in a staged manner that allows them to understand how treatment and lifestyle choices affect their health."

A randomized, double-blind, placebo-controlled, interventional, superiority study, CHIEF-HF will examine the use of canagliflozin compared to placebo in participants with chronic HF, with or without T2D. Investigators will analyze participant-reported outcomes through app-based clinical questionnaires, and physical activity data as logged by an app on the smartphone and actigraphy data from a wearable activity device, including daily step count and stairs climbed. The study plans to enroll approximately 1,900 participants in the United States.

CHIEF-HF will support clinical data specifically observed in participants enrolled in the Phase 3 clinical program for canagliflozin. Unlike other Phase 3 clinical programs, the CHIEF-HF trial incorporates an individualized patient-centric perspective that is not typically captured in a registrational trial.

CLICK TO TWEET: First-ever completely decentralized, mobile, indication-seeking clinical study seeks to break down barriers to traditional clinical trials #HF https://ctt.ec/f3CYX+

More about CHIEF-HF

CHIEF-HF will enroll participants 18 years or older who have clinically stable symptomatic HF with a baseline Kansas City Cardiomyopathy Questionnaire (KCCQ)* score of >40 and <80 who will be stratified based on their ejection fraction (HFrEF or HFpEF)† as recorded at study entry. Participants will be recruited by investigators at large integrated delivery networks (IDN)‡ using data systems (such as electronic patient records), email and smartphone, to screen, identify and onboard potential study participants. To be enrolled, participants must possess a smartphone.

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* The Kansas City Cardiomyopathy Questionnaire is a health-related quality of life measure for HF.
† HFpEF (heart failure with preserved ejection fraction, or diastolic failure) and HFrEF (heart failure with reduced ejection fraction, or systolic failure) are the two types of left-sided HF.
‡ An IDN represents a set of physicians working with hospitals to form a healthcare ecosystem where a person can receive any type of care needed.

The total study duration will be nine months and will be conducted in two phases. For the first phase, participants will be randomized in a 1:1 ratio with one group receiving canagliflozin and the other group receiving placebo for a period of three months. For the second phase, participants will enter an open-label collection period, with a staged roll-out of study outcomes, and be told what they had been receiving, to allow them to make a subsequent treatment decision. The goal of this second phase is to demonstrate the impact of knowledge from a randomized clinical trial on trial participants and their subsequent therapeutic choices and healthcare behaviors. Study results will then be returned to all participants at the end of the study.

Exclusion criteria include treatment with a sodium-glucose co-transporter 2 (SGLT2) inhibitor (current or within three months), type 1 diabetes, stage 4 or 5 diabetic kidney disease (DKD), current hospitalization or a history of amputation within the past 12 months.

More on Heart Failure

Heart failure contributes to one in nine deaths and is a leading cause of hospitalization in the U.S., yet there are limited treatment options for people living with this debilitating disease. It is highly prevalent and despite best-available therapy, is associated with poor patient outcomes.[1,2] HFpEF is well-recognized as the predominant type of HF in patients with T2D and is possibly related to insulin resistance and obesity. Such predisposing factors are thought to be at the crux of ineffectiveness of traditional HF therapies in treating HFpEF patients, making the need for impactful therapies in this patient population even more urgent.[3,4]

Canagliflozin is not indicated for HF in adults with or without T2D.

WHAT IS INVOKANA® (canagliflozin)?

INVOKANA® is a prescription medicine used:

- along with diet and exercise to lower blood sugar (glucose) in adults with type 2 diabetes
- to reduce the risk of major cardiovascular events such as heart attack, stroke, or death in adults with type 2 diabetes who have known cardiovascular disease
- to reduce the risk of end-stage kidney disease (ESKD), worsening of kidney function, cardiovascular death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic kidney disease (nephropathy) with a certain amount of protein in the urine

INVOKANA® is not for people with type 1 diabetes or with diabetic ketoacidosis (increased ketones in blood or urine). It is not known if INVOKANA® is safe and effective in children under 18 years of age.

IMPORTANT SAFETY INFORMATION

INVOKANA® can cause important side effects, including:

- **Amputations. INVOKANA® may increase your risk of lower-limb amputations. Amputations mainly involve removal of the toe or part of the foot; however, amputations involving the leg, below and above the knee, have also occurred. Some people had more than one amputation, some on both sides of the body.** You may be at a higher risk of lower-limb amputation if you: have a history of amputation, have heart disease or are at risk for heart disease, have had blocked or narrowed blood vessels (usually in leg), have damage to the nerves (neuropathy) in the leg, or have had diabetic foot ulcers or sores**. Call your doctor right away if you have new pain or tenderness, any sores, ulcers, or infections in your leg or foot.** Your doctor may decide to stop your INVOKANA® for a while if you have any of these signs or symptoms. Talk to your doctor about proper foot care
- **Dehydration. INVOKANA® can cause some people to become dehydrated (the loss of too much body water), which may cause you to feel dizzy, faint, lightheaded, or weak, especially when you stand up (orthostatic hypotension)**. You may be at higher risk of dehydration if you have low blood pressure, take medicines to lower your blood pressure (including diuretics [water

pills]), are on a low sodium (salt) diet, have kidney problems, or are 65 years of age or older

- **Vaginal yeast infection.** Women who take INVOKANA® may get vaginal yeast infections. Symptoms include: vaginal odor, white or yellowish vaginal discharge (discharge may be lumpy or look like cottage cheese), or vaginal itching
- **Yeast infection of the penis (balanitis or balanoposthitis).** Men who take INVOKANA® may get a yeast infection of the skin around the penis. Symptoms include: redness, itching, or swelling of the penis; rash of the penis; foul-smelling discharge from the penis; or pain in the skin around penis

Talk to your doctor about what to do if you get symptoms of a yeast infection of the vagina or penis.

Do not take INVOKANA® if you:

- are allergic to canagliflozin or any of the ingredients in INVOKANA®. Symptoms of allergic reaction may include: rash; raised red patches on your skin (hives); or swelling of the face, lips, mouth, tongue, and throat that may cause difficulty in breathing or swallowing
- have severe kidney problems and are taking INVOKANA® to lower your blood sugar
- are on kidney dialysis

Before you take INVOKANA®, tell your doctor if you have a history of amputation; heart disease or are at risk for heart disease; blocked or narrowed blood vessels (usually in leg); damage to the nerves (neuropathy) of your leg; diabetic foot ulcers or sores; kidney problems; liver problems; history of urinary tract infections or problems with urination; are on a low sodium (salt) diet; are going to have surgery; are eating less due to illness, surgery, or change in diet; pancreas problems; drink alcohol very often (or drink a lot of alcohol in short-term); ever had an allergic reaction to INVOKANA®; or have other medical conditions.

Tell your doctor if you are or plan to become pregnant, are breastfeeding, or plan to breastfeed. INVOKANA® may harm your unborn baby. If you become pregnant while taking INVOKANA®, tell your doctor right away. INVOKANA® may pass into your breast milk and may harm your baby. Do not breastfeed while taking INVOKANA®.

Tell your doctor about all the medicines you take, **including prescription and non-prescription medicines, vitamins, and herbal supplements**. Especially tell your doctor if you take diuretics (water pills), rifampin (used to treat or prevent tuberculosis), phenytoin or phenobarbital (used to control seizures), ritonavir (Norvir®, Kaletra® – used to treat HIV infection), or digoxin (Lanoxin®– used to treat heart problems).

Possible Side Effects of INVOKANA®

INVOKANA® may cause serious side effects, including:

- **Ketoacidosis** (increased ketones in your blood or urine). **Ketoacidosis has happened in people who have type 1 or type 2 diabetes**, during treatment with INVOKANA®. Ketoacidosis is a serious condition, which may need to be treated in a hospital. Ketoacidosis may lead to death. **Ketoacidosis can happen with INVOKANA® even if your blood sugar is less than 250 mg/dL. Stop taking INVOKANA® and call your doctor right away if you get any of the following symptoms: nausea, vomiting, stomach-area pain, tiredness, or trouble breathing**
- **Kidney problems.** Sudden kidney injury has happened to people taking INVOKANA®. Talk to your doctor right away if you: 1) reduce the amount of food or liquid you drink, if you are sick, or cannot eat or 2) you start to lose liquids from your body from vomiting, diarrhea, or being in the sun too long
- **Serious Urinary Tract Infections:** may lead to hospitalization and have happened in people taking INVOKANA®. Tell your doctor if you have signs or symptoms of a urinary tract infection such as: burning feeling while urinating, need to urinate often or right away, pain in the lower part of your

stomach (pelvis), or blood in the urine. Some people may also have high fever, back pain, nausea, or vomiting

- **Low blood sugar (hypoglycemia).** If you take INVOKANA® with another medicine that can cause low blood sugar, such as a sulfonylurea or insulin, your risk of getting low blood sugar is higher. The dose of your sulfonylurea medicine or insulin may need to be lowered while you take INVOKANA®. Signs and symptoms of low blood sugar may include: headache, drowsiness, weakness, dizziness, confusion, irritability, hunger, fast heartbeat, sweating, shaking, or feeling jittery
- **A rare but serious bacterial infection that destroys the tissue under the skin (necrotizing fasciitis) in the area between and around the anus and genitals (perineum).** Necrotizing fasciitis of the perineum has happened in women and men who take INVOKANA®. Necrotizing fasciitis of the perineum may lead to hospitalization, may require multiple surgeries, and may lead to death. **Seek medical attention immediately if you have fever or you are feeling very weak, tired, or uncomfortable (malaise) and you develop any of the following symptoms in the area between and around your anus and genitals:** pain or tenderness, swelling, or redness of the skin (erythema)
- **Serious allergic reaction.** If you have any symptoms of a serious allergic reaction, stop taking INVOKANA® and call your doctor right away or go to the nearest hospital emergency room
- **Broken Bones (fractures):** Bone fractures have been seen in patients taking INVOKANA®. Talk to your doctor about factors that may increase your risk of bone fracture

The most common side effects of INVOKANA® include: vaginal yeast infections and yeast infections of the penis; changes in urination, including urgent need to urinate more often, in larger amounts, or at night.

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 may**

report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Janssen Scientific Affairs, LLC at 1-800-526-7736.

Please read the full Product Information, including Boxed Warning, and Medication Guide for INVOKANA®.

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About Johnson & Johnson

At Johnson & Johnson, we believe good health is the foundation of vibrant lives, thriving communities and forward progress. That's why for more than 130 years, we have aimed to keep people well at every age and every stage of life. Today, as the world's largest and most broadly-based health care company, we are committed to using our reach and size for good. We strive to improve access and affordability, create healthier communities, and put a healthy mind, body and environment within reach of everyone, everywhere. We are blending our heart, science and ingenuity to profoundly change the trajectory of health for humanity.

About Janssen Cardiovascular & Metabolism

In Cardiovascular & Metabolism (CVM), we take on the most pervasive diseases that burden hundreds of millions of people and healthcare systems around the world. As part of this long-standing commitment and propelled by our successes in treating T2D and thrombosis, we advance highly differentiated therapies that prevent and treat life-threatening cardiovascular, metabolic and retinal diseases. Uncovering new therapies that can improve the quality of life for this large segment of the population is an important endeavor – one which Janssen CVM will continue to lead in the years to come. Our mission is global, local and personal. Together, we can reshape the future of cardiovascular, metabolic and retinal disease prevention and treatment. Please visit www.janssen.com/cardiovascular-and-metabolism.

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: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension.

Learn more at www.janssen.com. Follow us at www.twitter.com/JanssenGlobal. Janssen Pharmaceuticals, Inc. and Janssen Scientific Affairs, LLC are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding the potential benefits and further development of canagliflozin. 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., and any of the other Janssen Pharmaceutical Companies 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 30, 2018, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, 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 nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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