CHMP issues positive opinion to extend Invokana® (canagliflozin) indication to reflect improved renal outcomes in patients with diabetic kidney disease and type 2 diabetes

- Positive opinion is based on the Canagliflozin and Renal Endpoints in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) Phase III renal outcomes trial, which was stopped early based on the achievement of a pre-specified efficacy criterion
- If approved by the European Commission, canagliflozin will be the first therapy approved in nearly 20 years, for use on the background of diabetic kidney disease (DKD) standard of care, including angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs), to slow the progression of DKD in European patients with type 2 diabetes mellitus (T2DM), including patients with moderate and severe renal impairment.¹
- An estimated 59 million European adults have diabetes, around 90% of whom have T2DM.² Approximately 40% of people with T2DM will go on to develop kidney disease.³
- As commercial partner to Janssen Pharmaceutica NV, Mundipharma has exclusive distribution rights for canagliflozin in various countries within Europe.

Cambridge, 29th May 2020 – Mundipharma welcomes the news that the European Medicines Agency’s (EMA) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion to extend the indication of Invokana® (canagliflozin) to include important renal outcome data from the landmark Canagliflozin and Renal Endpoints in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) trial.⁴

If approved by the European Commission, canagliflozin would be the only SGLT2i with an indication extension to treat diabetic kidney disease (DKD) in European T2DM patients.⁴

“For the first time in nearly 20 years, patients with Diabetic Kidney Disease (DKD) will have a new treatment to reduce their risk of kidney failure requiring dialysis or transplantation.” said Dr Vinicius Gomes de Lima, European Medical Affairs Lead, Mundipharma. “The European Medicines Agency have indicated that the management of DKD should be regarded as an integral treatment goal of type 2 diabetes. Thus, this approach will provide a therapy for many patients affected by DKD across Europe. We are very excited by this decision as it fully aligns with Mundipharma’s purpose to Move Medicine Forward.”
The CREDENCE trial is the first dedicated renal outcomes study in patients with DKD and T2DM. The study enrolled 4401 subjects with an eGFR of 30 to <90ml/min/1.73m² and albuminuria (urinary albumin: creatinine ratio >300 to 5000 mg/g). All patients were treated on a background of standard of care for DKD, including ACE inhibitors and ARBs. The results showed that canagliflozin demonstrated a 30% reduction, compared to placebo, in the risk of the primary composite endpoint, comprising end-stage renal disease (ESRD), doubling of serum creatinine and renal or cardiovascular (CV) death, with event rates of 43.2 vs 61.2 per 1000 patient years, respectively (Hazard Ratio [HR]: 0.70; 95% Confidence Interval [CI]: 0.59 to 0.82; p<0.00001).

Rates of adverse events and serious adverse events were similar overall in the canagliflozin group and the placebo group. There were no observed differences in the incidence of lower limb amputations (12.3 vs 11.2 events per 1000 patient years; HR: 1.11; 95% CI: 0.79 to 1.56) or adjudicated bone fractures (11.8 vs 12.1 events per 1000 patient years; HR: 0.98; 95% CI: 0.70 to 1.37). The study was stopped early in July 2018, owing to positive efficacy findings.

Canagliflozin has been approved in the European Union since 2013, where it is indicated for the treatment of adults with insufficiently controlled T2DM as an adjunct to diet and exercise, either as monotherapy or in addition to other blood sugar-reducing medicinal products. Please visit https://www.ema.europa.eu/en/documents/product-information/invokana-epar-product-information_en.pdf for full prescribing information.

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Notes to the editors:

About Invokana (canagliflozin)
Canagliflozin is an oral, once-daily medication that belongs to a class of medications called sodium glucose co-transporter 2 (SGLT2) inhibitors. SGLT2 inhibitors work by inhibiting SGLT2 co-transporter, which promotes the excretion of glucose via the urine, and thus helps lowering blood glucose levels in adults with T2DM.

Canagliflozin was approved in the European Union by the European Commission in November 2013. It is indicated for the treatment of adults with insufficiently controlled T2DM as an adjunct to diet and exercise, as monotherapy when metformin is considered inappropriate due to intolerance or contra-indications and in addition to other medicinal products for the treatment of diabetes.

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The initiation dose is 100mg once daily in adults with an eGFR of ≥ 60 mL/min/1.73 m$^2$ and can be increased to 300mg once daily orally if tighter glycaemic control is needed. Canagliflozin should not be initiated if eGFR is < 60 mL/min/1.73 m$^2$. In patients tolerating canagliflozin whose eGFR falls persistently below 60 mL/min/1.73 m$^2$ the dose should be adjusted to or maintained at 100mg once daily. Canagliflozin should be stopped if eGFR falls persistently below 45 mL/min/1.73 m$^2$.

Approval in November 2013 was based on a comprehensive global Phase III clinical trial programme.

**About the CREDENCE Clinical Trial**¹

The CREDENCE (Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation) study was the first dedicated and fully recruited renal outcome trial evaluating renal and cardiovascular outcomes in people with type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD) with a sodium glucose co-transporter 2 (SGLT2) inhibitor. It was a phase III randomised, double-blind, event-driven, placebo-controlled, parallel-group, two-arm multicentre study of the effects of canagliflozin on renal and cardiovascular outcomes in subjects with T2DM and CKD. In particular, it compared the efficacy and safety of canagliflozin versus placebo in preventing clinically important kidney and cardiovascular outcomes in patients with T2DM and CKD when used in addition to standard of care, including a maximum tolerated daily dose of an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB).

**About the Mundipharma network**

Mundipharma is a global network of privately-owned independent associated companies whose purpose is To Move Medicine Forward. With a high performing and learning organisation that strives for innovation and commercial excellence through partnerships, we have successfully transformed and diversified our European portfolio of medicines to create value for patients, healthcare professionals, payers and wider healthcare systems across important therapeutic areas such as Diabetes, Oncology, Biosimilars, Anti-Infectives and Respiratory.

Invokana® is a registered trademark of Johnson & Johnson. The Marketing Authorisation Holder is Janssen-Cilag International NV.

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