INFORMATION FOR EUROPEAN MEDICAL/TRADE MEDIA ONLY

Mundipharma International welcomes positive phase III efficacy findings for *Invokana*® (canagliflozin) in type 2 diabetes patients with chronic kidney disease

- *Independent Data Monitoring Committee (IDMC) stops CREDENCE Phase III trial early, following positive efficacy findings of Invokana® (canagliflozin) in people with type 2 diabetes and chronic kidney disease (CKD)*[1]
- *3.15 million people in the UK are diagnosed with type 2 diabetes, 40% of which may develop chronic kidney disease at a cost of £8.8 billion to the NHS*[2,3,4]

CAMBRIDGE, UK: 18 July 2018 - As the European distributor of ***Invokana***® (canagliflozin) and Janssen's partner of choice in diabetes, the Mundipharma global network of independent associated companies welcomes the announcement from the Janssen Pharmaceutical Companies of Johnson & Johnson, that the Phase III CREDENCE (Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation) clinical trial has been stopped early based on a decision from the IDMC.[1,5] The recommendation is based on demonstration of efficacy as the trial achieved pre-specified criteria for the primary composite end points.[1]

CREDENCE is the first dedicated renal outcomes trial in patients with CKD and type 2 diabetes, which reviewed the efficacy and safety of ***Invokana***® (canagliflozin) versus placebo when used in addition to standard of care.[1] The trial assessed efficacy and safety by evaluating the risk and reduction of time to dialysis or kidney transplantation, doubling of serum creatinine, and renal or cardiovascular death.[1]

"This announcement highlights canagliflozin as a possible kidney protective treatment option for people living with type 2 diabetes and CKD, a condition that can be complex and difficult to manage. Canagliflozin is already helping to manage the early treatment and control of type 2 diabetes, and although we cannot comment on the data from the trial at this time, we look forward to seeing the full trial results and the positive impact this could have on patients" said Paul Schofield, European Medical Lead, Mundipharma International.

For further information and questions on the data specifically, please contact Janssen directly, who conducted the study.

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Notes to editors:

About *Invokana*® (canagliflozin)

Invokana® is a member of a class of drugs known as sodium glucose co-transporter 2 (SGLT2) inhibitors.[6]

SGLT2 inhibitors contribute to controlling blood glucose levels via the kidney.[6] As glucose is filtered from the blood into the kidneys, it is reabsorbed back into the bloodstream.[6,7] SGLT2is are an important transport carrier in the kidneys for this reabsorption.[6] Canagliflozin selectively inhibits SGLT2, and, as a result, promotes the loss of glucose via the urine, lowering blood glucose levels in adults with type 2 diabetes.[7,8] This mechanism of action is independent of insulin.[8]

In November 2013, the European Commission approved ***Invokana***® in the European Union for the treatment of adults with type 2 diabetes mellitus, to improve glycaemic (i.e blood sugar) control.[7,9]

Canagliflozin has been studied as monotherapy and in combination with other type 2 diabetes therapies including insulin.[9] It is recommended to start canagliflozin at 100mg once daily and if tolerated this can be increased to 300mg for tighter blood glucose control in patients with adequate kidney function (eGFR > 60ml/min/1.73m2).[9] The Phase III programme evaluated the safety and efficacy of canagliflozin across the spectrum of type 2 diabetes and included placebo and active comparator-controlled studies.[7,10] Three studies have compared canagliflozin to current standard treatments; two of which compared canagliflozin to sitagliptin (Januvia®) which showed non-inferior efficacy measured by HbA1c reduction (a marker of blood glucose control) at the 100mg dose, and a superior HbA1c reduction at the 300mg once daily dose, together with a similar tolerability profile.[7,11,12] The third study compared canagliflozin to glimepiride (Amaryl®) as dual therapy with metformin which showed a lower risk of hypoglycaemia.[13] The Phase III programme also included two large studies in special populations: patients over age 55 with type 2 diabetes and patients with type 2 diabetes who were considered to be at high risk for cardiovascular disease.[14,15]

Common adverse drug reactions associated with the use of ***Invokana***® include urinary tract infections (UTIs), hypoglycaemia, nausea, constipation, thirst, polyuria or pollakiuria, vulvovaginal candidiasis, balanitis or balanoposthitis, dyslipidemia and increased haematocrit.[9]

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About Type 2 Diabetes

Type 2 diabetes is a chronic condition that results in the body being unable to metabolise sugar (glucose).[16] A number of factors can increase the risk of developing type 2 diabetes, including obesity.[16,17] Obesity, specifically excess abdominal fat, can make the body less sensitive to insulin, causing a resistance by disrupting the function of insulin responsive cells and therefore the cells' ability to respond to insulin, leading to higher blood sugar levels (hyperglycemia).[16,17] If left uncontrolled, type 2 diabetes can lead to long-term complications such as heart attack, stroke, kidney damage (nephropathy), eye disease (retinopathy) and peripheral nerve damage (neuropathy).[16]

About the Mundipharma network

The Mundipharma global network of privately-owned independent associated companies was founded in 1956 by doctors and now operates in over 120 countries worldwide. We are focused on developing business partnerships to identify and accelerate meaningful technology across an increasingly diverse portfolio of therapy areas including respiratory, oncology, pain, and biosimilars. Consistent with our entrepreneurial heritage, we like to think we see what others don't by challenging conventional wisdom and asking different and challenging questions. By working in partnership with all our stakeholders, the Mundipharma network develops medicines that create value for patients, payers and wider healthcare systems.

For more information please visit: www.mundipharma.com.

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