The YODA Project
Research Proposal Due Diligence Assessment

Part 1: General Information	
YODA Project (Protocol) ID:	2024-0580
Date:	1-JUL-2024
Product Name:	**Team 1** INVOKANA® / Cardiovascular & Metabolic Diseases / sodium-glucose co-transporter 2 (SGLT2) inhibitor / Diabetes Mellitus, Type 2 & Obesity INVOKANA® / Cardiovascular & Metabolic Diseases / Diabetes Related- Other **Team 2** TOPAMAX® / Neuroscience / Anticonvulsants / Obesity & Diabetic Neuropathies **Team 3** OPSUMIT / Pulmonary Hypertension / Endothelin Receptor Antagonist / Pulmonary Hypertension **Team 4** UPTRAVI / Pulmonary Hypertension / Prostacyclin receptor agonist / Pulmonary Arterial Hypertension **Team 5** TRACLEER® / Pulmonary Hypertension / Endothelin Receptor Antagonist / Pulmonary Hypertension **Team 6** • THERMOCOOL® SMARTTOUCH™ Catheter / Heart and Blood Diseases / Cardiovascular devices / Atrial Fibrillation • Vitesse Intracranial Stent / Neuroscience / Neurovascular device / Ischemic Stroke
Therapeutic Area:	See above
Product Class:	See above
Condition(s) Studied:	See above
Protocol Number(s) and Title(s):	1. NCT02065791 - 28431754DNE3001 - A Randomized, Double-blind, Event-driven, Placebo-controlled, Multicenter Study of the Effects of Canagliflozin on Renal and Cardiovascular Outcomes in Subjects With Type 2 Diabetes Mellitus and Diabetic Nephropathy 2. NCT01032629 - 28431754DIA3008 A Randomized, Multicenter, Double-Blind, Parallel, Placebo-Controlled Study of the Effects of JNJ-28431754 on Cardiovascular Outcomes in Adult Subjects With Type 2 Diabetes Mellitus 3. NCT02243202 - 28431754OBE2002 - A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Investigate the Safety and Efficacy of the Co-administration of Canagliflozin 300 mg and Phentermine 15 mg Compared With Placebo for the Treatment of Non-diabetic Overweight and Obese Subjects 4. NCT00236613 - TOPMAT-OBES-001 - A Randomized, Double-Blind, Placebo-Controlled,Multicenter, Parallel Group, Dose-Response Study to Assess the Efficacy and Safety of Topiramate in the Treatment of Patients With Obesity

	5. NCT00231608 - TOPMAT-OBMA-001 - The Safety and Efficacy of Topiramate in Male Patients With Abdominal Obesity: A 6-Month Double-Blind, Randomized, Placebo-Controlled Study With a 6-Month Open-Label Extension 6. NCT00231634 - TOPMAT-OBDM-004 - A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study of the Efficacy and Safety of Topiramate in the Treatment of Obese, Type 2 Diabetic Patients Inadequately Controlled on Sulfonylurea Therapy 7. NCT00231660 - TOPMAT-OBDM-002 - A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study of the Efficacy and Safety of Topiramate in the Treatment of Obese, Type 2 Diabetic Patients Treated With Metformin 8. NCT00236626 - TOPMAT-OBDM-001 - A 9 Month, Double-Blind, Placebo-Controlled Study With a Blinded Crossover Transition to Open-Label Extension, Evaluating the Safety and Effectiveness of Topiramate on Insulin Sensitivity in Overweight or Obese Type 2 Diabetes Patients 9. NCT00231621 - TOPMAT-OBDL-001 - A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group, One-year Study of the Efficacy and Safety of Topiramate in the Treatment of Obese Subjects With Dyslipidemia 10. NCT00231647 - TOPMAT-OBD-202 - A Randomized, Double-Blind, Placebo-Controlled, Multicenter, Parallel-Group Study to Assess the Efficacy and Safety of Topiramate OROS Controlled-Release in the Treatment of Obese, Type 2 Diabetic Subjects Managed With Diet or Metformin 11. NCT01989754 - 28431754DIA4003 - A Randomized, Multicenter, Double-Blind, Parallel, Placebo-Controlled Study of the Effects of Canagliflozin on Renal Endpoints in Adult Subjects With Type 2 Diabetes Mellitus 12. NCT00231530 - TOPMAT-OBDM-003 - A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Assess the Safety and Efficacy of Topiramate in the Treatment of Obese, Type 2 Diabetic Patients on a Controlled Diet 13. NCT00231673 - TOPMAT-NP-005 - A Double-Blind, Placebo-Controlled, Parallel Group Study to Evaluate the Effect of Topiramate on Electrophysiological Parameters in Subjects With Diabetic Peripheral Polyneuropathy 14. NCT02025907 - 28431754DIA4004 - A Randomized, Double-blind, Placebo Controlled, 2-arm, Parallel-group, 26-week, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin in the Treatment of Subjects With Type 2 Diabetes Mellitus With Inadequate Glycemic Control on Metformin and Sitagliptin Therapy 15. NCT01340664 - 28431754DIA2003 - A Randomized, Double-Blind, Placebo-Controlled, 3-Arm, Parallel-Group, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin in the Treatment of Subjects With Type 2 Diabetes Mellitus With Inadequate Glycemic Control on Metformin

	16. NCT01381900 - 28431754DIA3014 - A Randomized, Double-Blind, Placebo-Controlled, Parallel Group, 18-Week Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin in the Treatment of Subjects With Type 2 Diabetes Mellitus With Inadequate Glycemic Control on Metformin Alone or in Combination With a Sulphonylurea 17. NCT01809327 - 28431754DIA3011 - A Randomized, Double-Blind, 5-Arm, Parallel-Group, 26-Week, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin in Combination With Metformin as Initial Combination Therapy in the Treatment of Subjects With Type 2 Diabetes Mellitus With Inadequate Glycemic Control With Diet and Exercise 18. NCT01137812 - 28431754DIA3015 - A Randomized, Double-Blind, Active-Controlled, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin Versus Sitagliptin in the Treatment of Subjects With Type 2 Diabetes Mellitus With Inadequate Glycemic Control on Metformin and Sulphonylurea Therapy 19. NCT01106690 - 28431754DIA3012 - A Randomized, Double-Blind, Placebo-Controlled, 3-Arm, Parallel-Group, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin in the Treatment of Subjects With Type 2 Diabetes Mellitus With Inadequate Glycemic Control on Metformin and Sulphonylurea Therapy 20. NCT01106651 - 28431754DIA3010 - A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin Compared With Placebo in the Treatment of Older Subjects With Type 2 Diabetes Mellitus Inadequately Controlled on Glucose Lowering Therapy 21. NCT00210808 - CAPSS-220 - A Multicenter, Randomized, Double-blind, Placebo-controlled, Flexible-dose Study to Assess the Safety and Efficacy of Topiramate in the Treatment of Moderate to Severe Binge-eating Disorder Associated With Obesity 22. NCT00650806 - 28431754OBE2001 - A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Dose-Ranging Study to Investigate the Safety and Efficacy of JNJ-28431754 in Nondiabetic Overweight and Obese Subjects 23. NCT00968812 - 28431754DIA3009 - A Randomized, Double-Blind, 3-Arm Parallel-Group, 2-Year (104-Week), Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of JNJ-28431754 Compared With Glimepiride in the Treatment of Subjects With Type 2 Diabetes Mellitus Not Optimally Controlled on Metformin Monotherapy 24. NCT01106677 - 28431754DIA3006 - A Randomized, Double-Blind, Placebo and Active-Controlled, 4-Arm, Parallel Group, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin in the Treatment of Subjects With Type 2 Diabetes Mellitus With Inadequate Glycemic Control on Metformin Monotherapy 25. NCT01081834 - 28431754DIA3005 - A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin as Monotherapy in the

	Treatment of Subjects With Type 2 Diabetes Mellitus Inadequately Controlled With Diet and Exercise 26. NCT01064414 - 28431754DIA3004 - A Randomized, Double-Blind, Placebo-Controlled, 3-Arm, Parallel-Group, 26-Week, Multicenter Study With a 26-Week Extension, to Evaluate the Efficacy, Safety and Tolerability of Canagliflozin in the Treatment of Subjects With Type 2 Diabetes Mellitus Who Have Moderate Renal Impairment 27. NCT01106625 - 28431754DIA3002 - A Randomized, Double-Blind, Placebo-Controlled, 3-Arm, Parallel-Group, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin in the Treatment of Subjects With Type 2 Diabetes Mellitus With Inadequate Glycemic Control on Metformin and Pioglitazone Therapy 28. NCT03267576 - 28431754DIA4026 - Canagliflozin Continuous Glucose Monitoring (CANA CGM) Trial: A Pilot Randomized, Double-Blind, Controlled, Crossover Study on the Effects of the SGLT-2 Inhibitor Canagliflozin (vs. the DPP-4 Inhibitor Sitagliptin) on Glucose Variability in Mexican Patients With Type 2 Diabetes Mellitus Inadequately Controlled on Metformin 29. NCT02139943 - 28431754DIA2004 - A Randomized Phase 2, Double-blind, Placebocontrolled, Treat-to-Target, Parallel-group, 3-arm, Multicenter Study to Assess the Efficacy and Safety of Canagliflozin as Add-on Therapy to Insulin in the Treatment of Subjects With Type 1 Diabetes Mellitus 30. NCT01385202 - Smart-AF - THERMOCOOL® SMARTTOUCH™ Catheter for the Treatment of Symptomatic Paroxysmal Atrial Fibrillation 31. NCT02382016 - AC-055-404 - A Randomized, Double-blind, Placebo-controlled, Prospective, Multicenter, Parallel Group Study to Assess the Safety and Efficacy of Macitentan in Patients With Portopulmonary Hypertension 32. NCT03078907 - AC-065A404 - A Multi-center, Double-blind, Placebo-controlled Phase 4 Study in Patients With Pulmonary Arterial Hypertension to Assess the Effect of Selexipag on Daily Life Physical Activity and Patient's Self-reported Symptoms and Their Impacts 33. NCT02471183 - AC-065A304 - Multicenter, Open-label, Single-group Study to Assess the Tolerability and the Safety of the Transition From Inhaled Treprostinil to Oral Selexipag in Adult Patients With Pulmonary Arterial Hypertension 34. NCT02070991 - AC-055G201 - A Prospective, Multicenter, Double-blind, Randomized, Placebocontrolled, Parallel-group, 12-week Study to Evaluate the Safety and Tolerability of Macitentan in Subjects With Combined Pre- and Post-capillary Pulmonary Hypertension (CpcPH) Due to Left Ventricular Dysfunction 35. NCT00313222 - AC-052-366 - Prospective, Randomized, Placebo-controlled, Double-blind, Multicenter, Parallel Group Study to Assess the Efficacy, Safety and Tolerability of Bosentan in Patients With Inoperable Chronic Thromboembolic Pulmonary Hypertension (CTEPH) 36. NCT00660179 - AC-055-302 - A Multicenter, Double-blind, Randomized, Placebo-controlled, Parallel Group, Event-driven, Phase III Study to

	Assess the Effects of Macitentan (ACT-064992) on Morbidity and Mortality in Patients With Symptomatic Pulmonary Arterial Hypertension 37. NCT00091715 - AC-052-364 - A Randomized, Double-blind, Placebo-controlled, Multicenter Study to Assess the Efficacy, Safety, and Tolerability of Bosentan in Patients With Mildly Symptomatic Pulmonary Arterial Hypertension (PAH) 38. NCT00303459 - AC-052-414 (COMPASS-2) - Effects of Combination of Bosentan and Sildenafil Versus Sildenafil Monotherapy on Morbidity and Mortality in Symptomatic Patients With Pulmonary Arterial Hypertension - A Multicenter, Double-blind, Randomized, Placebocontrolled, Parallel Group, Prospective, Event Driven Phase IV Study 39. NCT00319111 - AC-052-370 (BENEFIT OL) - Long-term Open-label Extension Study in Patients With Inoperable Chronic Thromboembolic Pulmonary Hypertension (CTEPH) Who Completed Protocol AC-052-366 (BENEFIT) 40. NCT01106014 - AC-065A302 - A Multicenter, Double-blind, Placebo-controlled Phase 3 Study Assessing the Safety and Efficacy of Selexipag on Morbidity and Mortality In Patients With Pulmonary Arterial Hypertension 41. NCT00236665 - TOPMAT-OBHT-001 - A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study of the Efficacy and Safety of Topiramate in the Treatment of Obese Patients With Mild to Moderate Essential Hypertension 42. NCT00642278 - 28431754DIA2001 - A Randomized, Double-Blind, Placebo-Controlled, Double-Dummy, Parallel Group, Multicenter, Dose-Ranging Study in Subjects With Type 2 Diabetes Mellitus to Evaluate the Efficacy, Safety, and Tolerability of Orally Administered SGLT2 Inhibitor JNJ-28431754 With Sitagliptin as a Reference Arm 43. NCT00816166 - VISSIT CA-2007-01 - Phase III Study of Pharos Vitesse Neurovascular Stent System Compared to Best Medical Therapy for the Treatment of Ischemic Disease 44. NCT00236639 - TOPMAT-OBES-002 - A Randomized, Double-Blind, Placebo-Controlled, Multicenter, Parallel Group, Dose-Response Study to Assess the Efficacy and Safety of Topiramate in the Treatment of Patients With Obesity 45. NCT00236600 - TOPMAT-OBES-004 - A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study of Efficacy and Safety of Topiramate in Weight Loss Maintenance in Obese Patients Following Participation in an Intensive, Non-Pharmacologic Weight Loss Program

Part 2: Data Availability	
Data Holder has authority to provide clinical trial data or development partner has agreed to share clinical trial data.	Yes

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Comments:	
Data Holder has sharable electronic clinical trial data or data can be converted to electronic format.	Yes
Comments:	
De-identification and redaction of clinical trial data in accordance with current HIPAA and EU criteria allows protection of participant privacy and confidentiality.	Yes
Comments:	
The product and relevant indication studied has either been approved by regulators in the US and EU, or terminated from development.	Yes
Comments:	
Data Holder has completed the clinical trial and trial has been completed for a period of at least 18 months (or results published in peer-reviewed biomedical literature).	Yes
Comments:	
Part 3: Data Availability Summary	
Based on the responses to the above Data Availability questions, the requested clinical trial data are available for a data sharing request.	Yes
Part 4: Proposal Review	
Question:	**Response:**
Summary-level CSR data is appropriate for the proposed analysis.	No
Participant-level data is appropriate for the proposed analysis.	Yes
A similar analysis is underway or completed/pending disclosure by Janssen.	No
Comments:	With regards to Selexipag: This project intends to develop or improve methodology to increase acceptance by health authorities for augmenting RCTs data with RWD. Janssen might have applied some existing methodology to augment RCTs with RWD. But I am not aware of developing or improving such methodology. With regards to Macitentan: The comment of a similar analysis pertains to the use of Macitentan studies for a similar meta-analysis.