prosciento®

ADVISE • ADVANCE • ACHIEVE

Specialized Expertise to Drive Advances in Diabetes Drug and Device Development

ProSciento provides comprehensive scientific and operational expertise in the design and management of all facets of clinical drug and device development for diabetes.

ProSciento's services and client-specific programs are initiated from a deep scientific expertise in disease pathophysiology, drug classes, methodologies and 16+ years of experience in clinical research, development and regulatory strategies exclusively for metabolic diseases. From that foundation, ProSciento provides clients:

- Customized, global CRO services from candidate selection through single or multinational clinical trial design and conduct, and
- Strategic clinical development consulting often beginning with a well-defined target product profile and clinical development plan through regulatory submissions, management of scientific advisory boards and often licensing opportunities.

ProSciento's Therapeutic Expertise in Diabetes

Founded in 2003, ProSciento's mission has been advancement of novel therapies for metabolic diseases, including diabetes, NASH and obesity. Led by a team of scientific, operational and regulatory experts, ProSciento has helped pioneer mainstays of therapy and devices that have greatly improved patient care for diabetes. This expertise has also driven important advances in clinical research methodologies that have helped shape today's clinical study design and protocol development for novel and biosimilar medicines for diabetes.

ProSciento's Track Record in Diabetes:

- More early phase type 1 and type 2 diabetes clinical studies than any other US provider*
- Clinical studies completed within every medically relevant glucose-lowering drug class
- Role in validating new diabetes drug and device classes and an active role in investigating new drug classes for NASH and obesity
- One of only three providers worldwide to utilize Automated Glucose Clamp technology, elevating data reliability for insulin-related drug trials
- Supporting clients in publishing outcomes with more than 300 poster presentations and peer-reviewed articles

*Data from Informa's Citeline January 2020

Diabetes Compound Experience

As the only clinical research organization in the U.S. exclusively focused on metabolic diseases, ProSciento has been involved in the development of all medically relevant classes of glucose-lowering drugs, including new insulin analogs, novel insulin formulations, and biosimilar insulins. An overview of ProSciento's diabetes compound experience includes:

BIOLOGICS:

Insulins
Rapid-, long- and ultralong-acting NCEs, biosimilar insulins, inhaled and oral insulins

Incretins mimetics
Glucagon-like peptide 1 (GLP-1) analogs, gastric inhibitory peptide (GIP) analogs, dual agonists, oxyntomodulin analogs

Other glucoregulatory peptides and proteins
Amylin analogues, peptide YY (3-36), fibroblast growth factors (FGF21), insulin-like growth factor 1

Immune-modulation and beta cell regeneration
Monoclonal antibodies, INGAP

SMALL MOLECULES:

Insulin secretagogues
Sulfonylureas, meglitinides, glucokinase activators, GPR40, GPR119, GPR44 agonists

Insulin sensitizers
Biguanides, PPAR agonists, SARMs, SIRT1 activators, 11beta-HSD1 inhibitors

Incretin/glucagon pathway modulators
Dipeptidyl peptidase-4 inhibitors, glucagon-receptor antagonists

SGLT-2 inhibitors

Other oral agents
Diacylglycerol acyltransferase and ACC inhibitors, farnesoid X receptor (FXR) agonists, niacin derivatives, CCR2 antagonists, iBAT inhibitors, PDF4 inhibitors

DEVICES:

Artificial pancreas

Continuous glucose monitoring systems

Alternative routes of peptide administration

mHealth applications

Unparalleled Expertise in Metabolic Clinical Research

305+ clinical projects conducted in diabetes, NASH and obesity

Contributions to **16+** drugs and devices on the market today

130+ clinical trials for biologics completed

220+ clinical trial sites across the Americas, Europe and Asia-Pacific

Specialized Expertise to Drive Advances in Diabetes Drug and Device Development

Utilizing Specialized Methods to Advance Clinical Research for Diabetes

ProSciento's advanced clinical research capabilities deliver detailed proof-of-concept and mechanistic studies. Mechanistic insights into diabetes pharmacotherapeutics requires a comprehensive range of quantitative investigative techniques that are well-tolerated, reproducible and of proven value in drug development. ProSciento's specialized repertoire of validated methodologies can provide evidence of differentiating properties, including ameliorating insulin resistance, increasing insulin secretion, restoring the integrity of the incretin axis, decreasing hepatic steatosis, and improving cardiovascular risk profiles. Moreover, ProSciento's science-driven approach enables simultaneous comprehensive profiling of multiple safety and efficacy signals and helps to minimize risk by maximizing the actionable data generated.

Assessment	Method
PK/PD of exogenous insulin (including biosimilar insulins)	Euglycemic clamp
Islet β-cell (insulin secretion)	Graded glucose infusion; hyperglycemic clamp
Islet α-cell function (glucagon secretion)	Stepped hypoglycemic clamp
Partitioning individual actions of islet hormones	Pancreatic (islet) clamp
Whole-body insulin action	Two-step hyperinsulinemic euglycemic clamp
Hepatic glucose production; muscle glucose uptake	Stable isotope labeled glucose methods
Hepatic de novo lipogenesis	Stable isotope labeled methods (^{13}C-acetate and deuterated water)
Whole-body substrate utilization (carbohydrate vs. lipid)	Indirect calorimetry
Glucose absorption from the intestine	Dual and triple stable isotope glucose tracer methods
Body composition, e.g. visceral vs subcutaneous fat	Dual-energy X-ray absorptiometry (DEXA, DXA)
Hepatic steatosis and fibrosis	Magnetic Resonance Imaging (MRI) and Magnetic Resonance Elastography (MRE)
Ectopic lipid deposition in muscle and pancreas	MRI
Cellular enzyme activity	Tissue biopsy (fat, muscle, liver)
Energy expenditure	Indirect calorimetry and doubly labeled water techniques
Electrocardiographic safety (thorough QT/QTc studies)	QT and electrocardiographic telemetry

Automated Glucose Clamp Technology

ProSciento's Automated Glucose Clamp is a proprietary clinical research technique to assess the pharmacokinetic and pharmacodynamic properties; time-concentration and time-action profiles; insulin sensitivity, and additional parameters of diabetes investigational drugs. This specialized approach utilizes a closed-loop system that determines and infuses exogenous glucose to maintain a predetermined target glucose level in which the challenges associated with manual glucose clamps, such as inconsistent results and inter-operator variability, are removed. Automated Glucose Clamp techniques include the euglycemic or isoglycemic clamp, hyperinsulinemic euglycemic clamp, the stepped hypoglycemic clamp, the islet cell or pancreatic clamp, and the hyperglycemic clamp.

ProSciento's specialized early phase clinical research unit (CRU) is the only center in the U.S. and one of only three centers worldwide with this proprietary Automated Glucose Clamp technology and expertise.

Partnering with ProSciento

ProSciento's science-driven approach provides clients seamless support from early development strategy to decision milestones. When partnering with ProSciento, all client interactions are with a ProSciento team of experts who are focused on tailoring services to meet individualized sponsor-specific programs. To learn more about ProSciento's clinical R&D services for single and multi-site studies, contact bd@prosciento.com or visit www.prosciento.com.

Contact us at bd@prosciento.com to discuss your diabetes drug development program

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