



**Celerion – A Global Contract Research
Organization, Leading Antidiabetic Drug
Development Locally**

November 14, 2014

Objectives

- Acquaint the ADC with Celerion.
- To understand the drug development process.
- To understand the unique obstacles to antidiabetic drug development.
- To understand the importance of community support for clinical research activity.

Terms

- Clinical Research
 - a branch of healthcare science that determines the safety and effectiveness of medications, devices, diagnostic products and treatment regimens intended for human use.
- Contract Research Organization (CRO)
 - an organization that provides support to the pharmaceutical, biotechnology, and medical device industries in the form of research services outsourced on a contract basis.

Ethics

- Clinical Research
 - Is a highly regulated industry guided and governed by
 - Ethics Committee / Institutional Review Board (EC / IRB)
 - International Conference of Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)
 - Good Clinical Practice (GCP)
 - Office for Human Research Protections (OHRP)
 - The Belmont Report
 - To ensure that participant protections of
 - Respect for persons
 - Beneficence
 - Justice
 - Right to informed consent
 - Shared decision-making
 - Privacy for research participants
 - Return of results
 - Right to withdraw

Celerion

- Celerion is the leading global provider of out-sourced early clinical development services to the pharmaceutical industry.
- Celerion specializes in early phase clinical research providing comprehensive data early in drug development to enable informed go/no go decisions on new drug candidates.
- Celerion employs more than 950 scientific and medical staff with the portfolio of skills to design, conduct and interpret complex clinical studies.
- Celerion has over 40 years of experience in early clinical research involving more than 6000 studies.

Global Clinical Research



Lincoln, Nebraska

- 200 beds
- 50,000 square feet
- 40 years of operation
- 119 employees

- AAHRPP Accredited
- ADME suite
- USP <797> Clean Room
- Radiolabel license
- 24 in-hospital beds at Bryan Health CPU



Neptune, New Jersey

- 150 beds
- 40,000 square feet
- 18 years of operation
- 102 employees

- AAHRPP Accredited
- Jersey Shore Hospital affiliation
- Renal center

Global Clinical Research



Phoenix, Arizona

- 300 beds
- 105,000 square feet
- State-of-the-art purpose built facility opened in 2008
- 245 employees

- AAHRPP accredited
- Highly Automated ECG Core Lab
- Cardiac center
- Ophthalmology Suite
- Diabetes Center of Excellence



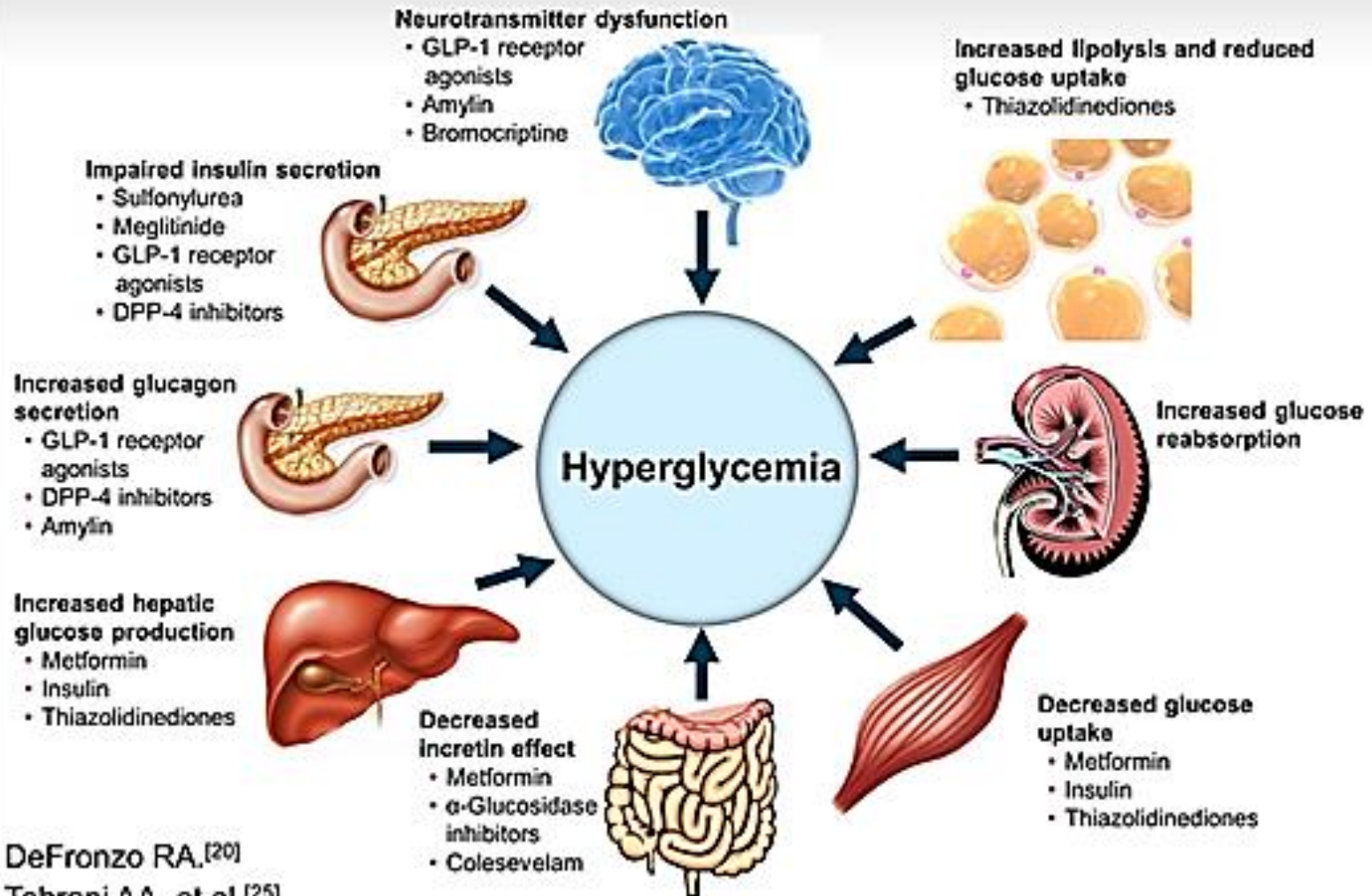
Belfast, Northern Ireland

- 78 beds
- 29,000 square feet
- 20 years of operation
- 98 employees

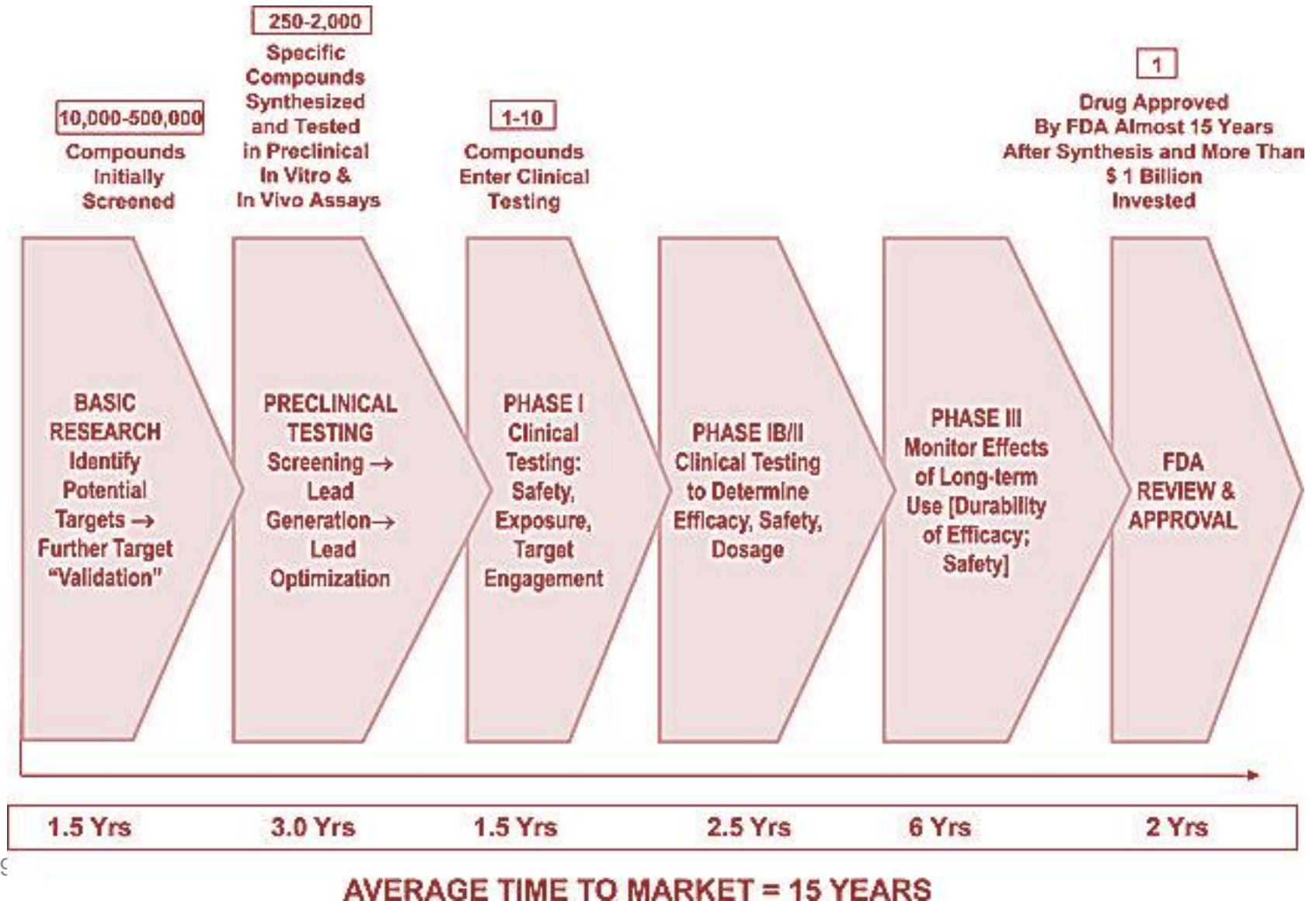
- MHRA accredited
- ANVISA certified
- Respiratory Centre of Excellence

The Ominous Octet: Pathologies, Therapies and Targets

Hyperglycemia in Type 2 Diabetes



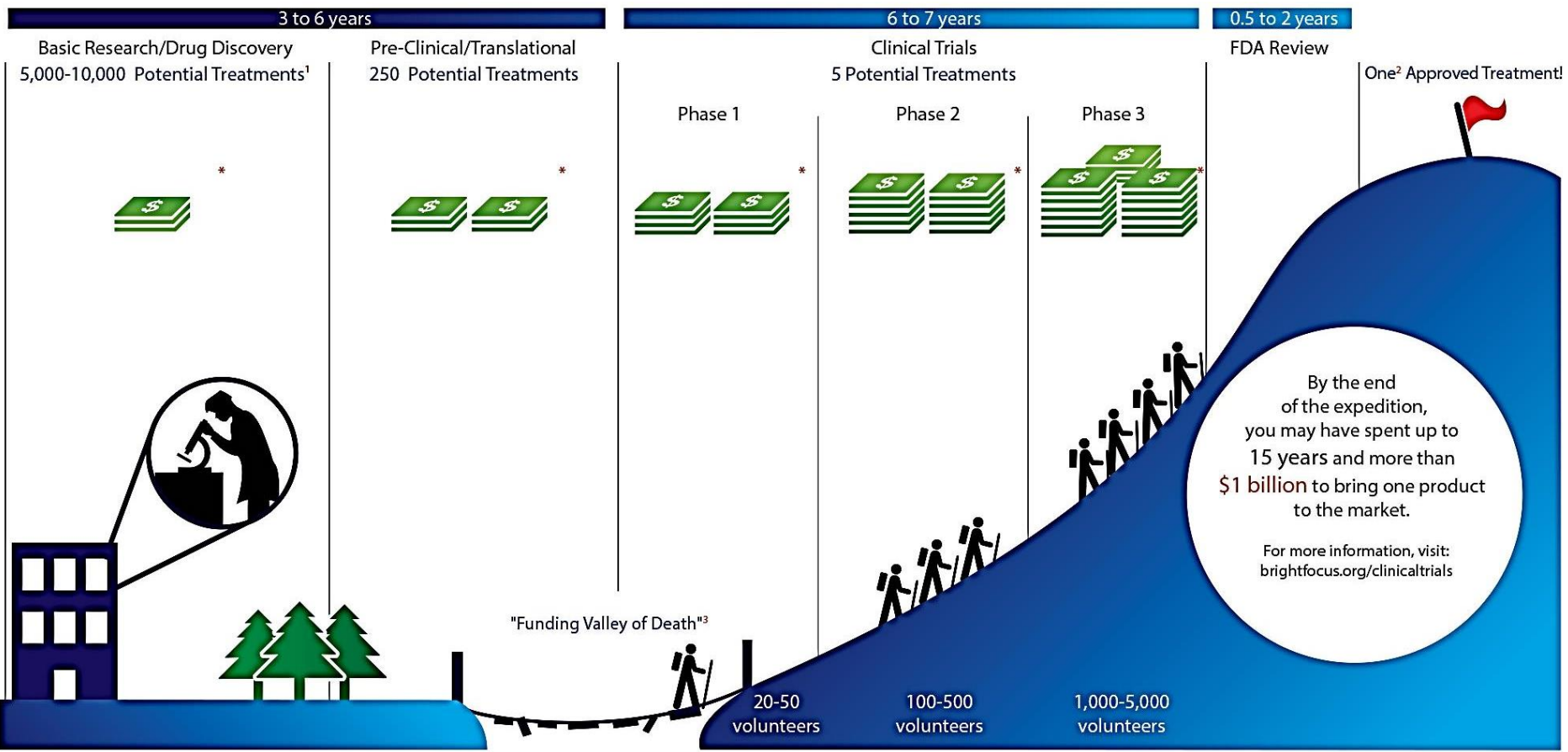
Drug Development Process



An Uphill Battle

Imagine leading an expedition where every step is more difficult than the last...

The long journey begins in the lab, where scientists spend years testing thousands of ideas. Next, crossing the so-called "Funding Valley of Death" requires the resources and time needed to complete clinical trials, testing safety and effectiveness among what could end up being thousands of volunteers. At the end of this steep financial and scientific climb: Food and Drug Administration approval for a new treatment. Ultimately, it may have taken up to 15 years and more than \$1 billion to bring this treatment to the market.



¹ Although we are using the word "treatment," clinical trials also involve medical research studies in which people participate as volunteers to test new methods of prevention, screening, and diagnosis of disease.

² After approval, the product is manufactured for sale on the market, and the process enters Phase 4 (Post-Marketing Monitoring/Clinical Trials). At this point, the FDA monitors for public safety and adverse events, and the sponsor company may begin Phase 4 Clinical Trials to obtain information about long-term effects or to test the product in special patient populations.

³ The "Funding Valley of Death" is the financial challenge many promising treatments face in having the opportunity to be scientifically tested in a clinical trial. In many cases, further financial support or partnerships are necessary to proceed.

⁴ The cost of bringing a drug to market depends on a number of variables, but could be more than \$1 billion, including approximately \$50-840 million for Basic Research/Drug Development and Pre-Clinical/Translational research, and approximately \$50-970 million to complete all three Phases of the Clinical Trials.

Challenges in Antidiabetic Drug Development

- In traditional drug development, discovery of these 3 critical elements is deferred to late phase. This is no longer a viable model of drug development.
 - Efficacy
 - FDA Guidance for Industry: Diabetes Mellitus – Developing Drugs and Therapeutic Biologics for Treatment and Prevention (2008)
 - Cardiovascular Risk Assessment
 - FDA Guidance for Industry: Diabetes Mellitus – Evaluating Cardiovascular Risk in New Antidiabetic Therapies To Treat Type 2 Diabetes (2008).
 - Durability
 - Time to failure of a treatment to control dysglycemia

Cardiovascular Risk Assessment

Adds at least a year to the drug development process and an estimated **250 to 500 million** US Dollars to the cost of developing a new diabetes medication.

In order to satisfy the initial approvability hazard ratio requirements of 1.8 to 1.3, drug development programs should target between approximately 120 to 700 CV events respectively. This will require studying between 4,500 and 15,000 T2DM patients.

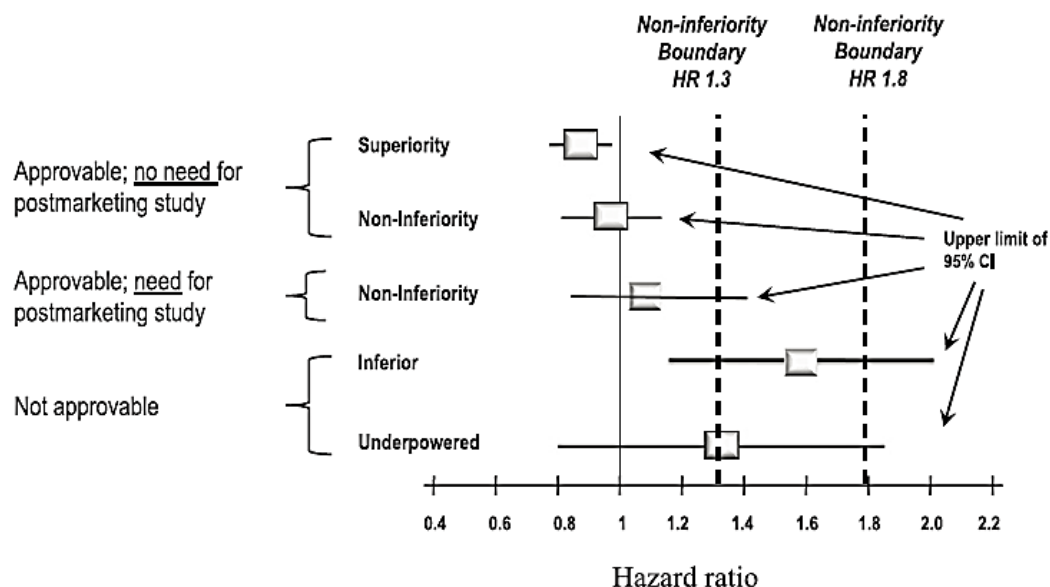


Figure 1—FDA CV safety: CI bars. The FDA guidelines provide statistical hurdles for approval. Five hypothetical examples of possible hazard ratios and the upper limit of the 95% CI of a development plan are shown as well as the regulatory consequences of each outcome.

Boaz Hirshberg, Arie Katz. "Cardiovascular Outcome Studies With Novel Antidiabetes Agents: Scientific and Operational Considerations" *Diabetes Care* 36.2 (2013): S253-S258.

David a. Fryburg, and Maria T. Vassileva. "Atherosclerosis Drug Development in Jeopardy: The need for Predictive Biomarkers of Treatment Response" *Science Translational Medicine* 3.72 (2011): 1-5.

Cardiovascular Risk Assessment

“Very few pharmaceutical companies have the resources, expertise, and financial capability to conduct such studies and it may no longer be feasible for small biotech and pharmaceutical companies to independently develop and launch antidiabetes medications.”

Celerion Metabolic Program: Overview of Available Services

- **Sample collection**
 - Closed-Loop Sampling: Intravenous cannula based blood sparing sampling technique. Eliminates blood volume lost to waste.
- **Glucose Analysis**
 - Fingertick glucometer
 - Laboratory Analyzer
 - Glucose hexokinase
 - Continuous Glucose Monitoring Systems (CGMS)
 - Yellow Springs Instruments (YSI)
 - Glucose oxidase method
 - Laboratory grade
 - Supports bedside and real time analysis
- **Metabolically Relevant Medical Imaging** (DEXA, MRI)*
- **Metabolically Relevant Biopsies** (Adipose, Muscle)*
- **Measures of Glucose Dysregulation**
 - Oral Glucose Tolerance Tests (OGTT)
 - Meal Tolerance Tests (MTT)
 - Intravenous Glucose Tolerance Tests (IVGTT)
 - Pancreatic Maximum Stimulation Tests
 - Graded Glucose Infusions (GGI)
 - Glucose Clamping
 - Isotope Dilution Methods
 - Stable and radioactive isotopes
- **Satiety**
 - Food intake models
- **Cardiometabolic Endothelial Function Testing**
 - Flow Mediated Dilation (FMD)
- **Substrate Utilization and Energy Expenditure**
 - Indirect Calorimetry

* Available with support from local medical communities

Questions ?