

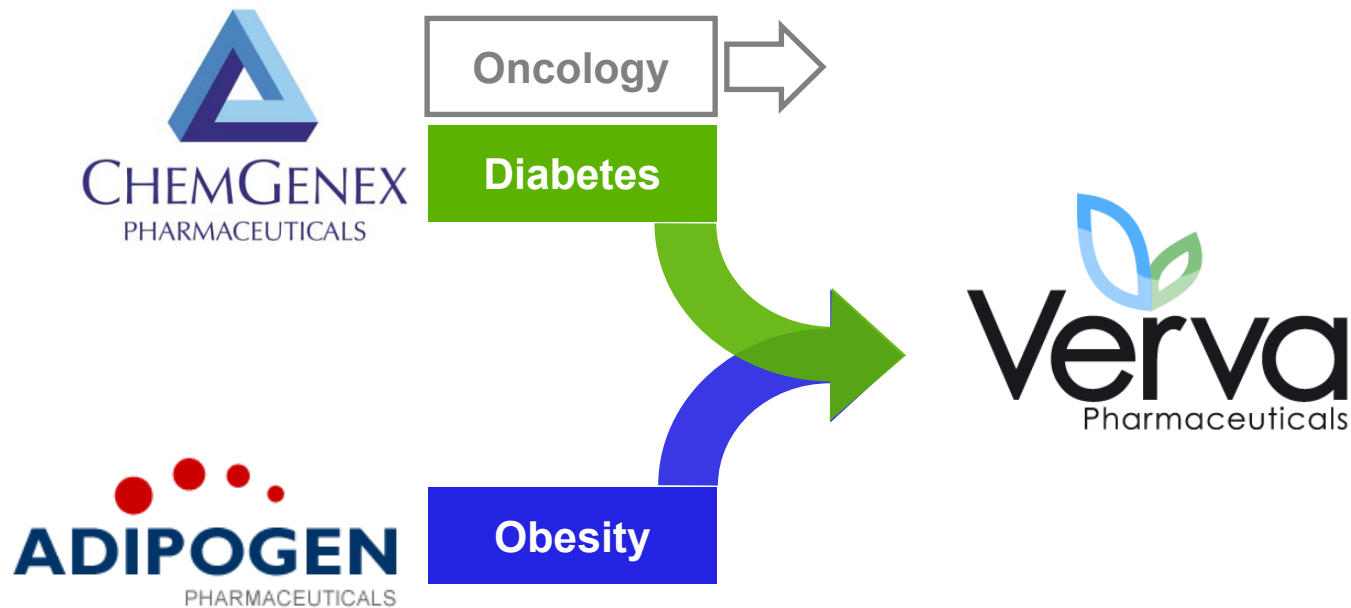


Novel Therapies for Metabolic Disease

Vince Wachter, CEO
vwacher@vervapharma.com

Verva Pharmaceuticals

- Clinical-stage pharmaceutical company formed Dec'07 to develop novel therapies for diabetes and obesity



Verva Leadership Team

Management

Vince Wacher, *CEO*

ex-CEO Adipogen; 14 yr US biopharma

Guy Krippner, *VP Drug Dev.*

ChemGenex, Starpharma, Biota

Ken Walder, *VP Biology*

ChemGenex, NIH

Board of Directors

Ian Nisbet, *Chairman*

ex-Millennium, Meditech, CSL

Greg Collier, *Director*

CEO, ChemGenex

Andrew Baker, *Director*

GBS Venture Partners

Andrew Macdonald, *Director*

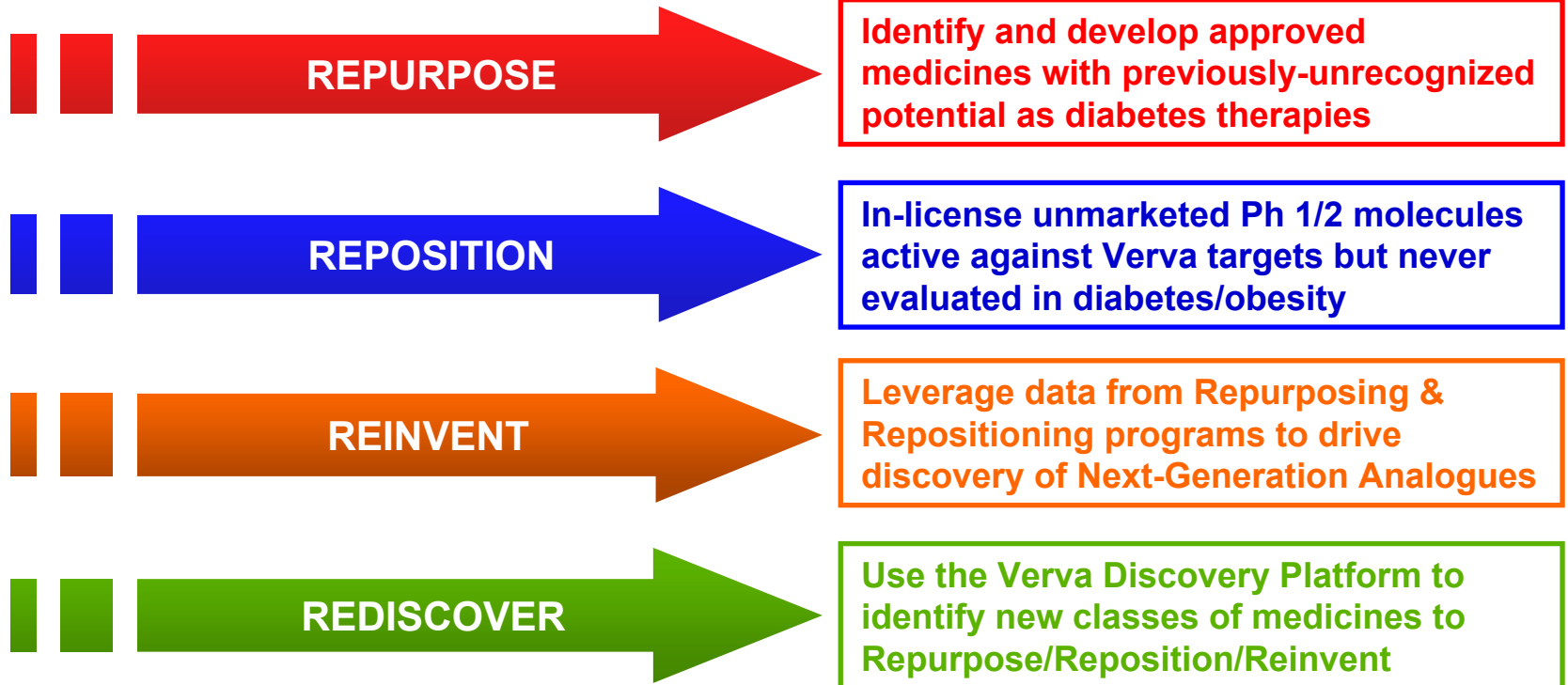
CEO, Cytopia Ltd.

Verva Expertise & Infrastructure



- Verva's founding laboratory
 - 10-year relationship
 - Ideal discovery partner
- Experienced scientific team
 - Decades of international metabolic diseases research
- Exceptional *in vitro* & *in vivo* capabilities
 - DIO mice/rats, *db/db* mice, Zucker rats, Israeli Sand Rats
- Verva Management & Board have extensive clinical trials experience

Multi-Tiered Value Generation Strategy



Verva Portfolio

PROGRAM	Discovery	Preclinical	Phase 1	Phase 2a	Phase 2b
VVP808 (diabetes)	Non-TZD Insulin Sensitizer *				
VVP100X (diabetes)	§				
GES Platform [¶]					
FGFR (obesity)	ASOs				
IMPDH (obesity)	†				

* Off-patent molecule with extensive clinical experience in an unrelated indication

§ Next-generation insulin sensitizers based on VVP808 structure and mode-of-action

¶ Gene Expression Signature technology applied to discovery of diabetes therapies

† Preclinical proof of concept with existing commercial product



VVP808 – A New Insulin Sensitizer

Diabetes Opportunity

- Multi billion dollar worldwide diabetes therapy market expected to double in the next 7 years
- Current therapies limited by safety, cost and loss of efficacy
- Developmental products are primarily “me too” drugs directed towards existing targets and modes-of-action
- Significant market demand for novel insulin sensitizers
 - TZD/PPAR insulin sensitizers dominated the oral therapy market prior to identification of cardiovascular safety issues

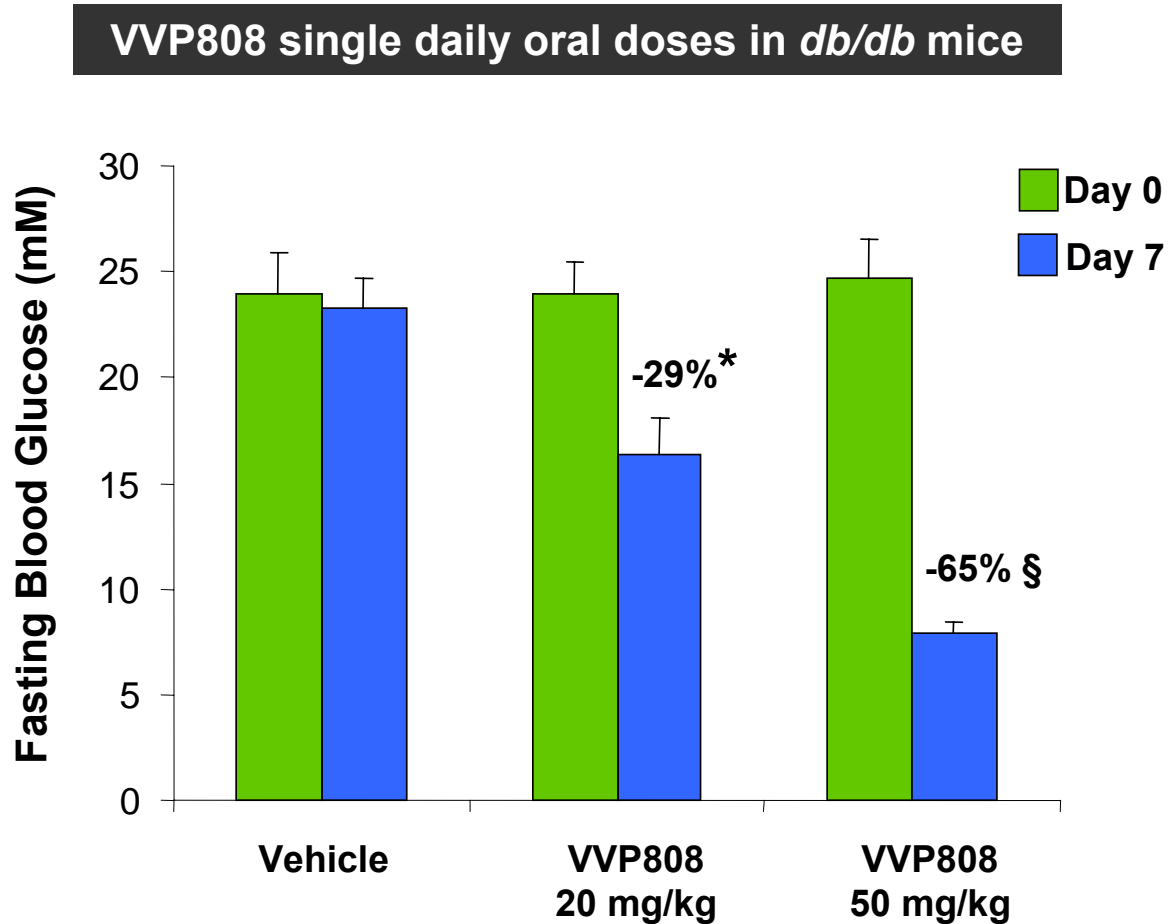
****VVP808 is a new non-TZD/non-PPAR insulin sensitizer****

VVP808 Clinical Repurposing

- **Off-patent enzyme inhibitor**
 - Identified using the Verva GES discovery platform
 - 40+ years of clinical use solely in North America in an unrelated indication
 - Established long-term safety profile
 - Limited current use; never evaluated as a diabetes therapy
 - No reported cardiovascular side-effects

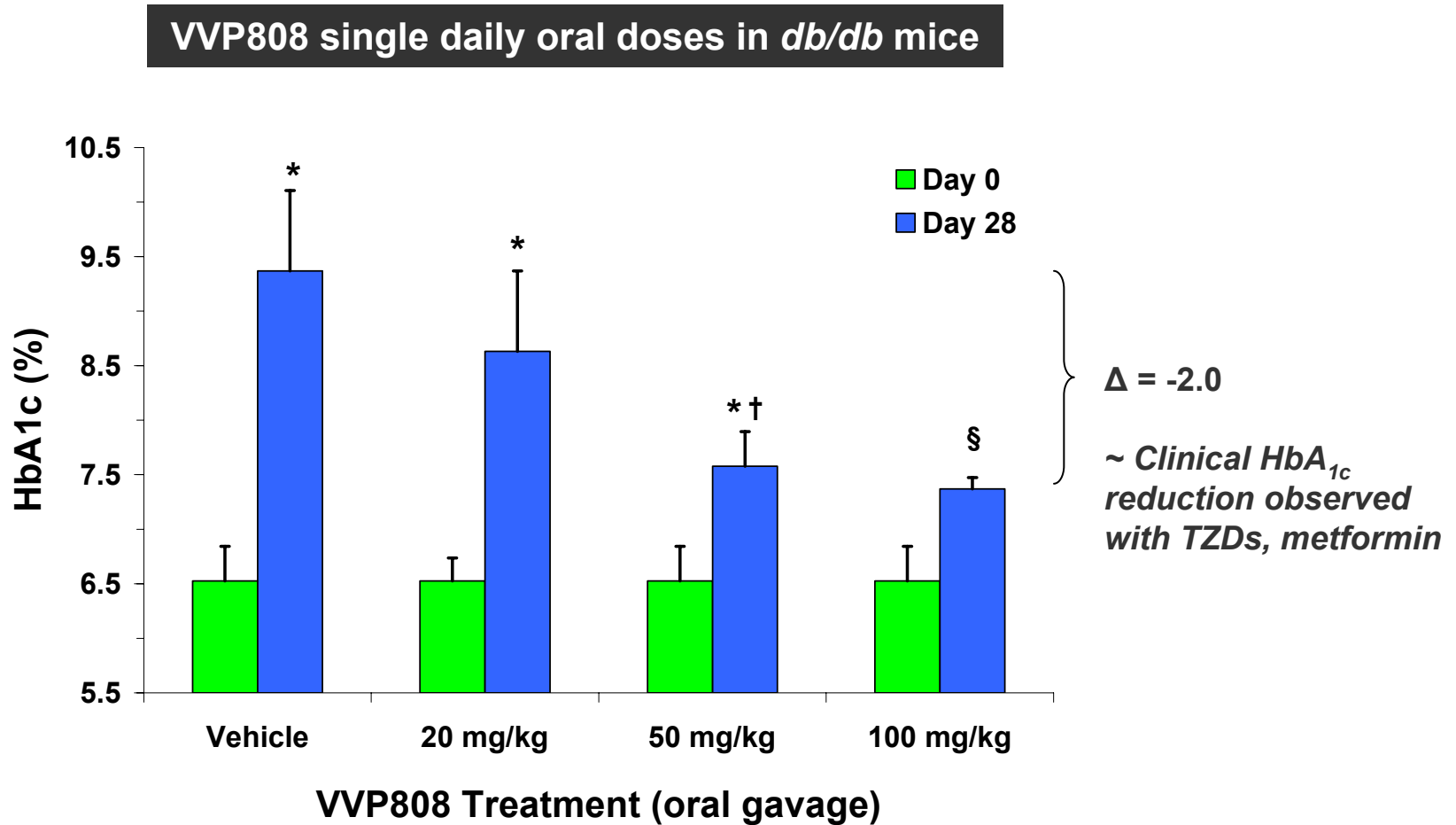
- **Diabetes activity is not due to the known enzyme inhibition**
 - Opportunity for dose-differentiation
 - Avoid effects associated with known enzyme inhibition

VVP808 Lowers Blood Glucose



Compared with Day 0: * $p=0.0008$, § $p=0.00004$

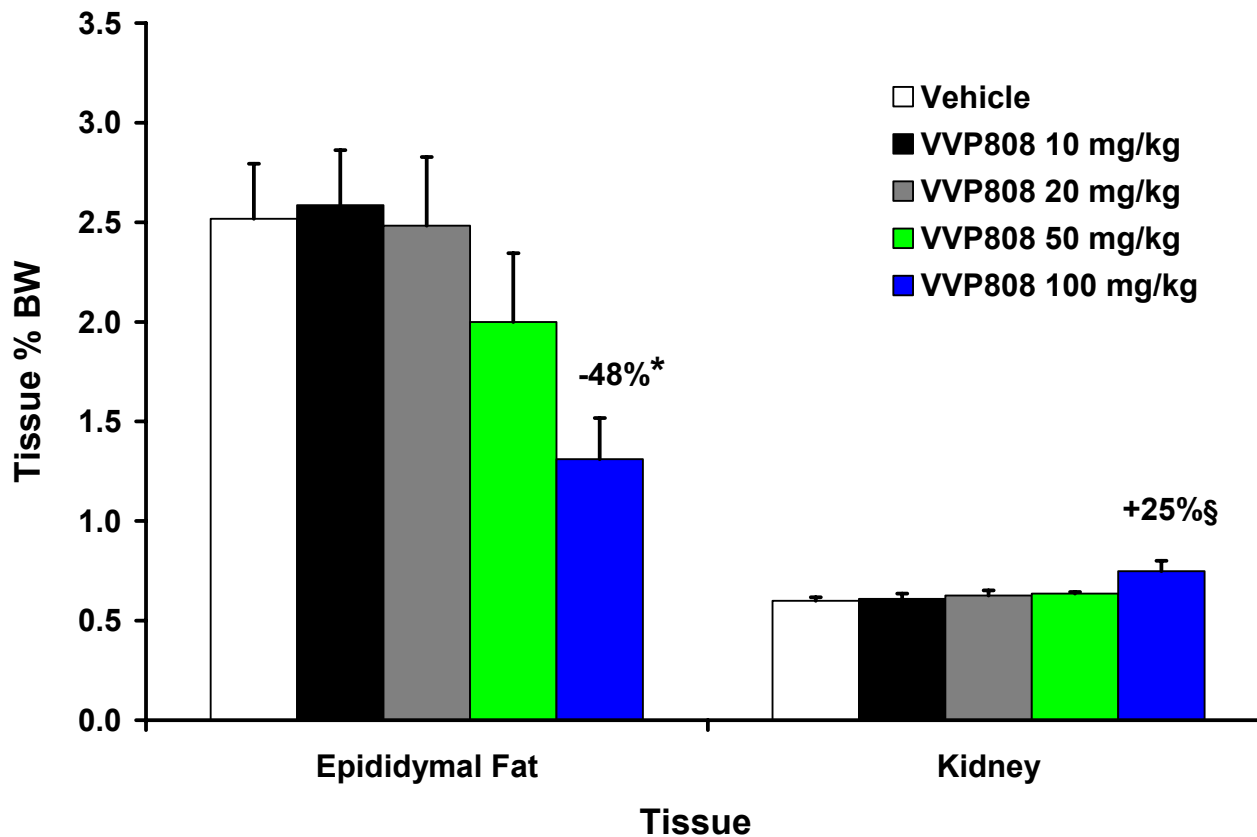
VVP808 Lowers HbA_{1c}



* $p \leq 0.04$ vs. day 0 † $p = 0.06$ vs. vehicle § $p = 0.04$ vs. vehicle

VVP808 Reduces Body Fat

VVP808 single daily oral doses in DIO mice

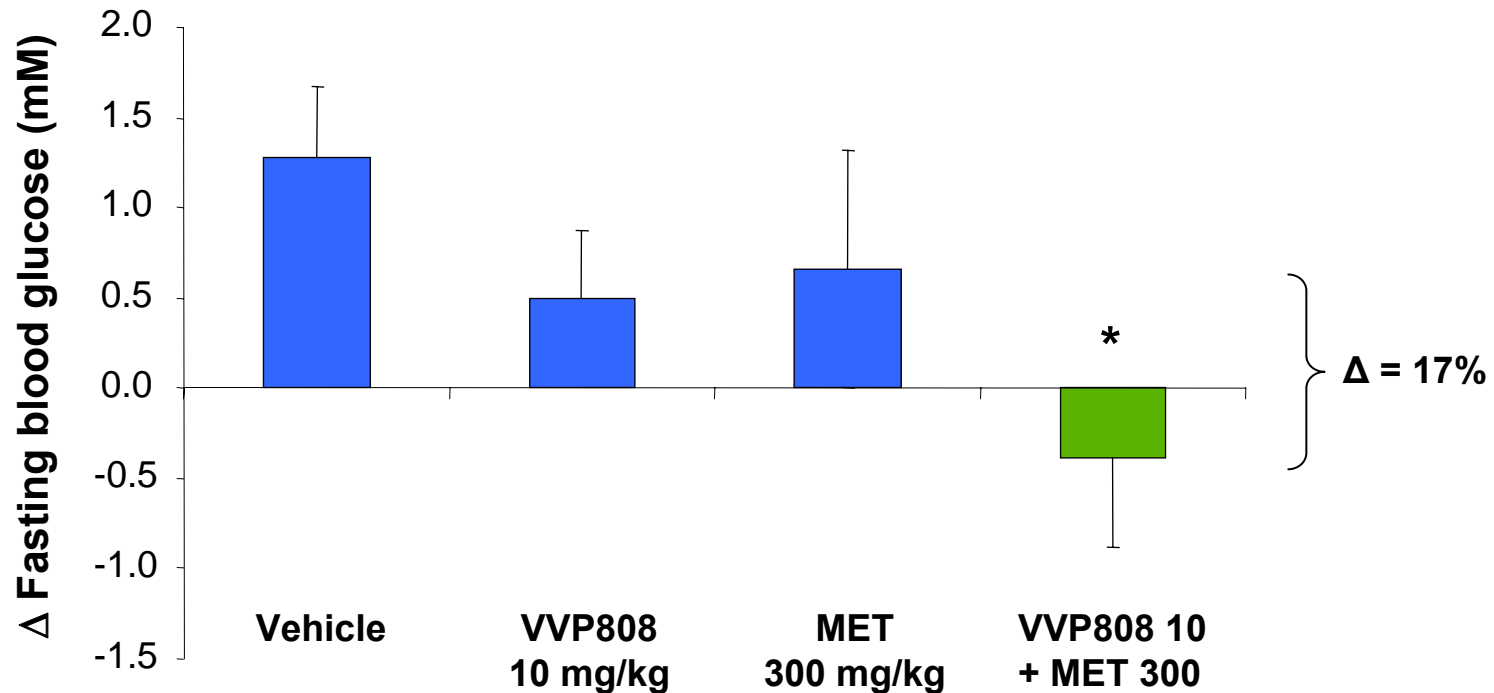


NO change in weights of:
- Quadricep muscle
- Liver

Animals dosed for 16 days. Compared with vehicle: * $p=0.01$ § $p=0.02$

Potential Synergy with Metformin

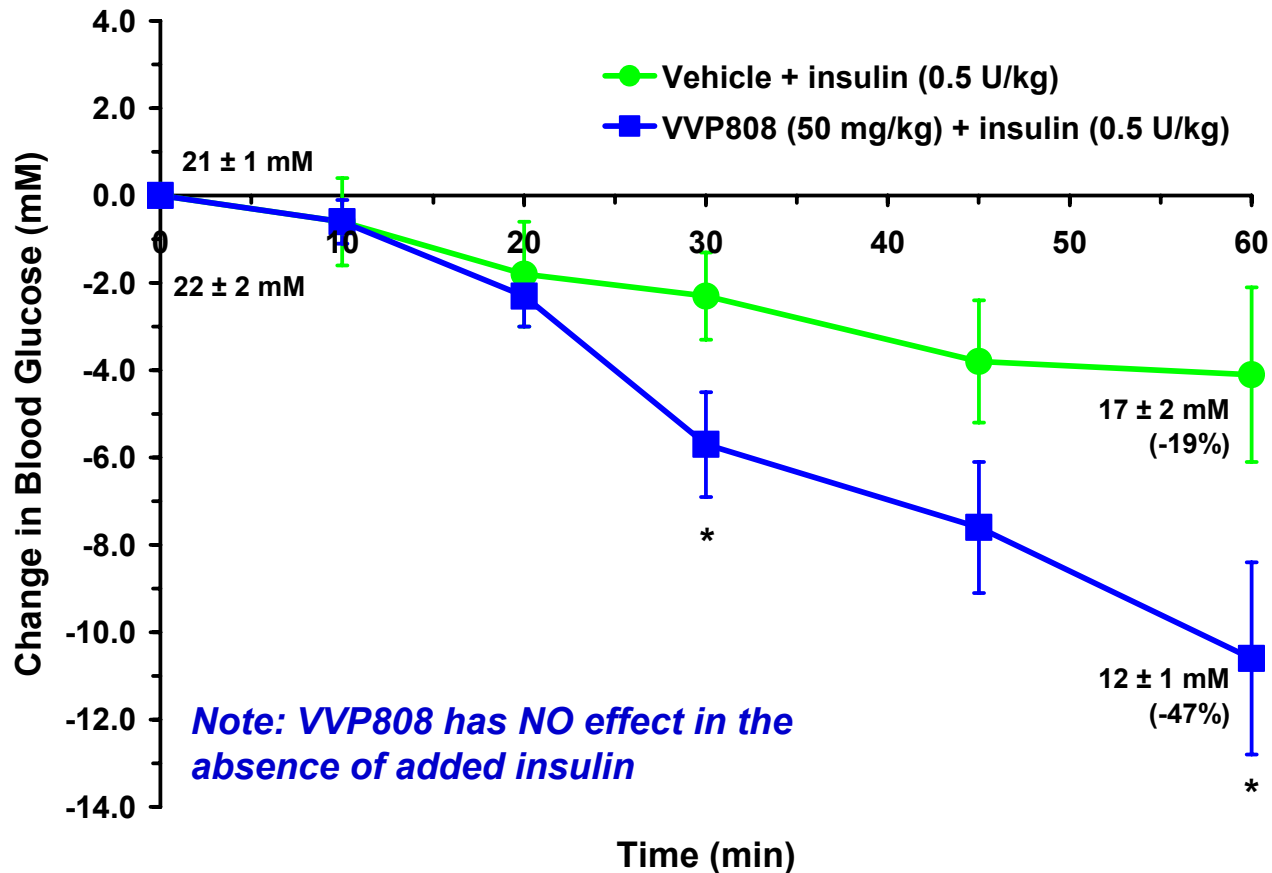
Combination therapy (single daily oral doses x 14 days)
reduced fasting blood glucose in DIO mice



* $p = 0.005$ vs. vehicle

VVP808 - A Novel Insulin Sensitizer

SD rats rendered diabetic (no insulin production) by STZ injection 60 mg/kg/day x 8 days) prior to 14 days VVP808



VVP808 Clinical Development

- **Phase 1b/2a clinical proof-of-concept study**
 - **Safety and efficacy of VVP808 in diabetes patients currently treated with metformin**
 - **Ethics approval obtained under the Australian CTN system**
 - **Primary site Geelong Hospital (PI Dr. Geoff Nicholson)**
 - **Second site Box Hill Hospital (Dr. Richard Simpson)**

- **Key objectives**
 - **Safe co-administration with metformin**
 - **Efficacy at lower doses than used in the approved indication**
 - **Reduction in HbA1c (0.5%), FPG, PPG**
 - **Weight loss, improved lipid profile**

VVP808 Differentiators

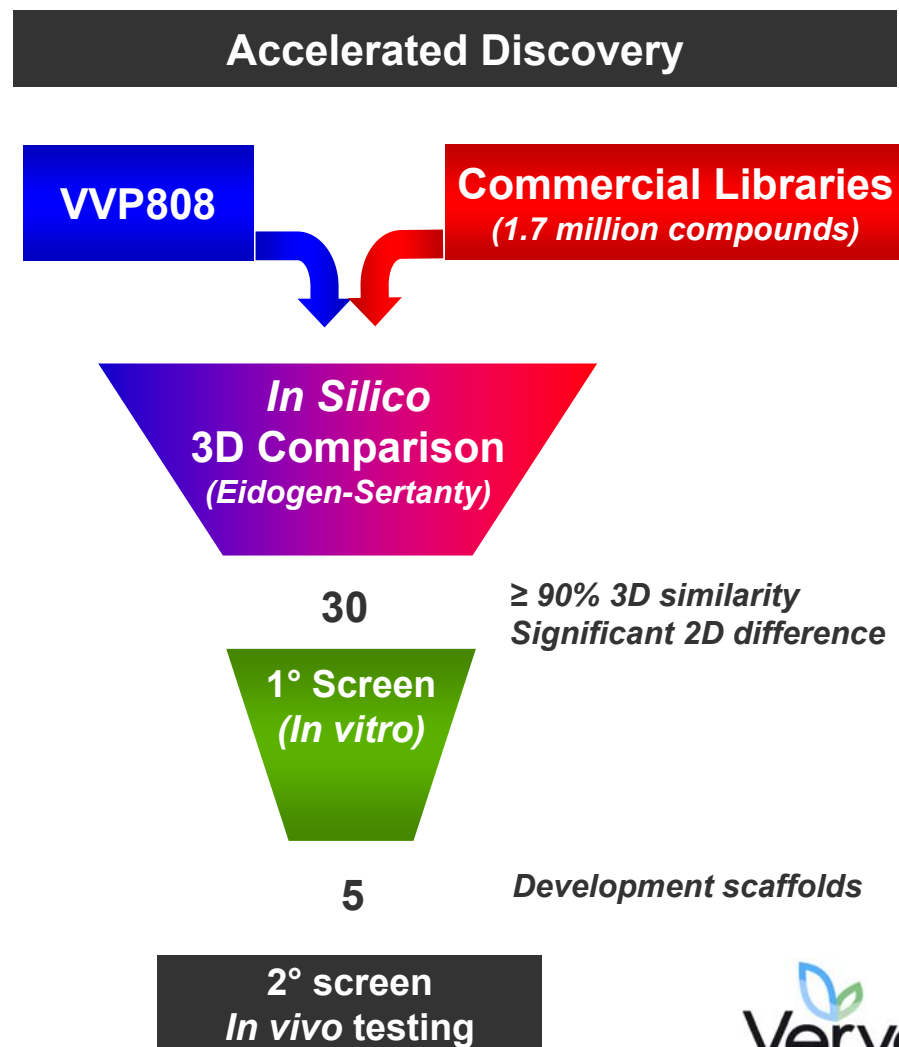
Feature	VVP808 Advantage
New diabetes MOA	→ Non-TZD/PPAR insulin sensitizer Decreased HGP
Long history of clinical use	→ Favourable safety profile Improved with lower doses
Additional benefits possible	→ Weight loss Synergy with metformin
Only approved in N. America Limited current use	→ First-to-market opportunity ROW Low risk of off-label prescribing
Simple structure; low COGS	→ Competitive, 'reimbursement friendly' pricing at good margin
IP differentiation	→ Lower doses; combinations; modified-release forms



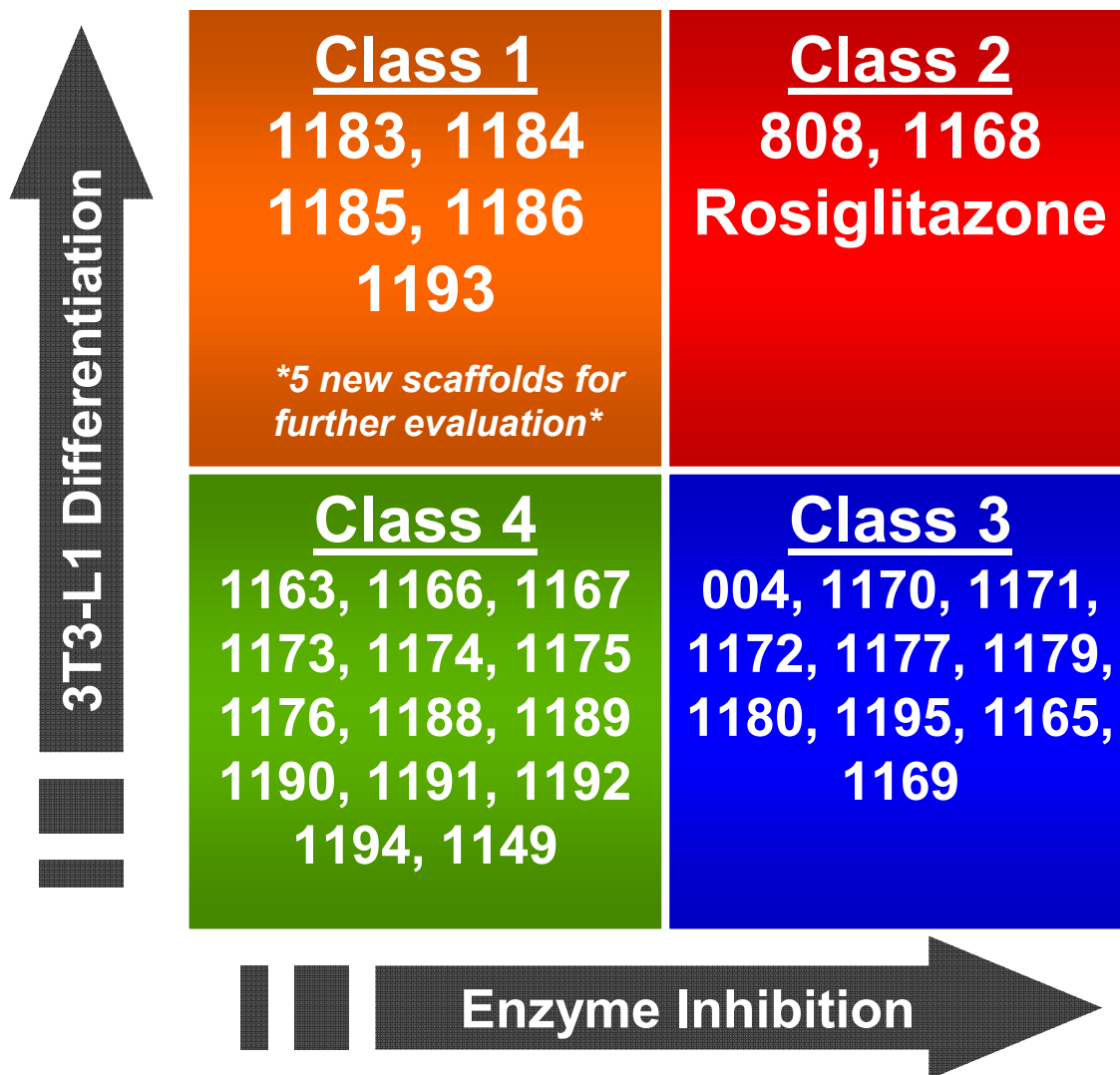
VVP808 Analogues

VVP100X: New Drugs From VVP808

- NCEs based on VVP808 structure & MOA
 - Optimize anti-diabetes effect
 - Engineer away from VVP808 enzyme inhibition
 - Improve efficacy & PK/PD
 - Improve safety profile
- Composition-of matter IP
- Longer-term value



Hit Stratification in Primary Screen





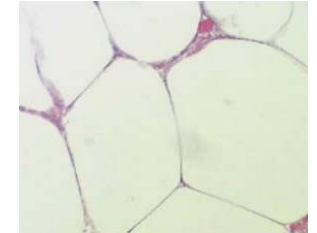
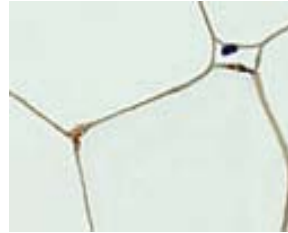
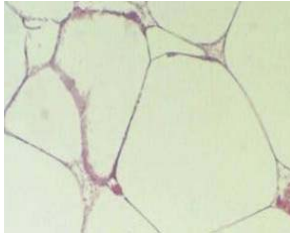
Discovery Platform

Diabetes Discovery Platform

- **Diabetes is not a homogeneous condition**
 - **A continuum of phenotypes and severity**
- **Modulation of multiple processes is required for truly effective diabetes therapy**
 - **Single target screening limits broader efficacy**
- **Verva Gene Expression Signature (GES) Technology**
 - **A 'fingerprint' of 7-12 genes from different pathways whose expression is modulated when diabetic cells are made healthy**
 - **Identifies drug effect on multiple disease-associated processes**

Verva Gene Expression Signature

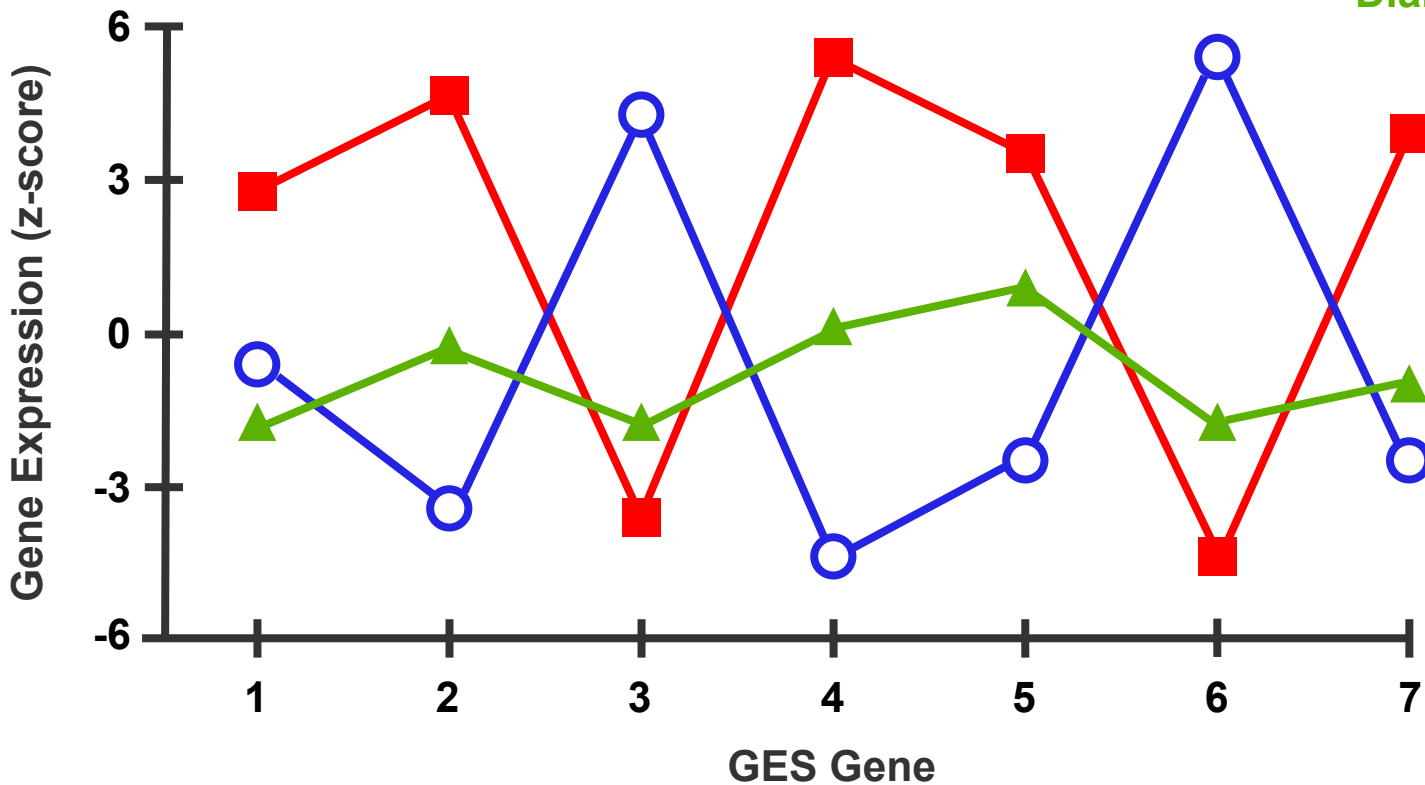
Adipocytes



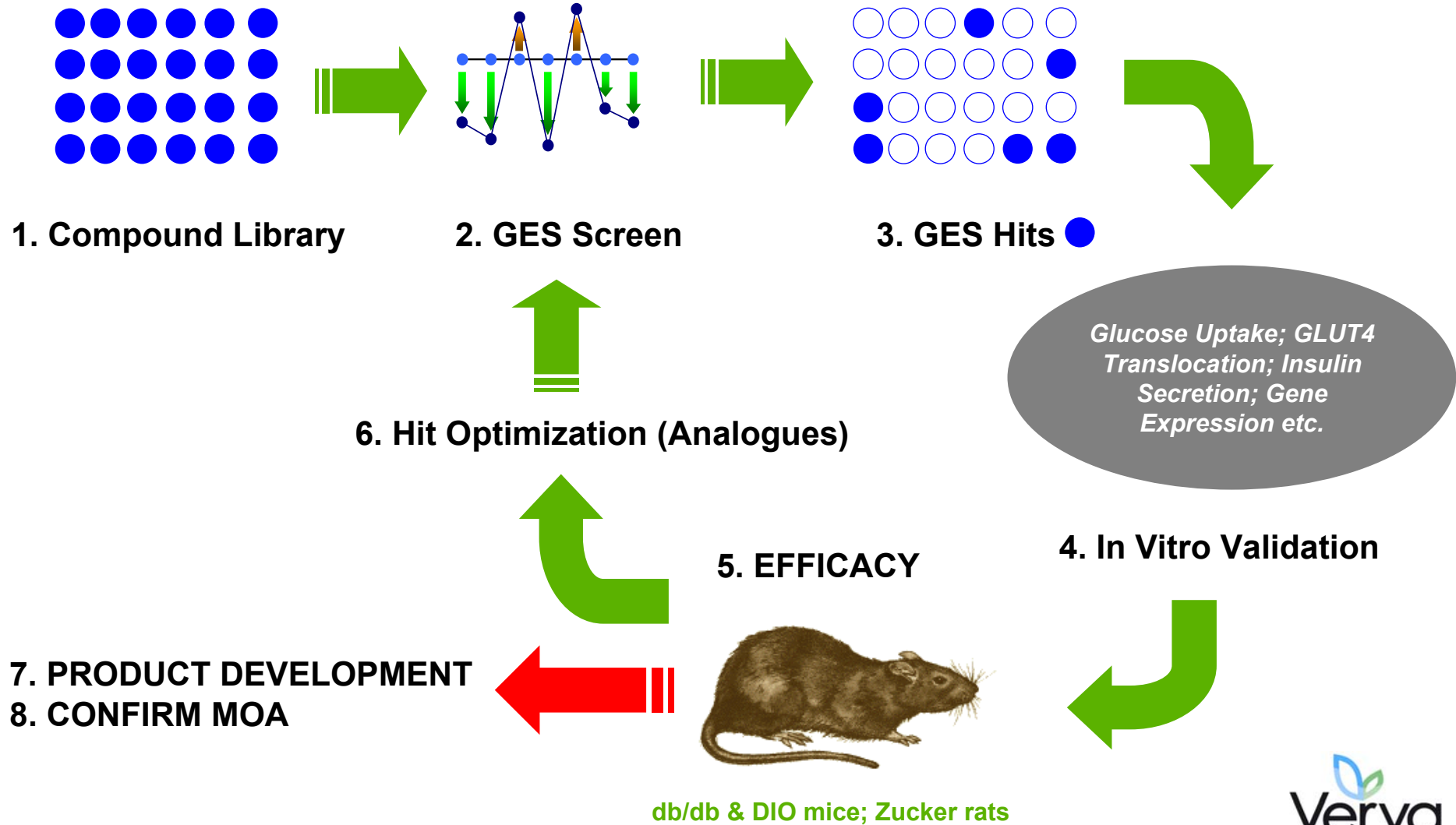
○ - Normal

■ Diabetic

▲ Treated Diabetic



GES-Based Product Discovery



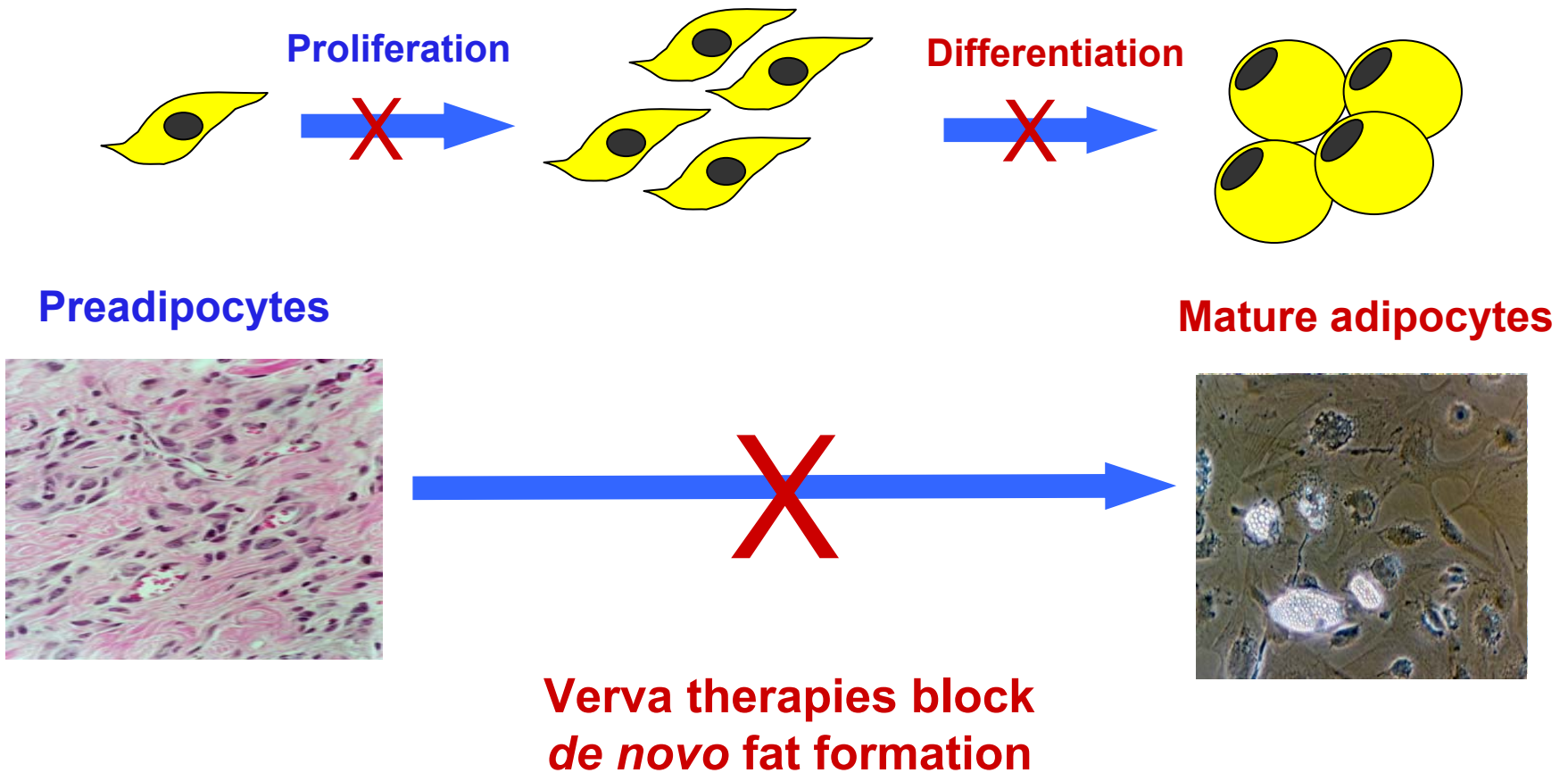
Pipeline Expansion using the GES

- **GES is powerful screening tool**
 - Target-, mechanism- and structure- independent
 - **Unlock value in partner libraries; rescue 'failed' compounds**
 - Knowledge of MOA not required to evaluate diabetes effect
 - Identify previously unrecognized potential for application in diabetes
- **GES is a flexible drug discovery platform**
 - **GES varies with cell type and underlying pathology**
 - May identify therapies optimized for different diabetes etiology
- **Pancreatic β -cell GES in development**
 - **Discover novel, oral, small molecule insulin secretion enhancers**



Verva Fat Reducers

Verva Fat Blockers



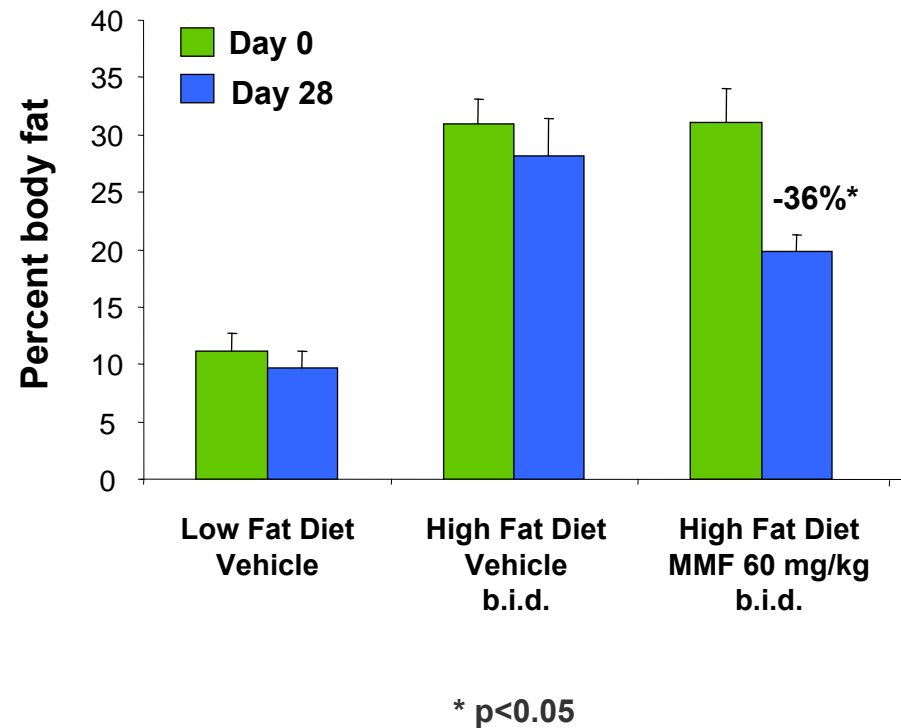
Benefits of Targeting Fat Formation

- **Novel mode of action at the target tissue**
 - Expect longer term efficacy, less resistance
 - Avoid CNS side-effects
- **Additional health benefits**
 - Fat removal can improve cardiovascular profile, reverse diabetes, ameliorate inflammation
- **Multiple clinical applications**
 - Weight/fat loss in obese subjects
 - Prevention of weight/fat gain (e.g. drug induced)
 - Prevention and treatment of diabetes

IMPDH - Small-Molecule Fat Blockers

- **Inosine 5'-Monophosphate Dehydrogenase**
 - **Well-known enzyme target**
 - Immunosuppression, hepatitis, cancer
 - **Not previously evaluated in metabolic diseases**
- **IMPDH Inhibitors**
 - **Weight and fat loss in DIO mice**
 - No changes to food intake; no toxicity
 - **Different mechanism in obesity?**
 - Block adipocyte differentiation but not proliferation
 - Reverse is true for T-cells and cancer cells
- **Accelerate progress through in-licensing**
 - **Access products with phase 1/2 clinical data in unrelated indications**

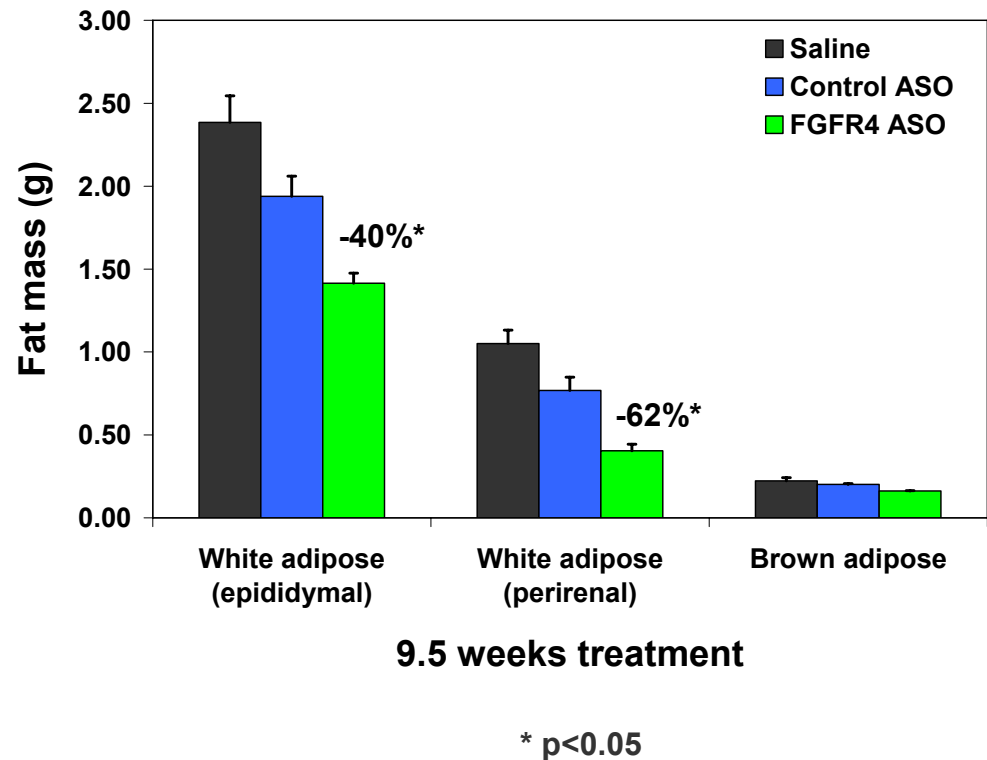
CellCept® (MMF; oral) decreased body fat of DIO mice maintained on a high fat diet



FGFR – Fat Blocking ASOs

- **FGF-1 is a potent promoter of adipogenesis**
 - Exerts its effects through multiple receptors (FGFRs)
- **Collaborated with ISIS Pharmaceuticals to evaluate FGFR in obesity**
 - **FGFR4 ASOs reduced body fat and weight in DIO mice**
 - No effect on food intake
 - Increased metabolic rate
 - Prevented fat gain in lean animals

**FGFR4 ASO (25 mg/kg s.c. q3d)
reduced body fat in DIO mice**





Milestones & Exits

Financing

- **Final stages of an equity financing**
 - **Conduct the VVP808 1b/2a clinical trial**
 - **Establish VVP808 diabetes mode-of-action**
 - **Partner/license other assets and IP in Verva portfolio**

- **Pursuing multiple value strategies**
 - **Partnerships**
 - **Joint development, licensing or options on product programs**
 - **Discovery collaborations around the GES platform**
 - **Strategic transaction**
 - **M&A with company seeking pipeline expansion**

Key Milestones & Newsflow

Event	Time
▪ Financing	Q3'09
▪ Obesity program(s) partnership/license	Q3'09
▪ VVP808 1b/2a clinical - start manufacture	Q3'09
▪ VVP808 phase 1b/2a clinical - initiate study	Q3'09
▪ VVP808 mode-of-action & target confirmed	Q1'10
▪ VVP808 phase 1b/2a clinical – final data	Q2'10
▪ VVP808 partnership/license	Q2'10