VTV THERAPEUTICS

Improving the Lives of Millions of People Living with Type 1 Diabetes

January 2025

Nasdaq: VTVT

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Pioneering Oral Drugs for Challenging Targets to Help Treat Diverse Chronic Diseases

VTV THERAPEUTICS

Advancing late-stage cadisegliatin program for type 1 diabetes

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CANTEX PHARMACEUTICALS

G42 Healthcare

NEWSOARA 恒翼生物医药

Partnerships for potential additional upside and shareholder value

VTV

Experienced Leadership with Decades of Life Sciences Expertise

Paul Sekhri
Chair, President & CEO

egenesis ENGINEERING HOPE
LYCERA
teva
sanofi
NOVARTIS

Steven Tuch
Chief Financial Officer

Rallybio
BMO
Deutsche Bank

Thomas Strack, MD
Chief Medical Officer

Lilly
Pfizer
Takeda
Progenics Pharmaceuticals
Daiichi-Sankyo
tem
faeth

Carmen Valcarce, PhD
Chief Scientific Officer

novo nordisk®

Rich Nelson
Chief Business Officer

VERICAST
Nielsen
IAC

Martin Lafontaine
Chief Commercial Officer

GSK
mont méd
Locemia SOLUTIONS

Dan Kirby
SVP Strategic Ops

axcella
CSL Seqirus
amag
parexel
sanofi

Cadisegliatin: Late-Stage Clinical Development

Product	Indication	Pre-clinical	Phase I	Phase II	Phase III*	Next Key Milestone	Partners + Regions
Cadisegliatin (TTP399) GK Activator	**Type 1 Diabetes**					Topline Ph 3 data	VTV THERAPEUTICS

*Currently on FDA clinical hold following discovery of a chromatographic signal in a human ADME study

Partnership with G42 Healthcare to advance cadisegliatin as an adjunct therapy to insulin for people living with Type 2 diabetes

G42 Healthcare

Cadisegliatin is under investigation and the safety and efficacy has not been established. There is no guarantee that this product will receive health authority approval or become commercially available for the use being investigated

Cadisegliatin: Potential to be First Oral Adjunct Therapy for T1D

Novel oral liver selective glucokinase activator in development to reduce hypoglycemia and improve glycemic control vs. insulin alone

Targets High Unmet Needs

~80% of 1.6M Americans living with T1D fail to achieve target blood glucose control with current SOC[1]

Hypoglycemia is often the major barrier to glycemic control[2]

Derisked by Ph1 and Ph2 Data

Dosed in 500+ subjects to date[3]

Positive impact on hypoglycemia and HbA1c[4]

In Late-Stage Development

Phase 3 trial* initiated Q2 2024

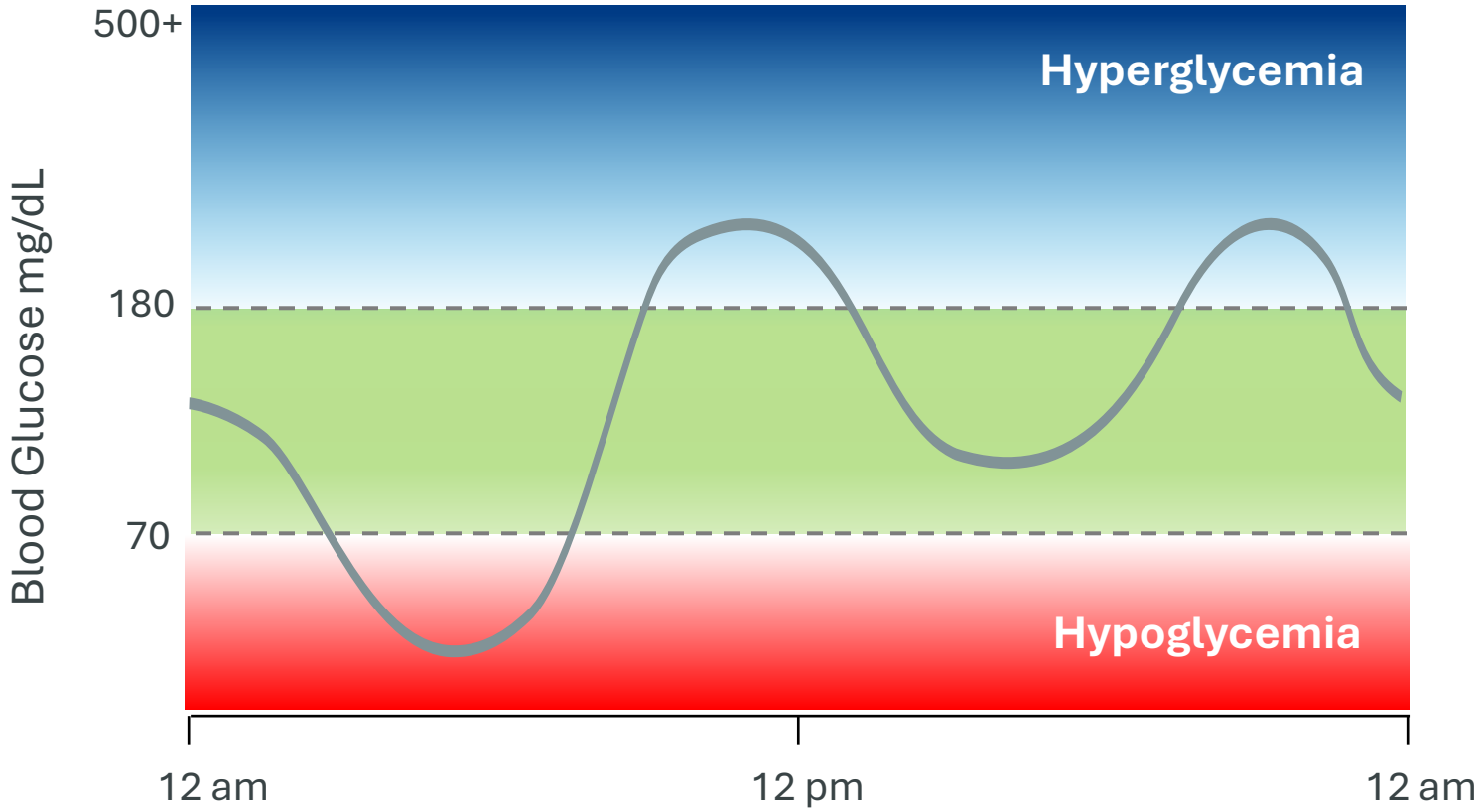
FDA Breakthrough Designation

**Working to resolve an FDA clinical hold on cadisegliatin program following discovery of a chromatographic signal in human ADME study*

1: Akturk HK, et al., T1D Exchange Quality Improvement Collaborative; Factors Associated With Improved A1C Among Adults With Type 1 Diabetes in the United States. Clin Diabetes 2 January 2023; 41 (1): 76–80. https://doi.org/10.2337/cd22-0067; 2: American Diabetes Association Standards of Care in Diabetes – 2023; 3: Internal studies – data on file; 4: Klein KR et al. The SimpliciT1 study: a randomized, double-blind, placebo-controlled phase 1b/2 adaptive study of TTP399, a hepatoselective glucokinase activator, for adjunctive treatment of type 1 diabetes. Diabetes Care. 2021 Apr 1;44(4):960-8

The Challenge: Lowering Blood Glucose to Target While Preventing Hypoglycemia

~80% fail to achieve ADA HbA1c target of <7.0%[1]



Insulin

The pharmacological standard of care with a narrow therapeutic window

Hypoglycemia

Often the major limiting factor in the glycemic management of patients with T1D[2]

1: Akturk HK, et al., T1D Exchange Quality Improvement Collaborative; Factors Associated With Improved A1C Among Adults With Type 1 Diabetes in the United States. Clin Diabetes 2 January 2023; 41 (1): 76–80. https://doi.org/10.2337/cd22-0067; 2: American Diabetes Association Standards of Care in Diabetes 2024

High Level Business Opportunity with Expansion Potential into Type 2 Diabetes

Large Established Markets

9.4 M

Patients globally with T1D, growing 3.5% annually[1]

$3 - 5 B

Annual gross sales opportunity globally with T1D[2]

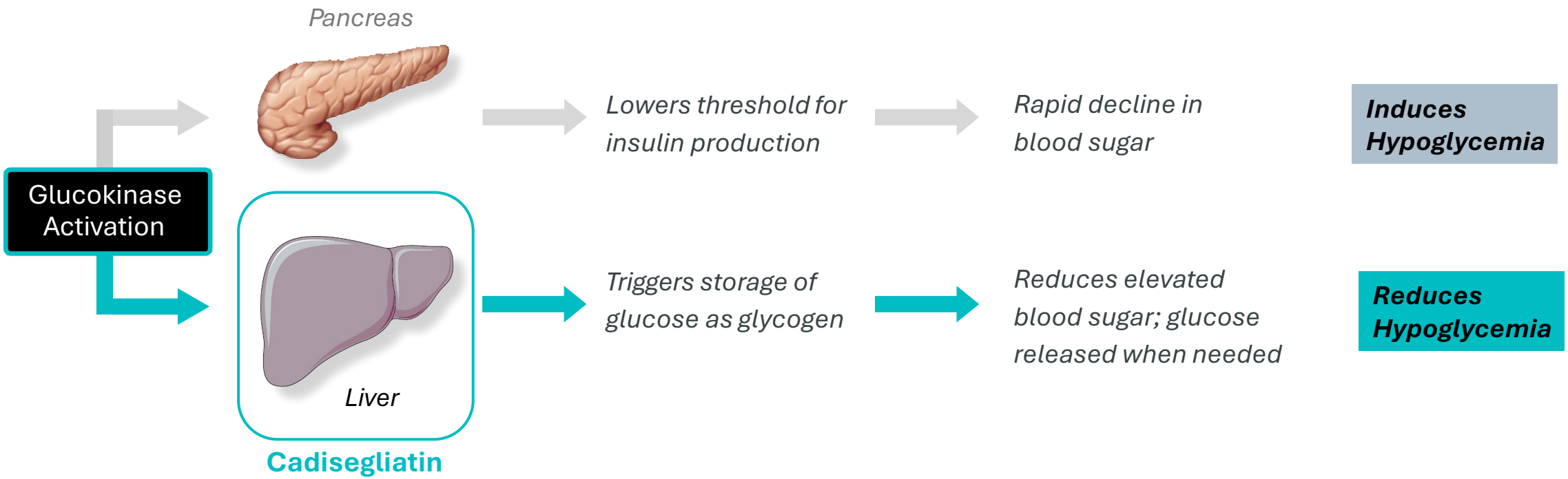
Upside

T2D global population

1: T1D Index 2: Internal company analysis - data on file

Cadisegliatin: Liver-Selective Glucokinase Activator

Glucokinase regulates glucose metabolism in liver and pancreatic β-cells

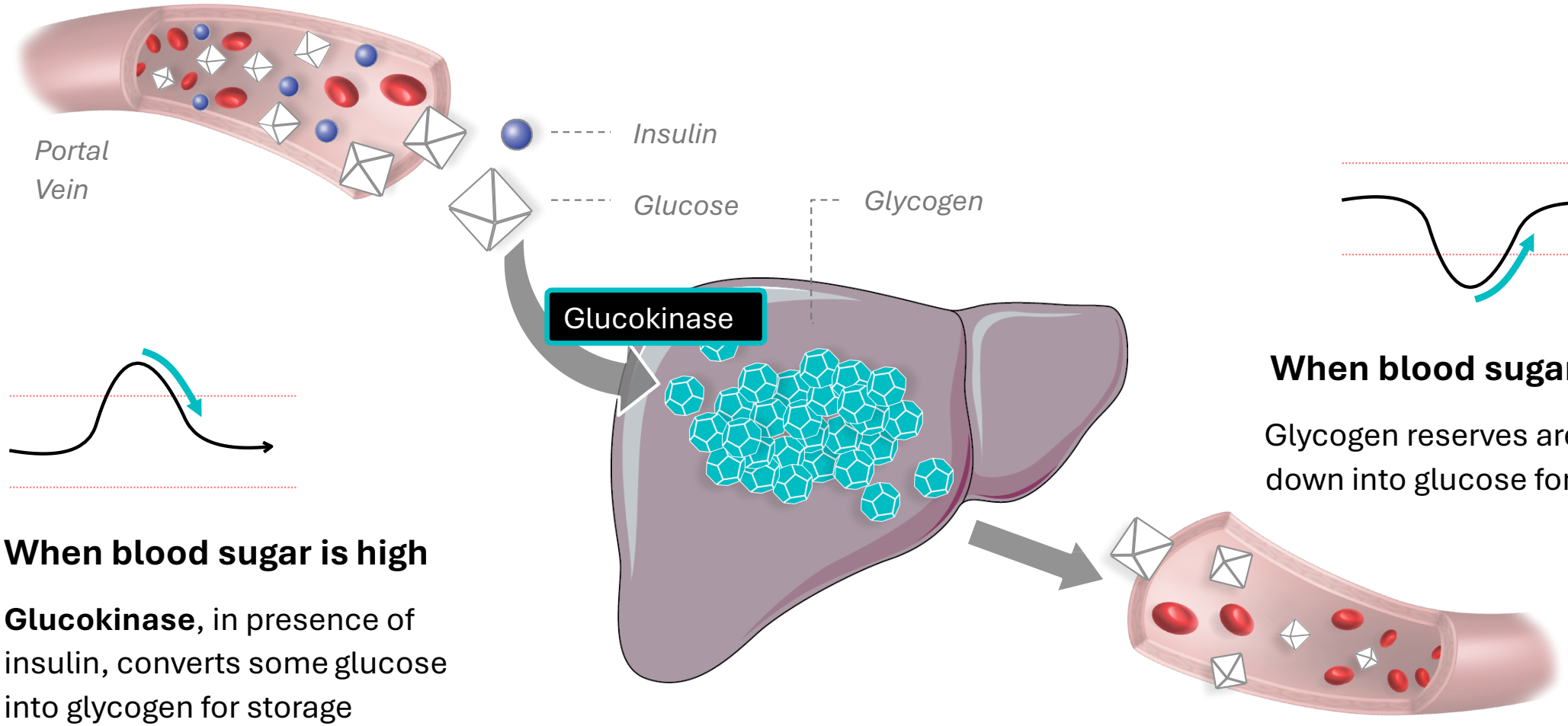


Cadisegliatin is in Development to Overcome Limitations of Past Approaches

Historical Limitations	Cadisegliatin's Goals
Increased hypoglycemia[1]	Reduction in hypoglycemia[2]
Elevated lipids[1]	No impact on lipids likely due to preservation of GK-GKRP interaction[2]
Loss of efficacy over time[1]	Maintain efficacy[2]
Liver toxicity[1]	Absence of liver toxicity[2]

GK: glucokinase GKRP: glucokinase regulatory protein; 1: Ren et al., Glucokinase as an emerging antidiabetes target and recent progress in the development of its agonists, J. of Enzyme Inhibition and Medicinal Chemistry, 37:1 606-615, DOI : 10.1080/14756366.2021.2025362; 2. : Vella A, et al. Targeting hepatic glucokinase to treat diabetes with TTP399, a hepatoselective glucokinase activator. Science translational medicine. 2019 Jan 16;11(475):eaau3441

In Non-Diabetic People, the Liver Acts as a Reservoir for Glucose with Insulin and Glucokinase being Key Gatekeepers



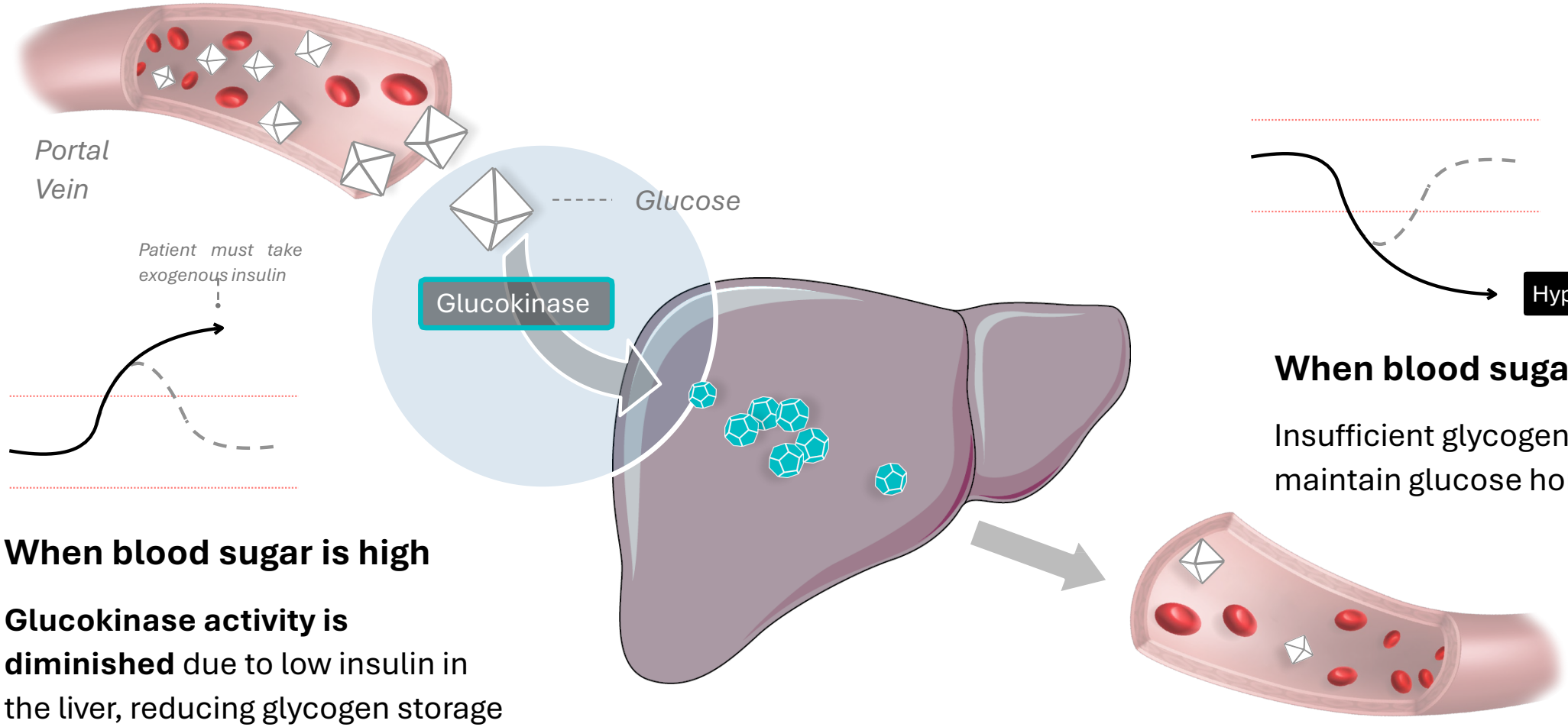
When blood sugar is high

Glucokinase, in presence of insulin, converts some glucose into glycogen for storage

When blood sugar is low

Glycogen reserves are broken down into glucose for release

With Type 1 Diabetes and Only Low Levels of Insulin Reaching the Liver, Glucokinase Activity Is Impaired



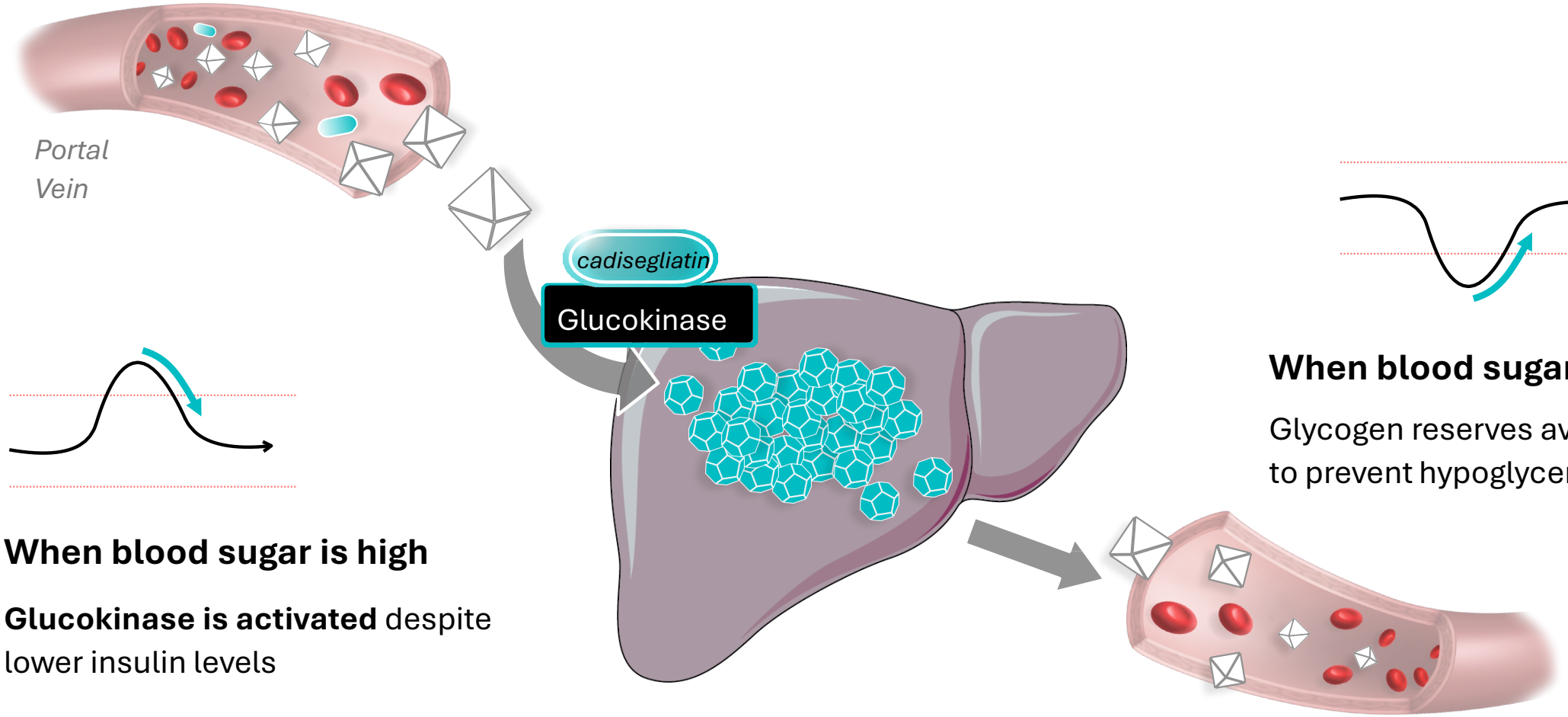
When blood sugar is high

Glucokinase activity is diminished due to low insulin in the liver, reducing glycogen storage

When blood sugar is low

Insufficient glycogen reserves to maintain glucose homeostasis

Cadisegliatin, as a Glucokinase Activator, Reactivates Innate Glucose-Regulating Capacity of the Liver Even in the Absence of Increased Insulin Levels



When blood sugar is high

Glucokinase is activated despite lower insulin levels

When blood sugar is low

Glycogen reserves available to prevent hypoglycemia

Proof-of-Concept Data for Cadisegliatin in T1D and T2D

SimpliciT1 Phase 2 Study in T1D[1]

50% fewer symptomatic hypoglycemic episodes ($p<0.04$) and no ketoacidosis

Reduction of HbA1c by 0.36 vs. insulin alone ($p < 0.001$)

40% of cadisegliatin treated patients had reductions of total daily insulin dose **and** HbA1c (by 0.41%) vs. insulin alone

N = 100; US Study

Insulin Withdrawal Study in T1D[1]

No increased risk of ketoacidosis vs. insulin alone

Despite short treatment for only 7-10 days:

- Improved fasting plasma glucose levels
- Fewer hypoglycemic events

N = 23; US Study

AGATA Phase 2 Study in T2D[2]

Reduction of HbA1c by 0.9% vs. metformin ($p < 0.01$)

No difference to metformin with regards to hypoglycemia or hyperlipidemia over 6 months

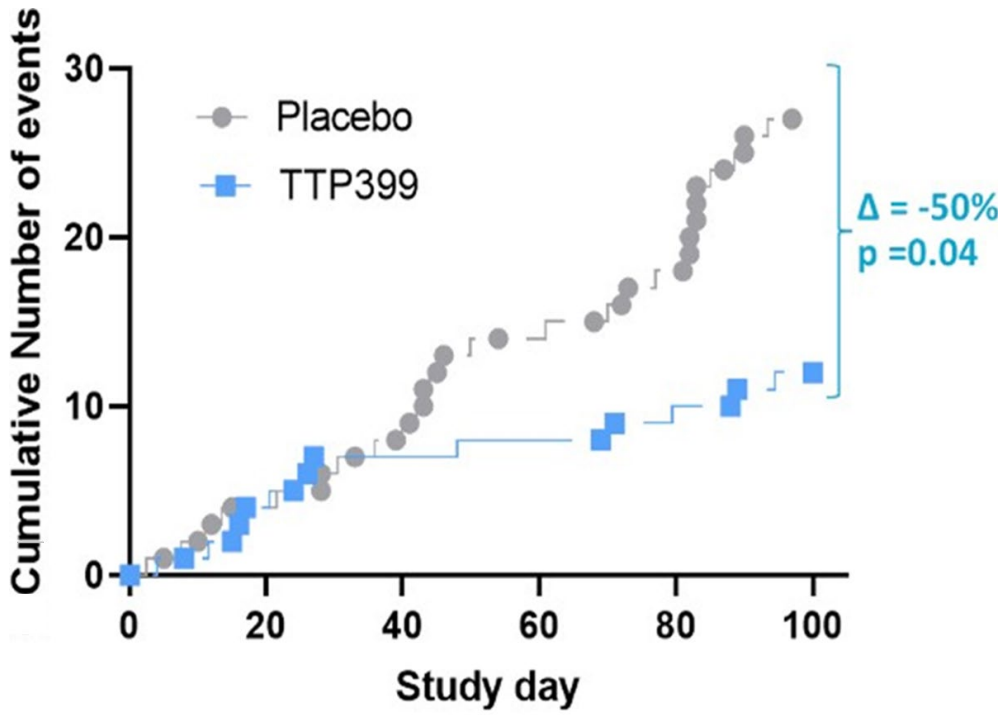
N = 190; US Study

1: Klein KR et al. The SimpliciT1 study: a randomized, double-blind, placebo-controlled phase 1b/2 adaptive study of TTP399, a hepatoselective glucokinase activator, for adjunctive treatment of type 1 diabetes. Diabetes Care. 2021 Apr 1;44(4):960-8; 2: Diabetes Obes Metab. 2022 August ; 24(8): 1439–1447. doi:10.1111/dom.14697

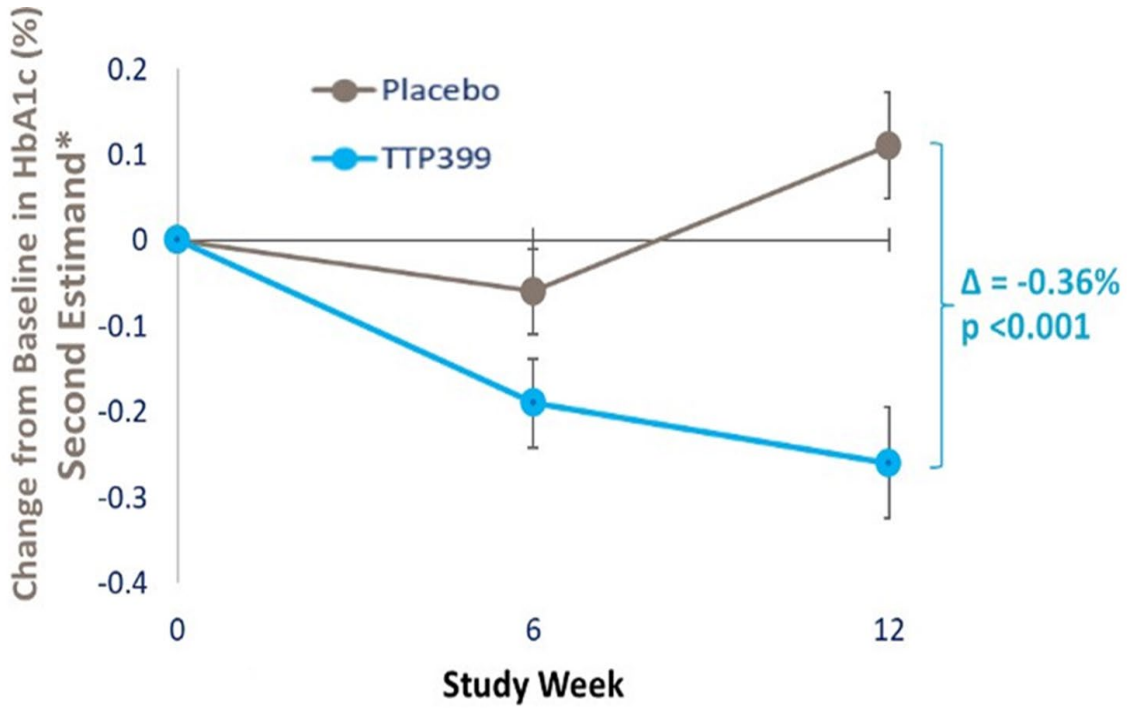
Cadisegliatin Significantly Reduced Hypoglycemia and HbA1c v. Insulin Alone[1]

SimpliciT1 Phase 2 Trial in patients with T1D

Fewer Hypoglycemic Events



Improved Glycemic Control

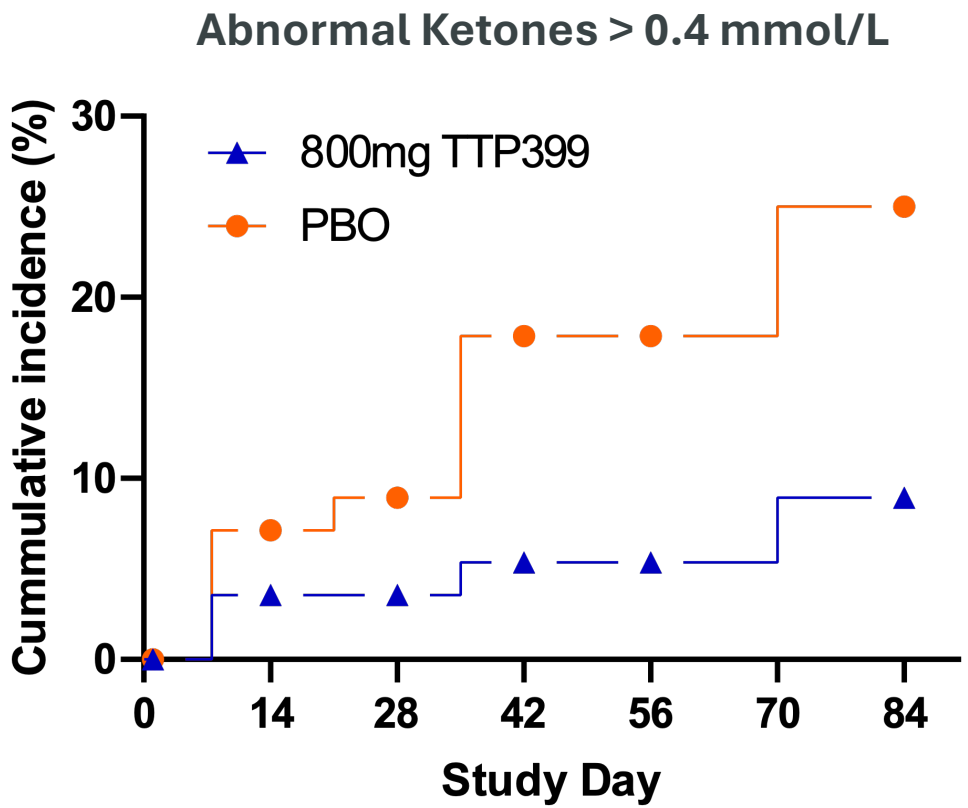


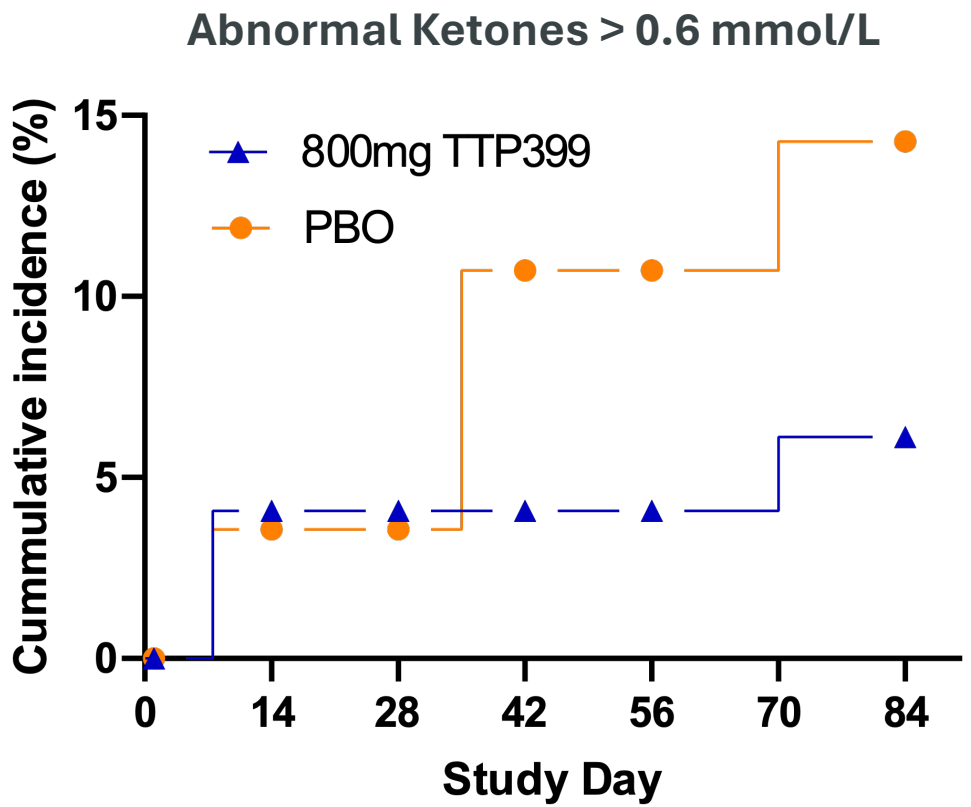
Randomized, Double-Blind, Placebo Controlled 2-Part Study of ~100 patients. A total of 49 patients in the treatment groups received 800mg daily of *cadisegliatin*.

1: Klein KR et al. The SimpliciT1 study: a randomized, double-blind, placebo-controlled phase 1b/2 adaptive study of TTP399, a hepatoselective glucokinase activator, for adjunctive treatment of type 1 diabetes. Diabetes Care. 2021 Apr 1;44(4):960-8

No Observed Increased Risk of Ketoacidosis with Cadisegliatin vs. Insulin Alone[1]

SimpliciT1 Phase 2 Trial in patients with T1D





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Cadisegliatin was Well-Tolerated Across People Living with T1D or T2D[1,2]

	Type 1 Diabetes – Phase 2, 3-month trial		Type 2 Diabetes – Phase 2, 6-month trial			
	Cadisegliatin 800 mg (n=56)	Placebo (n=49)	**Cadisegliatin** 400 mg (n=50)	**Cadisegliatin** 800 mg (n=42)	Placebo (n=48)	Sitagliptin (n=49)
Treatment Emergent and Serious Adverse Events[1,2]						
Subjects with ≥1 TEAE (%)	**36 (64)**	**32 (65)**	**26 (52)**	**21 (50)**	**29 (60)**	**30 (61)**
Subjects with ≥1 related TEAE (%)	**3**	**5**	**3 (6)**	**8 (19)**	**4 (8)**	**8 (16)**
SAEs	**1**	**1**	**0**	**0**	**0**	**0**
Subjects with ALT, AST, ALP > 1.5 UNL and/or bilirubin >2 ULN (%)	**2 (4)**	**1 (2)**	**1(2)**	**0**	**0**	**0**
Subjects with AST or ALT >3 ULN and bilirubin >1.5 ULN	**0**	**0**	**0**	**0**	**0**	**0**
DKA Events	**0**	**0**	**N/A**			
Subjects with ≥ 1 BOHB > 1mmol/l	**1 (2)**	**3 (5)**				

1: Vella A, et al. Targeting hepatic glucokinase to treat diabetes with TTP399, a hepatoselective glucokinase activator. Science translational medicine. 2019 Jan 16;11(475):eaau3441. 2: Klein KR et al. The SimpliciT1 study: a randomized, double-blind, placebo-controlled phase 1b/2 adaptive study of TTP399, a hepatoselective glucokinase activator, for adjunctive treatment of type 1 diabetes. Diabetes Care. 2021 Apr 1;44(4):960-8

Cadisegliatin Did Not Adversely Impact Lipids, Cholesterol or Liver Enzymes[1]

Phase 2 trial, 6-months

Fasting Lipid Changes from Baseline in Type 2 Diabetes Patients[1]			
	Cadisegliatin 400 mg (n=50)	**Cadisegliatin** 800 mg (n=42)	Sitagliptin (n=49)
Triglycerides (mg/dl)	**+1.5**	**-13.3**	**-27.4**
LDL-Cholesterol (mg/dl)	**+7.9**	**+2.9**	**-2.0**
HDL-Cholesterol (mg/dl)	**-0.4**	**+3.2***	**+0.9**

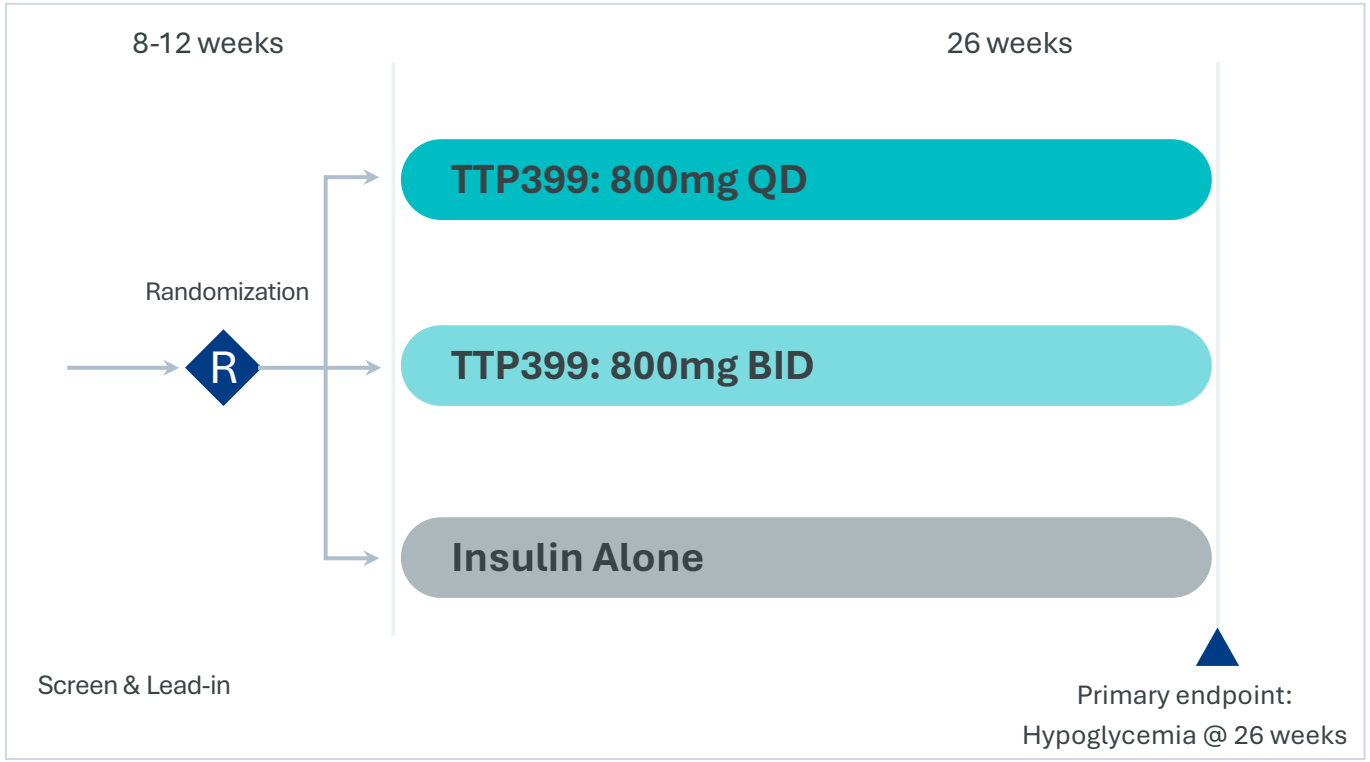
*P < 0.05

1: Vella A, et al. Targeting hepatic glucokinase to treat diabetes with TTP399, a hepatoselective glucokinase activator. Science translational medicine. 2019 Jan 16;11(475):eaau3441

Cadisegliatin CATT1 Study – Informed by FDA Advice and Published Guidance for Endpoint Selection, Exposure and Population Criteria

Working to resolve an FDA clinical hold following discovery of a chromatographic signal in human ADME study

CATT1 Study
Target Enrollment:
150 subjects at
~20 US sites



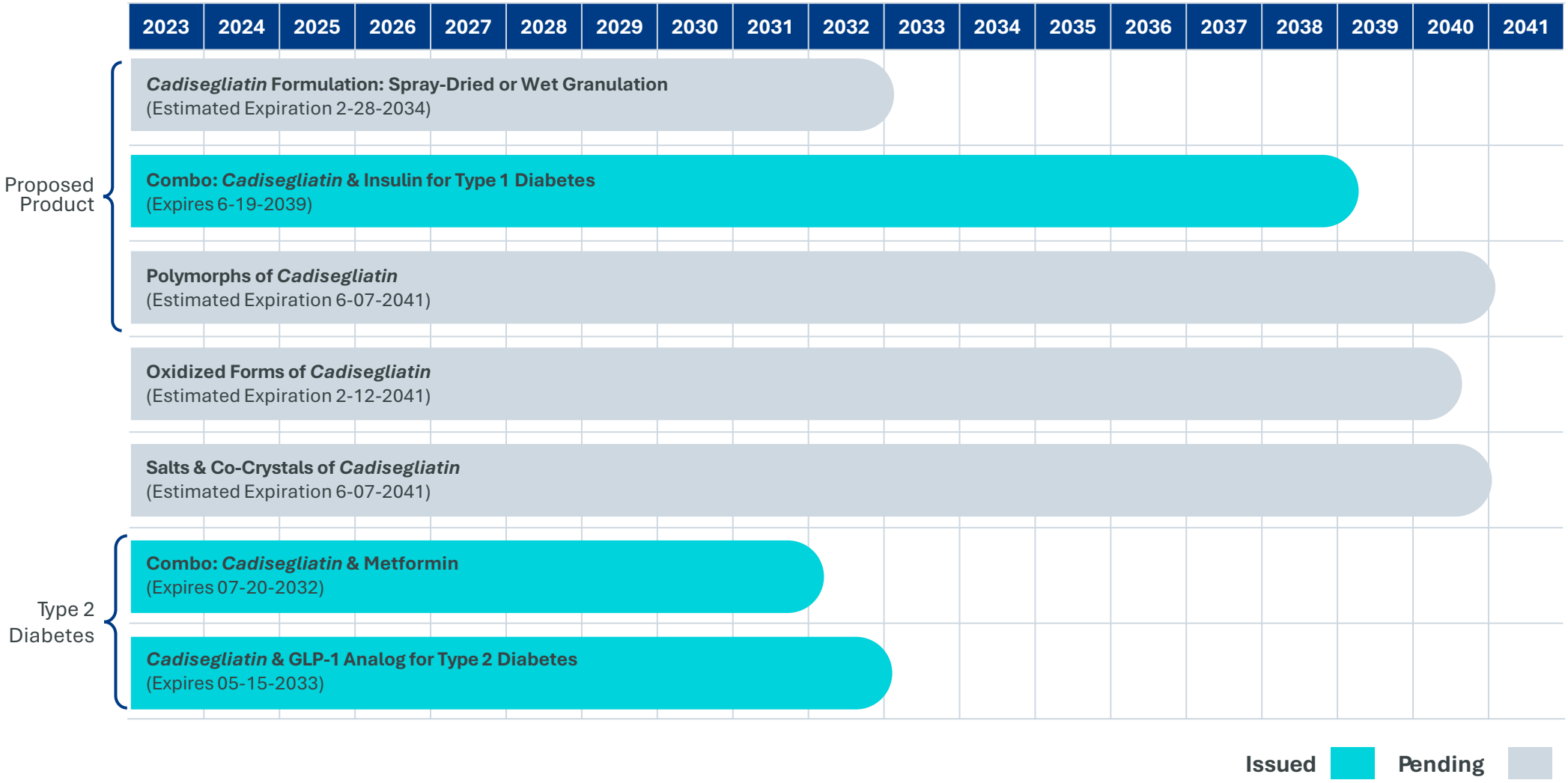
Primary endpoint
Incidence of Level 2 or Level 3 hypoglycemic events

Key secondary endpoint
Change in Hemoglobin A1C

CATT1 (TTP399-302) is the first Phase 3 trial to assess the efficacy of cadisegliatin in patients utilizing continuous glucose monitoring (CGM)

Strong IP Protection for Cadisegliatin in T1D and T2D through 2041

Exclusivity Period*



* Dates are provided for informational purposes only; actual results may differ from expectations.

Small Molecule Portfolio

Broader Portfolio Continues to Offer Additional Upside and Shareholder Value

Partnered Programs With Global Rights

Product	Indication	Pre-clinical / Phase I / Phase II / Phase III	Partners + Rights
PDE4 Inhibitor HPP737	**Psoriasis**		NEWSOARA 恒翼生物医药 China
	COPD		
	Atopic Dermatitis		
RAGE Antagonist Azeliragon	**Glioblastoma**		CANTEX PHARMACEUTICALS Global
	Pancreatic Cancer		
	Breast Cancer		
	Pneumonia		

Additional Programs With Global Rights

Oral GLP-1R Agonist TTP273	**Type 2 Diabetes**		VTV THERAPEUTICS
Nrf2/Bach1 Modulator HPP971 /HPP3033	**Oxidative Inflammatory Indications**		

Pipeline candidates are under investigation and the safety and efficacy has not been established. There is no guarantee that these products will receive health authority approval or become commercially available for the use(s) being investigated

Partnerships Provide Potential Independent Revenue Streams

Cadisegliatin (TTP399) *GK Activator*	**HPP737** *PDE4 Inhibitor*	**Azeliragon** *RAGE Antagonist*
Type 2 Diabetes *Phase 2 initiation 2025* *Middle East*	**Psoriasis*, COPD, Atopic Dermatitis** *Ongoing Phase 2 and Phase 3* trials* *China*	**Pneumonia**, Glioblastoma, Breast Cancer, Pancreatic Cancer** *Ongoing Phase 2 and Phase 3** trials* *US*
G42 Healthcare	NEWSOARA 恒翼生物医药	CANTEX PHARMACEUTICALS
Certain countries in the Middle East, Africa, and Central Asia	China	Global
Royalties in high single digits	**Over $100 M potential value**	**Potential for 20 - 40% of economics from commercialization or acquisition**

HPP737: Oral, Novel, Potent and Selective PDE4 Inhibitor

NEWSOARA 恒翼生物医药

Clinically Advanced

Phase 3 in psoriasis in China completed with once daily dosing [1]

Ongoing long-term open label extension study in psoriasis (week 16-52) [1]

Differentiated Profile

Preclinical potency on par with or superior to competitor PDE4 inhibitors (e.g., OTEZLA, Amgen®)[2]

Did not cross the blood-brain barrier in preclinical studies[2]

No significant GI intolerance (nausea, vomiting, diarrhea)[3]

No need for titration[3]

Potential Newsoara Global Partnership

Additional $20 M upfront

Up to $41 M in development milestones

Up to $35 M in sales-related milestones

Royalties in the mid to upper single digits based on sales

Global license effective upon payment of the $20M upfront fee

1. Internal Study Report provided by Newsoara – data on file; 2: vTv Internal Studies - Data on File; 3. Internal Studies – Data on File

VTV

Azeliragon: Novel, Oral Full Spectrum RAGE Antagonist

Cantex has an exclusive global license to develop and commercialize azeliragon

Mid- to Late-Stage Trials

Several ongoing US Phase 2 trials for the treatment of various cancer indications[1]

Three FDA Orphan Drug Designations: glioblastoma, pancreatic cancer and brain metastasis from breast cancer[2]

US Phase 3 trial in hospitalized patients with pneumonia to prevent acute kidney injury[1]

Characterized Clinical Profile

Well-tolerated safety profile in more than 2000 individuals dosed for periods up to 18 months[3]

Once daily dosing[3]

Clinical data showed inhibition of mechanisms that stimulate cancer growth[3]

Cantex Global License

With potential for 20-40% economics from acquisition or commercialization

Exclusive worldwide license for all indications except for diabetes, psoriasis and Alzheimer's disease

1: https://cantex.com/pipeline/ 2: https://cantex.com/2024/12/09/cantex-pharmaceuticals-receives-fda-orphan-drug-designation-for-azeliragon-for-the-treatment-of-brain-metastasis-from-breast-cancer/; 3: Cantex Corporate Presentation August 2024

Additional Programs: Differentiation in Large Market Opportunities

TTP273 *Oral GLP-1 agonist*	**HPP971 /HPP3033** *Nrf2/Bach1 Modulator*
Obesity *Phase 2 ready*	**Oxidative inflammation** *Phase 1 assets*
Negligible observed GI side effects[1]	**Franchise opportunity**
Potential for improved tolerability, convenience and accessibility vs. current standards of care[1]	Diverse compounds with proof-of-concept efficacy data in multiple animal models[2]
Expansion opportunities in weight management, T2D and beyond	Broad application

1: Internal Studies – Data on File 2: internal Studies – Data on File

TTP273: Oral Small Molecule GLP-1 Receptor Agonist

Targets High Unmet Needs

42% of adults in the U.S. are obese[1]

GI side effects like nausea and vomiting compromise adherence and efficacy[2]

Current peptide standards of care are limited by high cost and low supply[3]

Negligible observed GI side effects

No nausea and vomiting with improved satiety, HbA1c and body weight[4]

No need for titration or administration with meals[4]

Binds to an allosteric site distinct from the peptide site[5]

Expansion Potential

Ph1 and Ph 2 efficacy and tolerability profile support use for obesity, weight loss and T2D

Ideal for fixed dose combinations with oral agents

1: https://www.niddk.nih.gov/health-information/health-statistics/overweight-obesity; 2: Blue Health Intelligence, Real World Trends in GLP-1 Treatment Persistence and Prescribing for Weight Management, May 2024; 3: Heather P. Whitley, Jennifer M. Trujillo, Joshua J. Neumiller; Clin DiabActivation of the GLP-1 receptor by a non-peptidic agonist. *Nature* **577**etes 1 July 2023; 41 (3): 467–473; 4: Internal Studies – Data on File; 5: Zhao, P., Liang, YL., Belousoff, M.J. *et al.* , 432–436 (2020). https://doi.org/10.1038/s41586-019-1902-z

HPP971 /HPP3033: Nrf2-Bach 1 Modulator Platform

Potential to advance multiple distinct compounds targeting reduced oxidative stress and inflammation

Franchise Opportunity

Multiple non-electrophilic small-molecule compounds with distinct profiles

Opportunity to advance multiple molecules into different indications

Phase 1 Asset

Completed 1 month toxicology studies

Completed SAD and MAD studies

No dose limiting toxicities[1]

Preclinical Efficacy/ Proof Of Concept

Observed in disease relevant animal models[1] related to:

Liver disease (NASH)
Kidney disease
Autoimmune disease (MS, IBD)
Reperfusion injury/hypertension
Neurodegeneration (Parkinson's disease, AD)
Bone Loss (Periodontitis, Osteoarthritis)
Ocular disease (Presbyopia)

1: Internal studies - data on file

Summary: Cadisegliatin has Potential to be First Oral Adjunct Therapy for T1D

Novel oral liver selective glucokinase activator in development to reduce hypoglycemia and improve glycemic control vs. insulin alone

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Thank You