Therapeutics

Corporate Presentation

First-in-class small molecules for the treatment of metabolic and inflammatory disorders

August 2021

Forward looking statements

The statements made in this presentation may include forward-looking statements regarding the type 1 diabetes, psoriasis, and other markets, the development and attributes of investigational and marketed products to treat these diseases and other conditions, and the future operations, opportunities or financial performance of vTv Therapeutics Inc.

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For a more detailed discussion of our risks, see the Risk Factors section in our prospectus filed with the SEC and our other filings with the SEC, including our most recent 2020 Annual Report on Form 10-K.

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Our Focus

We are focused on treating **metabolic and inflammatory disorders** to minimize their long-term complications and improve the lives of patients

Our innovative pipeline of internally discovered **first-in-class small molecules, emphasis on clinical trial execution,** and **strategic partnerships** are the keys to our success

Our People

Steve Holcombe, B Sc
President, CEO

35 years experience growing start-up companies

18 years at vTv; founding team member

Negotiated 10 vTv partnerships

Raised $200 million equity capital

Focused on operational excellence: Assembled teams that moved projects forward on time and on budget

Carmen Valcarce, PhD
Executive Vice President, CSO

30+ years of R&D experience focused on diabetes and metabolic disease

Managed 12+ INDs

Part of the vTv IPO team

Involved in over 50 due diligence and partnership deals

Ran multiple positive clinical studies

+20 patents

7 years at Novo Nordisk

Trained biochemist and molecular biologist focused on mitochondrial metabolism

Rudy Howard, BA CPA
Executive Vice President, CFO

20+ years as CFO of 5 publicly held companies, ranging from early stage to $1B in revenues, and up to 7,000 employees

As CFO, led three companies through IPOs

Raised over $500M in public markets

Significant role in over 30 M&A transactions

Former partner with PWC

Aaron Burstein, PharmD
Senior Vice President, Clinical Development

24+ years clinical research and drug development experience across academia, federal government, large pharma and small biotech companies.

Supported 60+ clinical studies across Phases 1-4

48 peer reviewed scientific publications

Fellowship training in Clinical Neuropharmacology including PK/PD data analysis techniques

Pipeline

Indication	Preclinical	Phase I	Phase II	Phase III
Type 1 Diabetes (T1D)	TTP399 (GKA)			
Psoriasis	HPP737 (PDE4)			
Cystic Fibrosis Related Diabetes (CFRD)	TTP273 (Oral GLP1-R)			
Type 1 Diabetes (T1D) Prevention	TTP7059 (RAGE)			
Under Evaluation to Select Indication	HPP3033 (Nrf2)			

Partnered Programs	Preclinical	Phase I	Phase II	Partner / Territory
Type 2 Diabetes (T2D)	TTP273 (Oral GLP1-R)			华东医药 HUADONG MEDICINE — China and other Pacific Rim Countries (excl. Japan)
Primary Mitochondrial Myopathy	HPP593 (PPAR-δ)			Reneo — Worldwide
COPD/Atopic Derm/Psoriasis	HPP737 (PDE4)			NEWSOARA 恒翼生物医药 — China and other Pacific Rim Countries (excl. Japan)
Cancer	Azeliragon (RAGE)			CANTEX PHARMACEUTICALS — Worldwide
Renal Diseases	HPP971 (Nrf2 Activator)			Anteris Bio — Worldwide

Key Milestones in Next 12 Months

	TTP399 (GKA)	HPP737 (PDE4 inhibitor)
2021	▪ **Mechanistic Study Readout – Q3/Q4 2021** Mechanistic study of Diabetic Ketoacidosis (DKA) risk to inform Ph3 study design ▪ **Complete dialogue with FDA regarding TTP399 phase 3 program**	▪ **Multiple Ascending Dose Study Readout - Q3 2021** Phase 1 Multiple Ascending Dose clinical study to determine MTD and inform dose selection for POC study ▪ **Engage with FDA to discuss proposed phase 2 study design**
2022	▪ **Initiate TTP399 phase 3 studies**	▪ **HPP737 Phase 2 Study in Psoriasis** **Study start: Q1 2022**

Diabetes

TTP399
Liver-Selective Glucokinase Activator (GKA) as an Adjunctive Treatment to Insulin in T1D

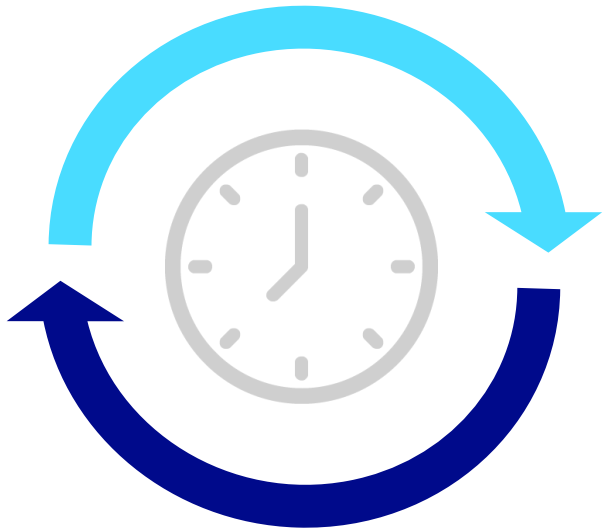
VTV Therapeutics

T1D is a Burdensome Disease

People with T1D never get a day off from managing it

It requires constant monitoring of blood glucose levels

People with T1D must wear a pump or use injections to dose insulin



It requires constant management, 24 hours a day

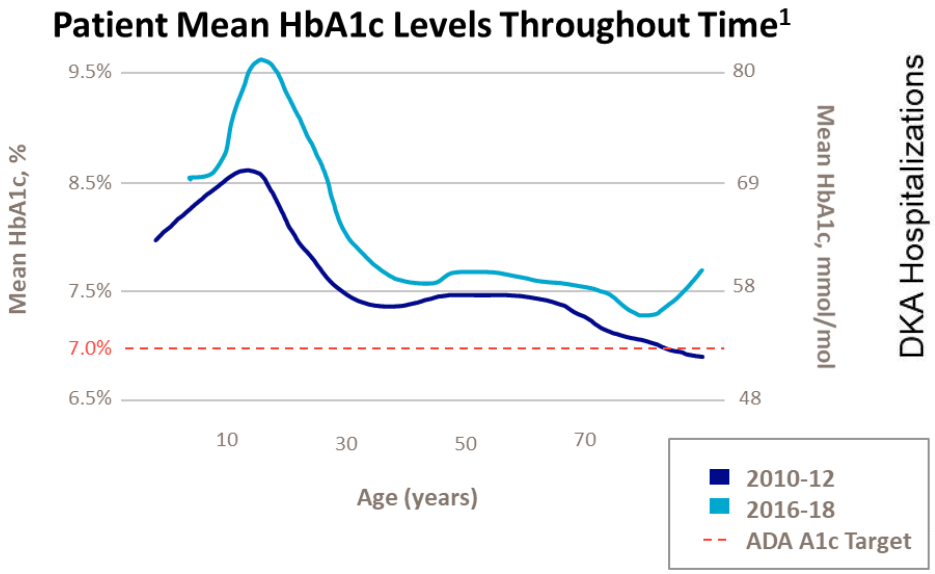
Must count the carbs and account for everything they eat

It is exhausting and has long-term dangerous complications

Clinical Outcomes Continue to Decline Despite New Diabetes Technologies[1]

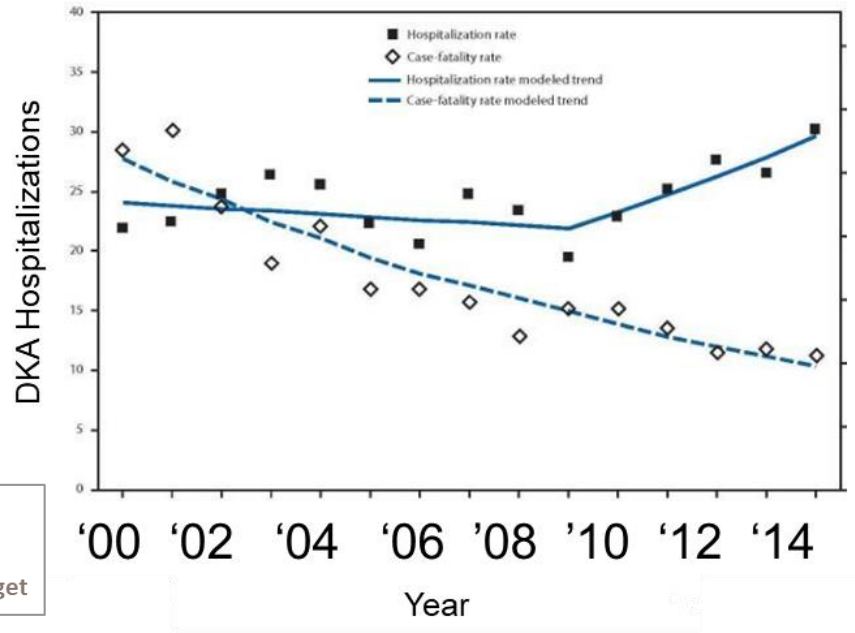
Nearly 80% of people with type 1 diabetes fail to achieve ADA target A1c levels[2]

Patient Mean HbA1c Levels Throughout Time[1]

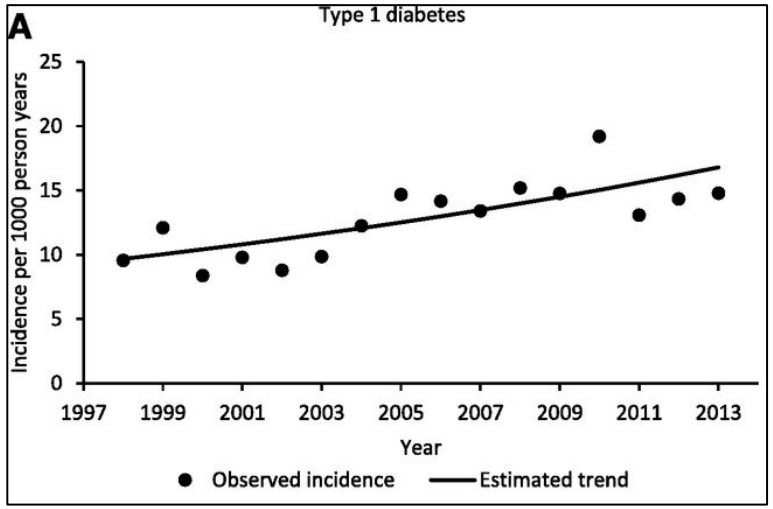


Life-threatening, short-term complications of poor glycemic control

The incidence of DKA-hospitalization is increasing[3]



The incidence of hypoglycemia-hospitalization is increasing[4]



[1] *Foster et al. Diabetes Technology and Therapeutics (2019) 21:66-72; DOI: 10.1089/dia.2018.0384*
[2] Diabetes Technol Ther. 2019 Feb;21(2):66-72. doi: 10.1089/dia.2018.0384. Epub 2019 Jan 18
[3] Gosmanov et al. Hyperglycemic Crises: Diabetic Ketoacidosis (DKA), And Hyperglycemic Hyperosmolar State (HHS) South Dartmouth (MA): MDText.com, Inc.; 2000
[4] Zhong et al, Diabetes Care 2017 Dec; 40(12): 1651-1660.

Severe Hypoglycemic Events Result in a Substantial Burden on Patients and Healthcare System*

~7.4 Million Americans with diabetes (T1D and T2D) take insulin, including 1.5M T1D patients[1]

36% of US diabetic patients (T1D and T2D) had ≥1 episode of severe hypoglycemia in the last year [2]

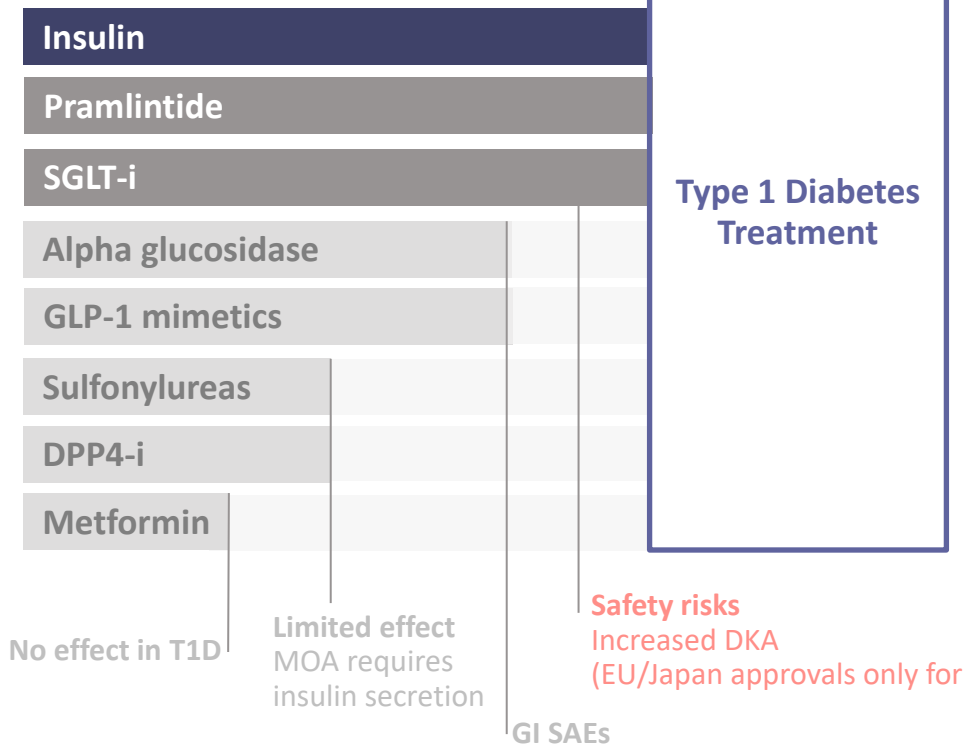
245,000 Emergency Room visits due to severe hypoglycemia by adults with diabetes (2014)[3]

$1.8 Billion in total direct medical costs of hypoglycemic events (2009)[4]

(1) https://care.diabetesjournals.org/content/41/6/1299
(2) The iNPHORM study (NCT04219514) is one of the first prospective, longitudinal investigations in the world to be conducted in the area of hypoglycemia. It will take place across the United States and involve 12 months of data collection using multiple self-reported, self-administered questionnaires. Results presented at EASD 2020 https://www.uwo.ca/diabetesalliance/img/iNPHORM_posters_full_sized/EASDposter_Sept%2023-Large.jpg
(3) CDC National Diabetes Statistics Report 2017
(4) Zhao Y. et al. DOI:10.1080/13696998.2016.1178126

Limited Treatment Options for a Significant Patient Population

No approved Oral Therapies for T1D in the US, and Available T2D Treatments have Limited Potential in T1D[(1)]



TTP399 GKA

Product attributes:

- Oral treatment
- Reduce hypoglycemia
- Improve glycemic control
- Reduce insulin dose

Without:

- Diabetic ketoacidosis (“DKA”)
- Weight gain

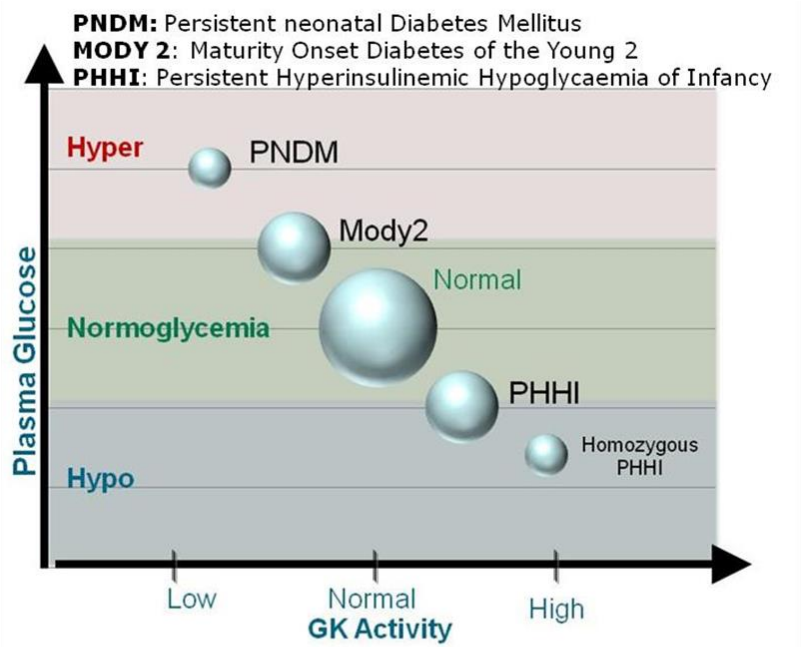
(1) American Diabetes Association: Diabetes Care 2019; 42 (Supplement 1):S90-S92, https://doi.org/10.2337/dc19-S009.

Hepatic Glucokinase Activation

A New Strategy to Treat T1D

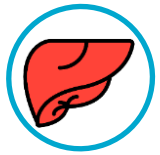
Glucokinase (GK) is the glucose sensor of the body

Key role in glucose homeostasis supported by strong genetic evidence



- In humans, abnormal GK activity due to activating or inactivating mutations is linked to hyperglycemic and hypoglycemic conditions respectively

TTP399: A liver selective Glucokinase Activator[1]



TTP399 activates GK in the liver

TTP399 does not activate GK in β-cells

TTP399 does not disrupt the interaction between GK and GKRP (GK Regulatory Protein) keeping physiological control of GK

In patients with T2D, TTP399 significantly reduced HbA1bc after 6-months of treatment without signs of tachyphylaxis or hypoglycemia

In patients with T1D, TTP399 significantly reduced HbA1bc after 3-months of treatment and reduced the number of hypoglycemic events

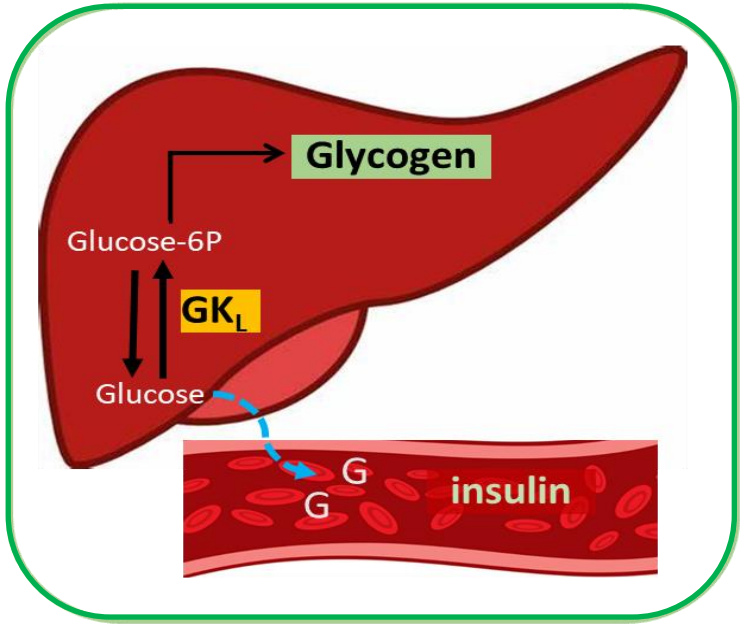
1. Vella A, Freeman J, Dunn I, Keller K, Buse J, Valcarce C. Targeting hepatic glucokinase to treat diabetes with TTP399, a hepatoselective glucokinase activator. Science Translational Medicine 16 Jan 2019

Proposed Mechanism of Action in T1D - Normalization of Glucose Metabolism in the Liver

Glucokinase (GK) is the glucose sensor of the body

→ Key role in glucose homeostasis supported by strong genetic evidence

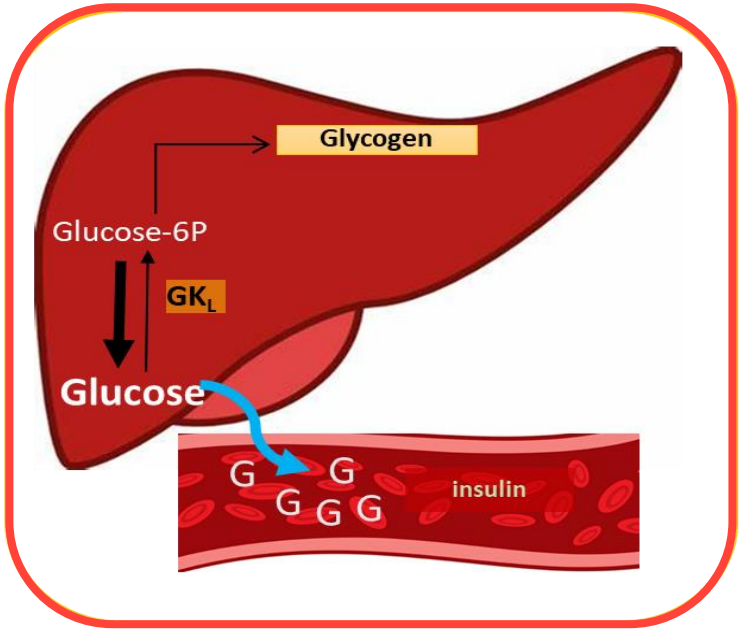
Healthy (Non-Diabetic)



Normal Glucose metabolism:

- GK activity
- Glycogen storage

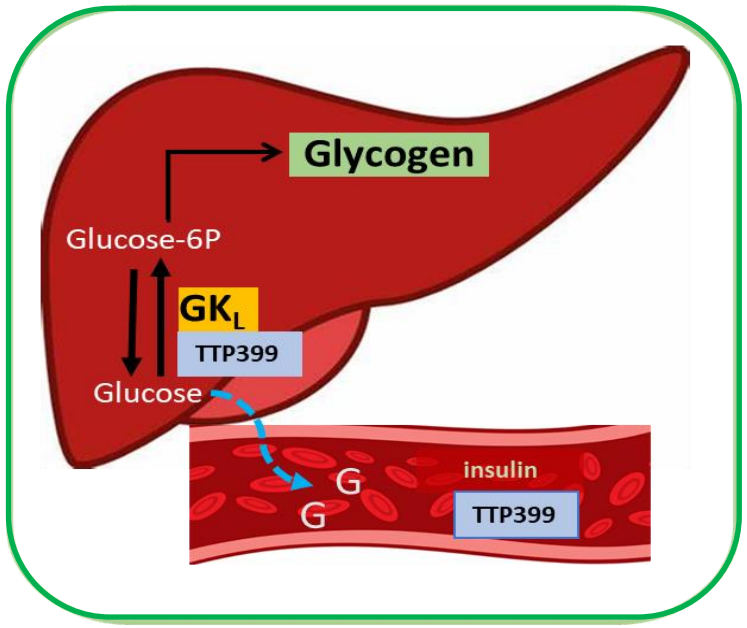
Type 1 Diabetes



Abnormal Glucose metabolism:

- Lower GK activity
- Lower Glycogen storage

Type 1 Diabetes + TTP399



Normalization of Glucose metabolism:

- GK activation
- Normalization of Glycogen storage

Simplici-T1 – Key Phase 2 Study Results

- **Statistically significant reduction in HbA1c** under a treat-to-target design (i.e. compared to intensive insulin treatment)
- **~40% reduction in hypoglycemic episodes** with TTP399 vs. placebo
- **No report of diabetic ketoacidosis,** trends towards reduction in ketone events were observed in the TTP399 treated group compared to placebo
- **~2 hour increase in time in range** relative to placebo
- **Reduced total daily mealtime bolus insulin** relative to baseline
- **No detrimental safety signals across multiple parameters** in TTP399 treated group when compared to placebo, unlike other oral MOAs investigated for T1D

Klein et al. *Diabetes Care*, **2(16)**, 2684 (2021)

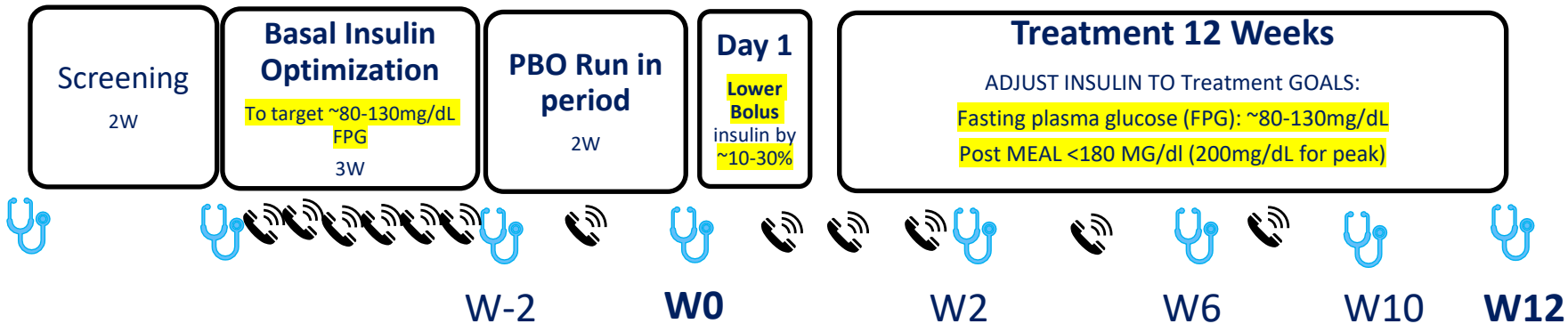
Simplici-T1 — Adaptive Phase 1b/2 Study Trial Design

- Simplici-T1 study designed to explore the **safety and efficacy** of TTP399, as an oral adjunctive therapy for T1D

- Double-blind Placebo controlled **12 weeks of dosing, 800mg QD** or placebo (1:1) in **104 patients with T1D**

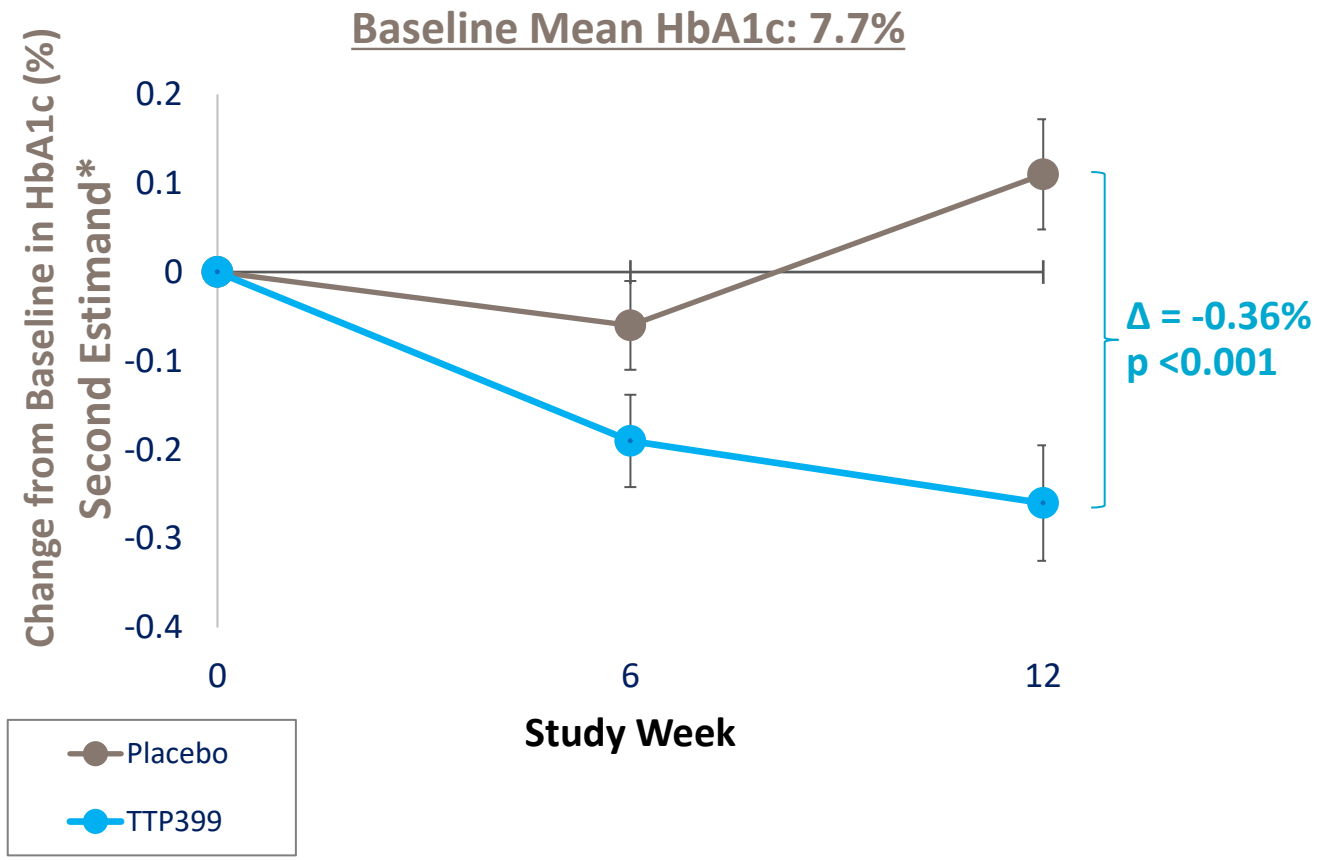
- **Treat-to-target design** allowed changes in insulin dose after the insulin-optimization period in all participants via frequent PI follow-up to achieve and maintain the pre-specified targets (FPG: ~80-130mg/dL; post meal glucose: <180-200 mg/dL)

Study Design

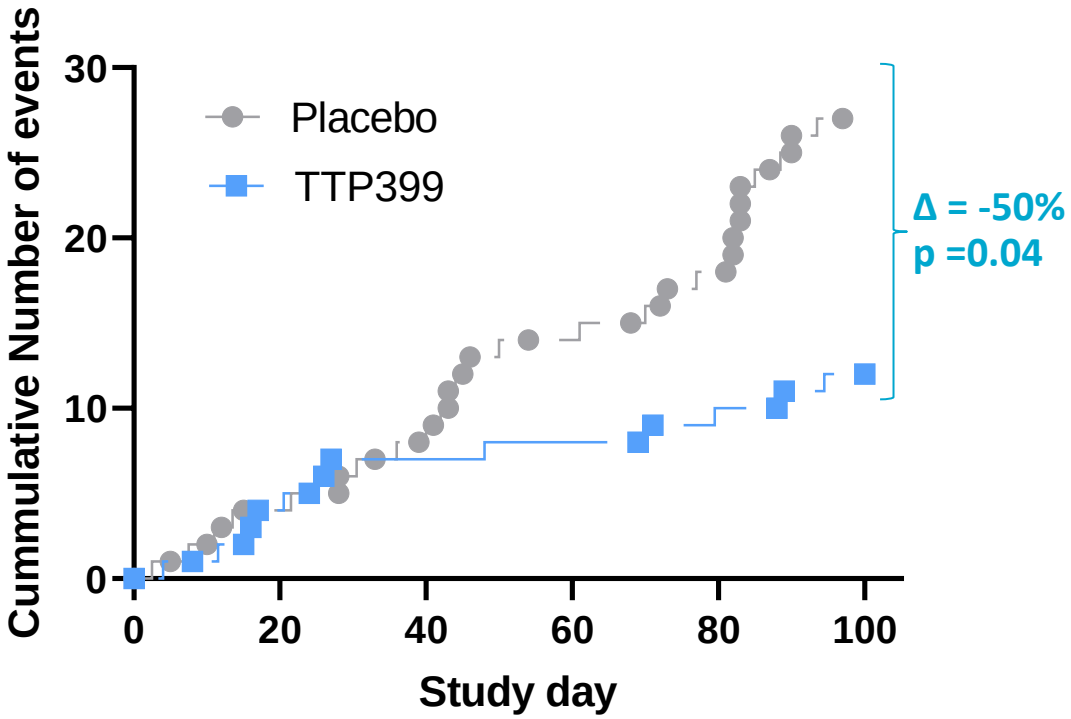


Simplici-T1: TTP399 Treated Subjects Achieved Better Glycemic Control while Reducing Hypoglycemic Events

Change in HbA1c



Hypoglycemic Events



*The pre-specified second estimand analysis evaluated the effect on HbA1c for patients without evidence of noncompliance with prescribed treatment who did not administer notable increases of bolus insulin of three or more units. This second estimand analysis was conducted consistent with current regulatory guidance. Data shown for Part 1 and Part 2 combined (n=104).

Klein et al. *Diabetes Care*, **2(16)**, 2684 (2021)

Pivotal Study Development Plan Under Breakthrough Therapy Designation*

Q3/Q4 2021

- DKA mechanistic study top-line results
- Continue dialogue with FDA on an efficient development path to registration
- Initiate other NDA supporting studies

1H 2022

- Goal to initiate two 6-month pivotal trials early 2022 including a 6 month Open Label Extension study

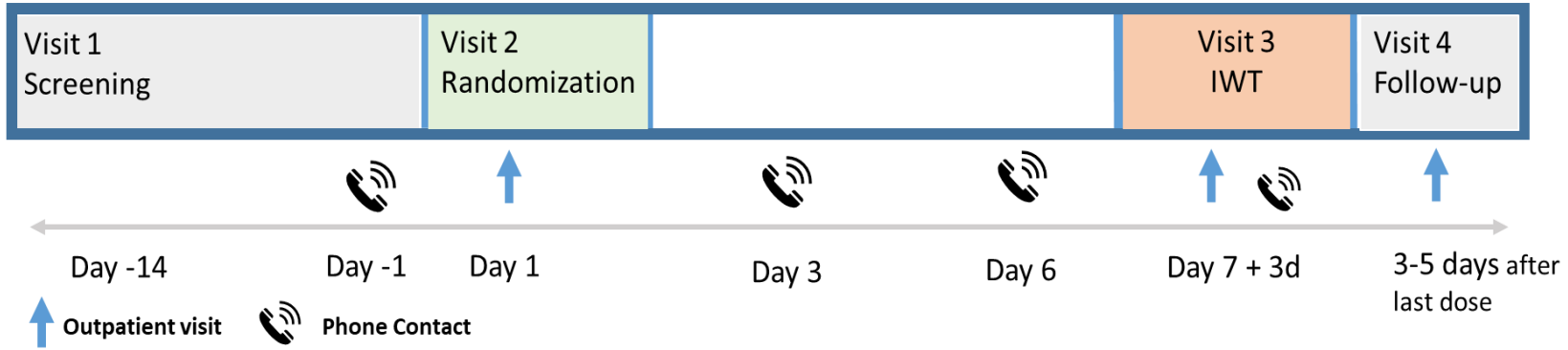
*Current development plan may change based on continued dialogue with FDA and other stakeholders

Mechanistic Study of DKA Risk (TTP399-118)

Study Objective: Evaluate effects of TTP399 on ketogenesis during insulinopenia to inform Ph3 study design

Study Design:

- **Participants:** 20-30 adults with T1D on insulin pumps
- **Dosing:** TTP399 800mg or placebo once daily for 7 days (randomized 1:1)
- **Insulin withdrawal test**: on day 7, insulin pumps will be stopped and physically removed at 6 am and serial measurements of plasma glucose and ketones (β-hydroxybutyrate) will be collected for 10h



Study Initiation: Q1 2021
Study Readout: Q3/Q4 2021

- **Study design similar to clinical studies using SGLT2 inhibitors[1,2]**
- **Results from similar preclinical study using TTP355[3]**
  - **Decreased ketones** in plasma after insulin withdrawal **with liver selective GKA** compared to placebo

JDRF vTv received JDRF Industry Discovery & Development Partnerships Grant for the TTP399-118 study

(1) Herring et al, Diabetes Care 2020 https://doi.org/10.2337/dc19-2579
(2) Patel et al. Diabetes Technology & Therapeutics 19,618-622, 2017) https://doi/10.1089/dia.2017.0267
(3) https://vtvtherapeutics.com/wp-content/uploads/2020/08/GKA-Poster-Keystone-2017_01182017_final-minipigs.pdf TTP355: liver-selective GKA (first generation)

Inflammation

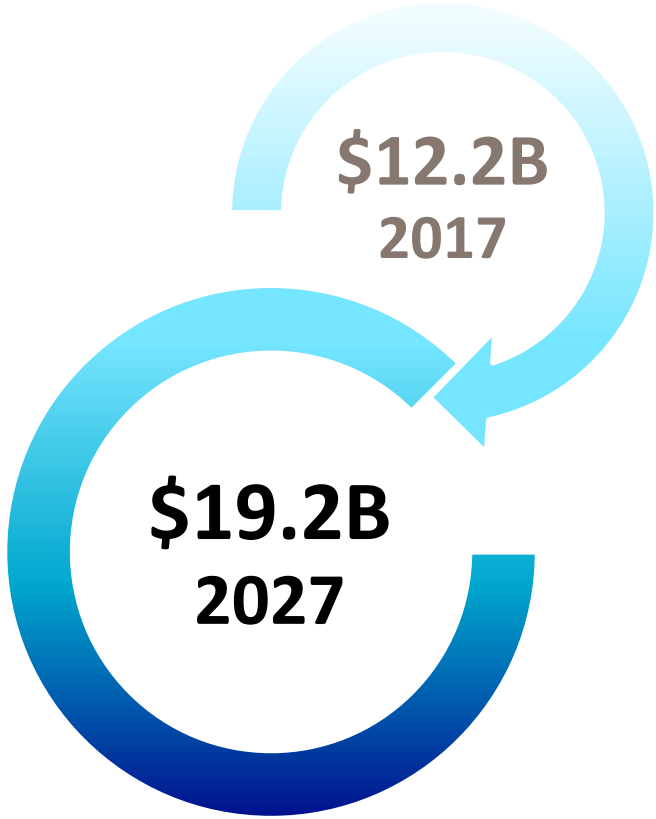
HPP737:
PDE4 Inhibitor as an Oral Treatment of Psoriasis

VVT Therapeutics

Program Overview

- **PDE4 is a validated target** in the treatment of a variety of inflammatory disorders. Targeting PDE4 is a multi-billion dollar market and growing rapidly
- HPP737 is an oral, novel, potent and **selective PDE4 inhibitor**
- HPP737 exhibits in vitro, in vivo and ex vivo potency **on par with or superior to competitor PDE4 inhibitors** affording opportunity to potentially demonstrate improved efficacy at lower doses
- **HPP737 does not cross the blood-brain barrier**
  - Expected to reduce incidence of PDE4 associated GI intolerance and CNS side effects
- **No significant GI intolerance (i.e. nausea, vomiting, diarrhea)** observed in completed Phase 1 SAD and MAD clinical studies
- **PK supports once daily dosing**

Psoriasis Market Sales*



* Psoriasis market sales in US, Japan, 5EU (France, Germany, Italy, Spain, and UK).
Source: Global Data, Plaque Psoriasis Global Drug Forecast and Market Analysis to 2027. Published Dec 2018

HPP737: *in vitro* (sRICA model)

HPP737 10-100x More Potent than Apremilast in Skin Resident Immune Cell Assay (sRICA) Model

Compound	Inhibition (IC_{50} nM)					
	TNF-α	GM-CSF	MIP-1a	IL-2	IP-10	IL-17a
HPP737	3	20	25	4	2	2.4
Apremilast	100	200	250	120	200	n/a

sRICA Model

- Th17 model of "psoriatic like inflammation"
- *Ex vivo* tissue model mimicking the inflammation in skin biopsies from patients with psoriasis
- Culture of normal human skin with inflammatory stimuli that allows for cellular and molecular interactions between stromal and resident immune cells in presence of inflammatory stimuli

Development Plan

3Q 2021

- Phase 1 healthy subject MAD study results
- Dialogue with FDA on Phase 2 study design

1Q 2022

- Goal to initiate psoriasis phase 2 study
- Proposed study design:
  - 12-week study in patients with moderate to severe plaque psoriasis
  - 120 subjects randomized 1:1 to HPP737 or placebo
  - Primary efficacy outcome: PASI-75, defined as % of participants achieving a 75% improvement (response) in Psoriasis Area and Severity Index (PASI), at Week 12

*Current development plan may change based on continued dialogue with FDA and other stakeholders

Partnered Development Programs

VTV Therapeutics

Creating Value Through Partnerships

Asset	Partner	Territory	Target Indications	Economics for vTv
TTP273 (Oral GLP-1r)	华东医药 HUADONG MEDICINE	China and other Pacific Rim Countries (excl. Japan)	Type 2 Diabetes	Milestones and Royalties Utilization of data to advance development in ROW
HPP737 (PDE4i)	NEWSOARA 恒翼生物医药	China and other Pacific Rim Countries (excl. Japan)	COPD/Atopic Dermatitis/Psoriasis	Milestones and royalties Utilization of data to advance development in ROW
HPP591 (PPAR-δ Agonist Program)	Reneo	Worldwide	Primary Mitochondrial Myopathy, Fatty Acid Oxidation Disorder, McArdle Disease	Equity interest in Reneo Milestones and Royalties
HPP971 (Nrf2 Activator)	Anteris Bio	Worldwide	Renal diseases	Equity interest in Anteris Bio Milestones and Royalties
Azeliragon (RAGE Antagonist)	CANTEX PHARMACEUTICALS	Worldwide	Cancer and complications (cachexia and pain from bone metastasis)	Allocate profits under a tiered arrangement

Thank you

VVT Therapeutics