



Corporate Presentation

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

January 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 2019 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 long-term sponsor support** 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
Type 1 Diabetes (T1D)	TTP399 (GKA)		
Psoriasis	HPP737 (PDE4)		
Cystic Fibrosis Related Diabetes (CFRD)	TTP273 (Oral GLP1-R)		
Type 1 Diabetes (T1D) Prevention	Azeliagon (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)			 China and other Pacific Rim Countries (excl. Japan)
Primary Mitochondrial Myopathy	HPP593 (PPAR-δ)			
COPD/Atopic Derm/Psoriasis	HPP737 (PDE4)			 Worldwide
Renal Diseases	HPP971 (Nrf2 Activator)			 China and other Pacific Rim Countries (excl. Japan)
				 Worldwide

Data Readouts Expected Across Pipeline in 2021

TTP399 (GKA)

Mechanistic Study

Mechanistic study of Diabetic Ketoacidosis (DKA) risk to inform Ph3 study design

Initiation Q1 2021
Readout Q2 2021

HPP737 (PDE4 inhibitor)

Multiple Ascending Dose study

Phase 1 Multiple Ascending Dose clinical study to determine MTD and inform dose selection for POC study

Initiation Q1 2021
Readout Q2 2021

Diabetes

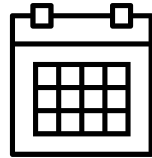
TTP399

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

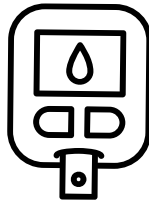


T1D is a Burdensome Disease

People with T1D never get a day off from managing it



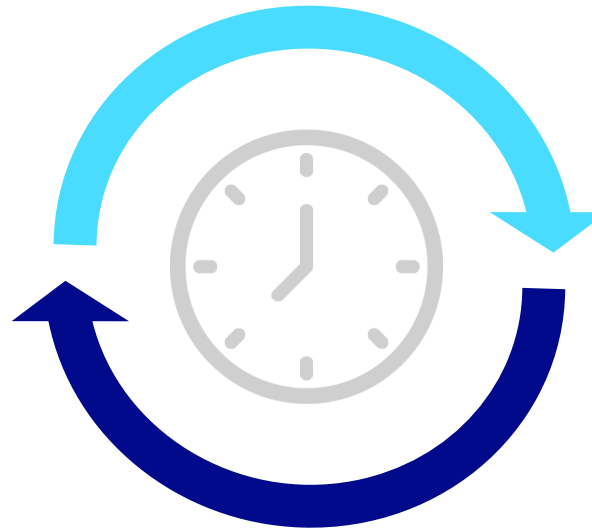
It requires constant monitoring of blood glucose levels



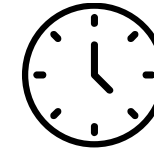
People with T1D must wear a pump or use injections to dose insulin



Risk of daytime hypoglycemia



Risk of nighttime hypoglycemia and seizures



It requires constant management, 24 hours a day



Must count the carbs and account for everything they eat

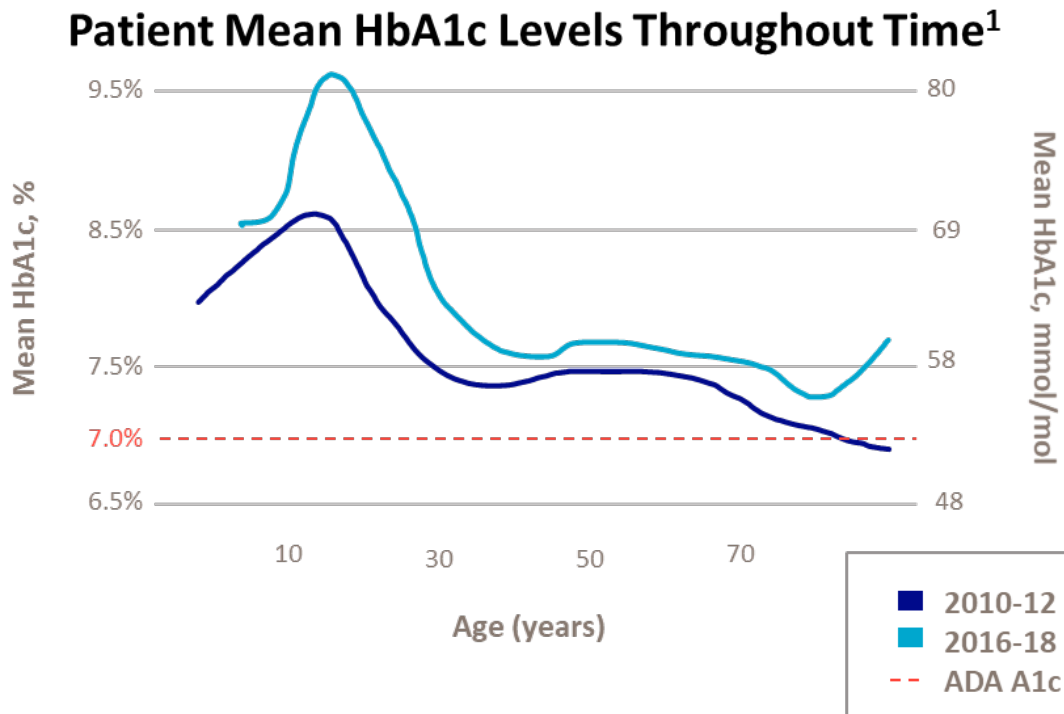


It is exhausting and has long-term dangerous complications

Insulin Alone is Not Enough

Nearly 80% of people with type 1 diabetes fail to achieve ADA target A1c levels¹

Despite improved and more widely adopted diabetes technology, clinical outcomes continue to decline²



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

Severe Hypoglycemia:

- Patients' fear of hypoglycemic events is one of the **barriers to achieving glycemic control** in diabetes

Diabetic Ketoacidosis (DKA):

- DKA accounts for **14% of all hospital admissions** of patients with diabetes and **16% of all diabetes-related fatalities**³

1. Diabetes Technol Ther. 2019 Feb;21(2):66-72. doi: 10.1089/dia.2018.0384. Epub 2019 Jan 18.
2. Foster et al. Diabetes Technology and Therapeutics (2019) 21:66-72; DOI: 10.1089/dia.2018.0384
3. Osama Hamdy, et al. [Medscape May 31, 2019, Diabetic Ketoacidosis \(DKA\)](#)

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 patients¹



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

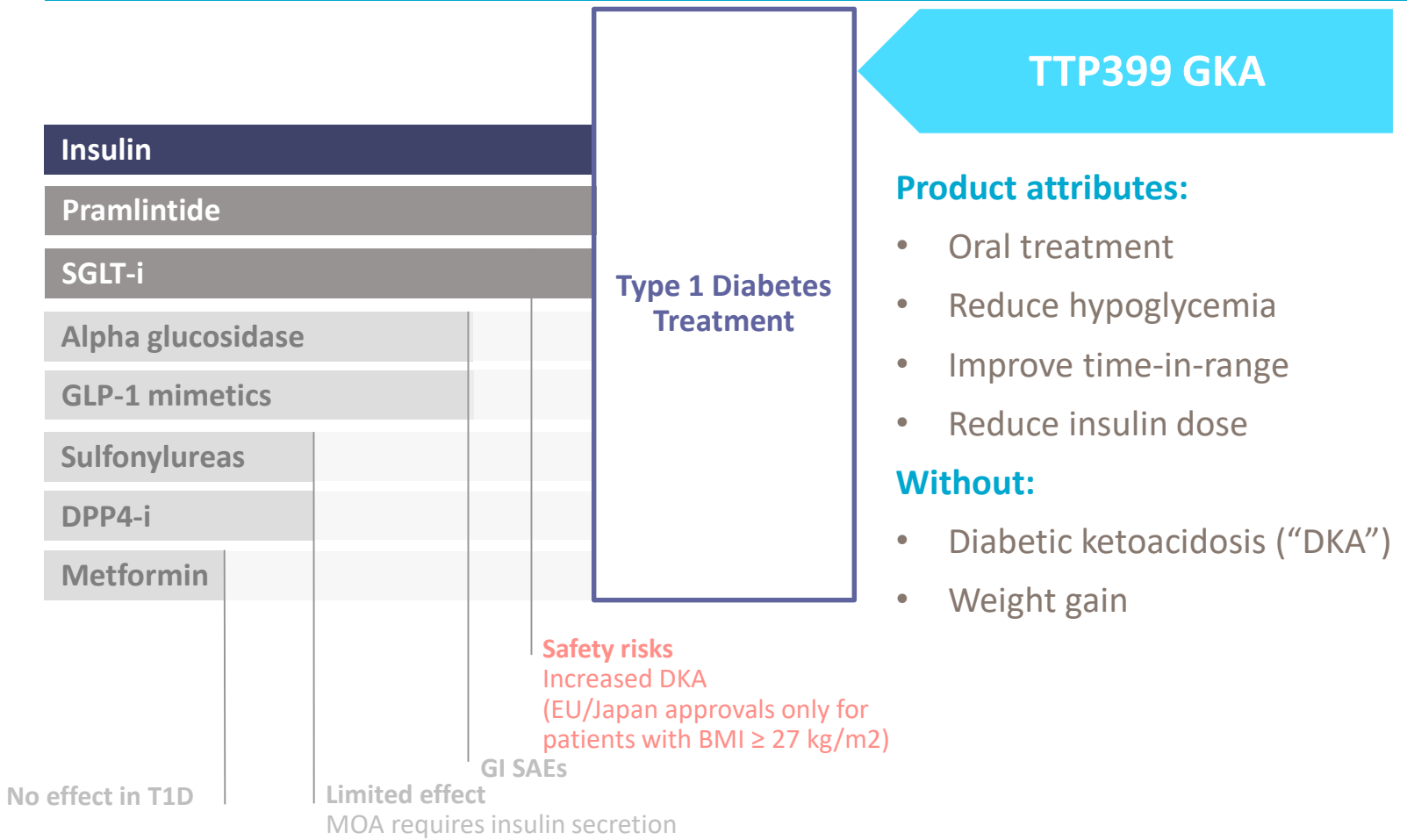
(4) Zhao Y. et al. DOI:10.1080/13696998.2016.1178126

Limited Treatment Options for a Significant Patient Population

Large commercial opportunity with significant unmet need

- **In the US, 1.6 million** adult and pediatric T1D patients⁽¹⁾ ; ~64k new T1D patients diagnosed each year in US⁽²⁾
- **Nearly 80%** of people with T1D **fail to achieve ADA target A1c levels**⁽³⁾
- Limited historical innovation for current standard of care
 - Requires constant management and monitoring to avoid hyperglycemia, hypoglycemia, and DKA
- Potential >\$1 billion market for oral adjunctive treatments to insulin in T1D

No approved oral therapies for T1D in the US, and available T2D treatments have limited potential in T1D⁽⁴⁾



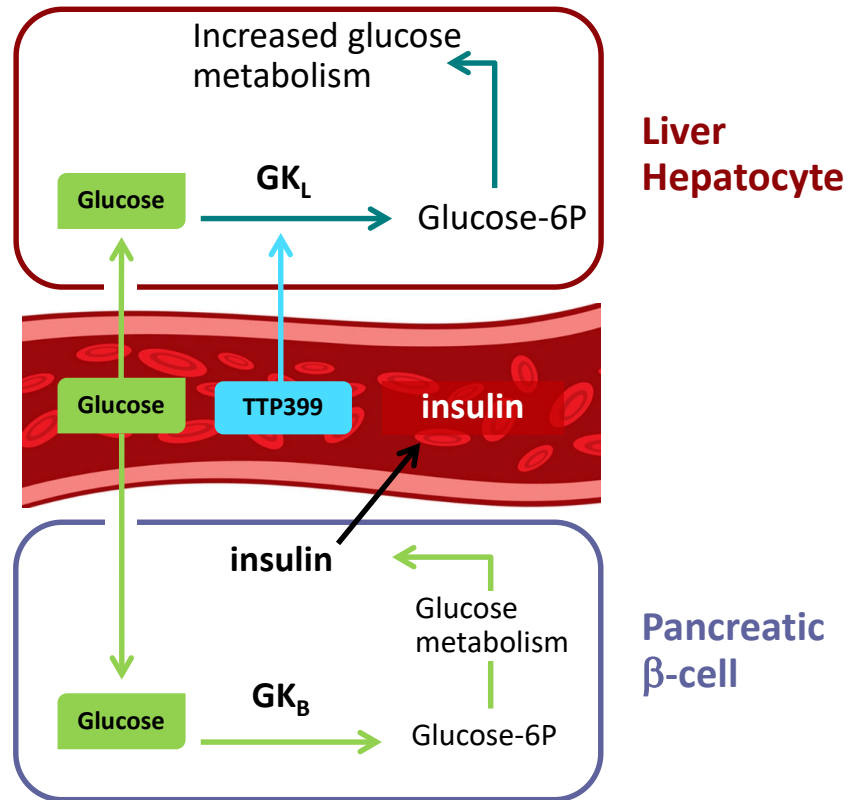
(1) CDC National Diabetes Statistics Report, 2020
 (2) Rogers, et al. 2017. BMC Medicine 15:199
 (3) Diabetes Technol Ther. 2019 Feb; 21(2):66-72. doi: 10.1089. Epub 2019 Jan 18.
 (4) American Diabetes Association: Diabetes Care 2019; 42 (Supplement 1):S90-S92, <https://doi.org/10.2337/dc19-S009>.

GKA, a Unique Biological Strategy to Support T1D Patients

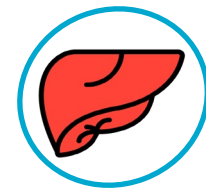
Glucokinase facilitates a critical step in sugar metabolism

Glucokinase is the glucose sensor of the body

Key role in glucose homeostasis supported by strong genetic evidence



TTP399: A liver selective Glucokinase Activator¹



TTP399 activates GK in the liver and normalizes glycogen storage



TTP399 does not activate GK in the pancreas

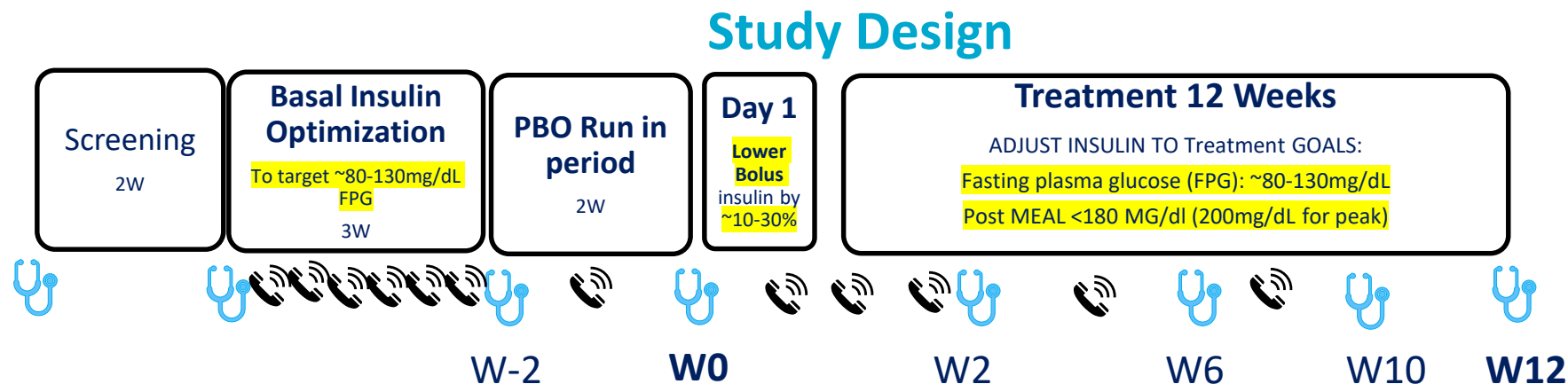


TTP399 does not interrupt the interaction between GK and its regulatory protein

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

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)



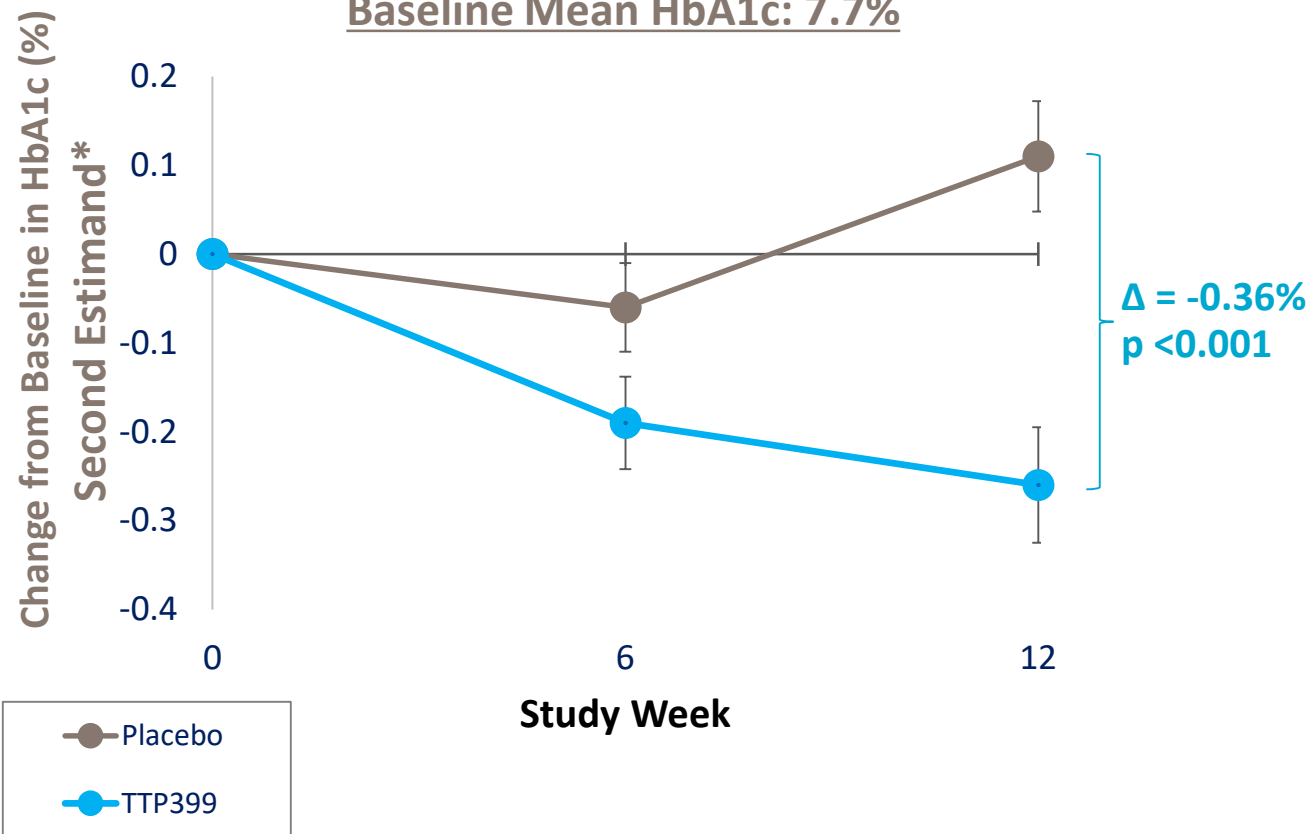
Simplici-T1 - Key Study Results

- **Statistically significant reduction in HbA1c** under a treat-to-target design (i.e. compared to intensive insulin treatment)
- **~50% 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

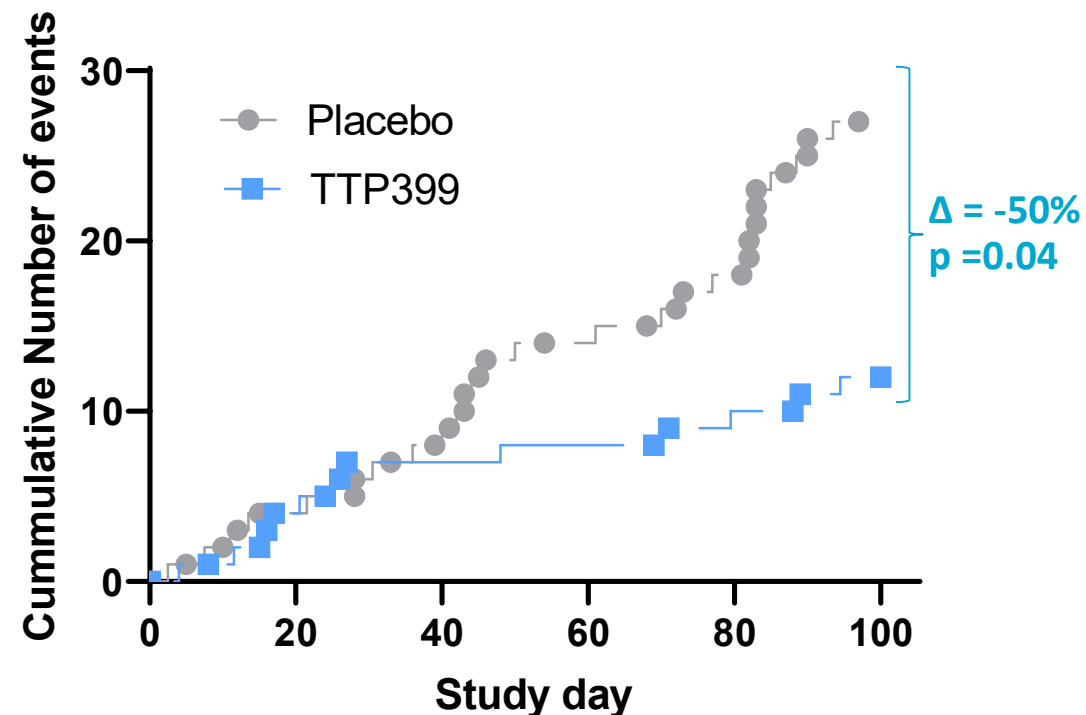
Simplici-T1: TTP399 Treated Subjects Achieved Better Glycemic Control while Reducing Hypoglycemic Events

Change in HbA1c

Baseline Mean HbA1c: 7.7%



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).

Pivotal Study Development Plan*

Advice Received

Received guidance from FDA regarding development via Type C meeting

- Guidance on Ph3 primary endpoints of HbA1c and/or reduced hypoglycemia
- Mechanistic study supporting reduced risk of DKA encouraged by FDA to inform Ph3 design

2021

Conduct DKA mechanistic study

Initiate 6 month pivotal trial followed by 6 mo Open Label Extension

2022

Second 6 month pivotal trial to start 9-12 months after first pivotal study

Estimated cost for entire development plan \$75M-\$90M
(including pivotal trials, clin pharm, API and drug product manufacturing)

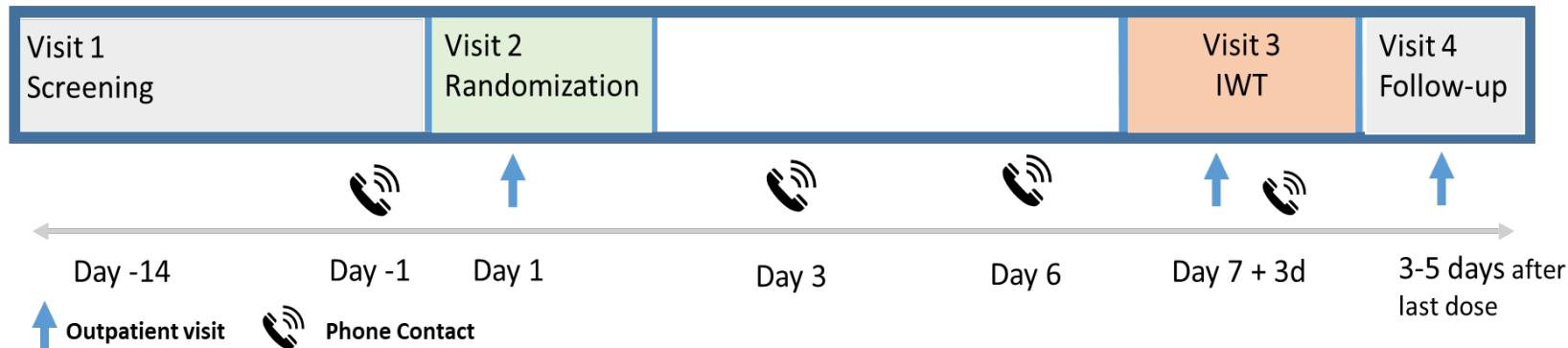
*Current development plan may change based on continued dialogue with FDA and other stakeholders and capital availability.

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



Initiation: Q1 2021

Readout: Q2 2021

- **Study design similar to clinical studies using SGLT2 inhibitors^{1,2}**
- **Results from similar preclinical study using TTP355³**
 - **Decreased ketones** in plasma after insulin withdrawal **with liver selective GKA** compared to placebo

(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:

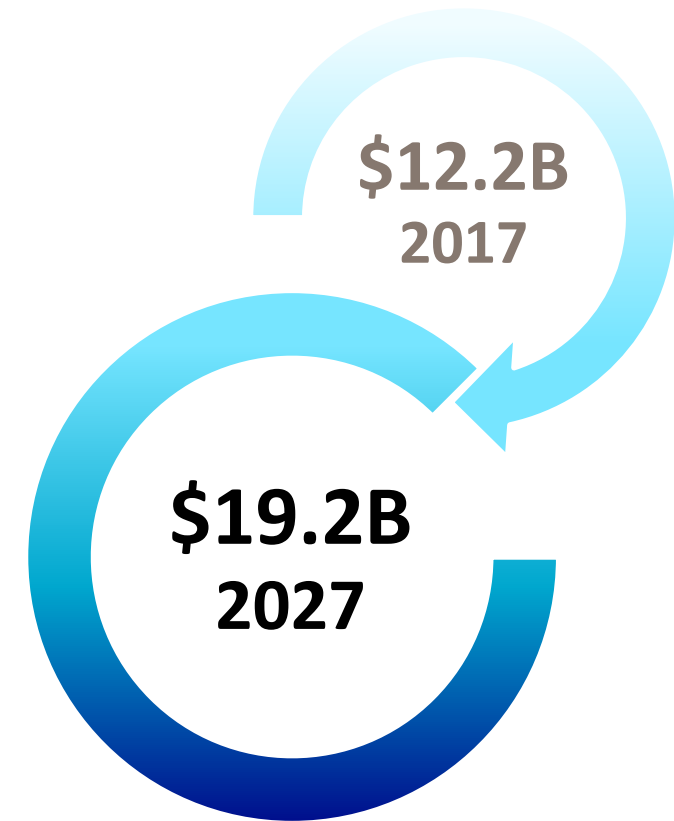
PDE4 Inhibitor as an Oral Treatment of Psoriasis



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 clinical studies

Psoriasis Market Sales*



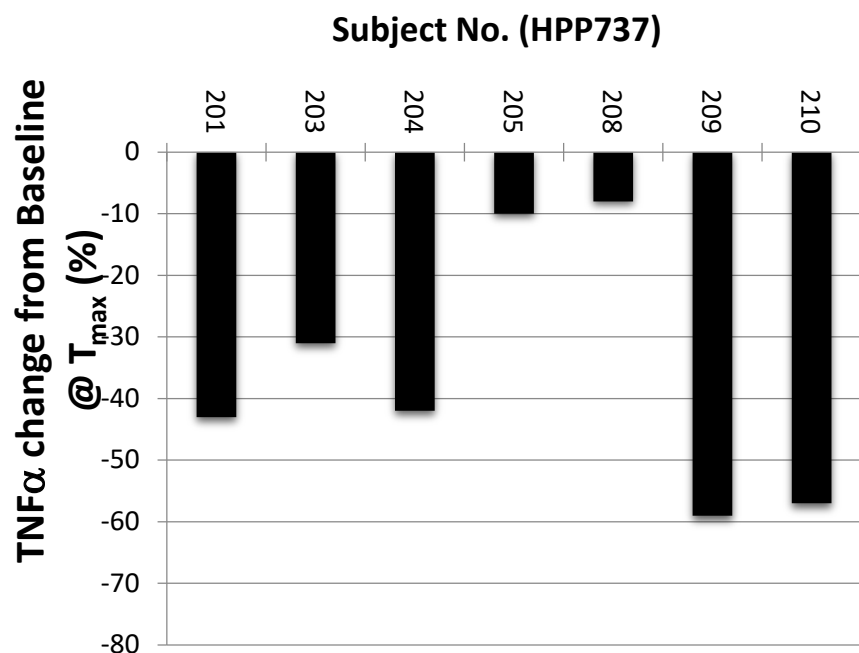
* Psoriasis market sales in US, Japan, 5EU (France, Germany, Italy, Spain, and UK).

HPP737 Shows Differentiated Profile from other PDE4 Inhibitors in Phase 1 Studies in Healthy Volunteers

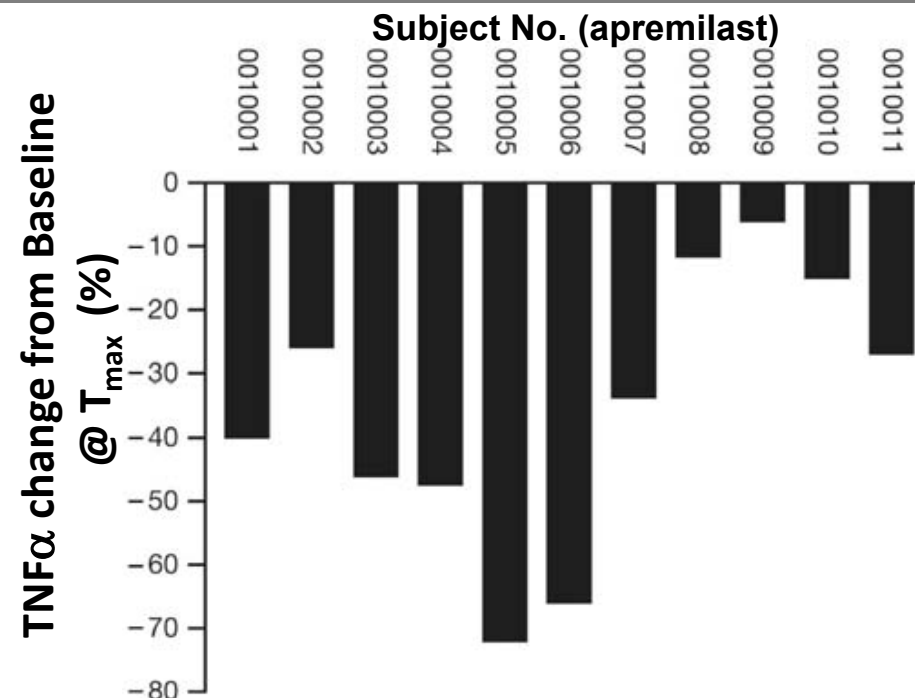
In completed Single and Multiple Ascending dose studies in healthy volunteers

- No significant treatment related GI intolerance observed (i.e. nausea, vomiting or diarrhea)
- Reduction in TNF α similar to published data with Apremilast* but at ~10x lower drug concentrations

HPP737 12 mg single dose
Healthy Volunteers
 C_{\max} 21ng/mL



Apremilast 20mg single dose*
Psoriasis Patients
Day 29: C_{\max} 207 ng/mL
Day 1: TNF α response



* Gottlieb AB et al. An open-label single-arm pilot study in patients with severe plaque-type psoriasis treated with an oral anti-inflammatory agent apremilast. *Current Medical Research and*

HPP737-103: Multiple Ascending Dose Study

Study Objective: Demonstrate proof-of-principle and select dose(s) for POC study

- Determine Maximum Tolerated Dose (MTD)
 - Demonstrate minimal to no GI intolerance (i.e. nausea, vomiting and/or diarrhea)
- Characterize pharmacokinetics / pharmacodynamics
 - Functional pharmacologic activity on Th-17 cells consistent with PDE4 target engagement
- Goal: Once daily dosing; no need for titration

Study Design:

- Healthy volunteer Multiple Ascending Dose (MAD) study
- 2-week dosing
- 2 planned cohorts, 1 additional optional cohort as needed
- Biomarkers: IL-17A, IL-17F, IL-22 and TNF- α

Initiation: Q1 2021

Readout: Q2 2021

Azeliragon

Antagonist of RAGE (Receptor for Advanced Glycation Endproducts)

Exploring Opportunities for Azeliragon in New Disease Areas through Partnerships

- Alzheimer's disease program has been discontinued
- vTv has fielded multiple in-bound inquiries to partner on testing azeliragon in diseases of interest beyond Alzheimer's disease
- vTv is evaluating these various inquiries and will pursue strategic opportunities of interest
- **In addition to potential future collaborations, vTv has an ongoing pre-clinical collaboration for testing azeliragon for the prevention of type 1 diabetes:**

Disease	Partner/Collaborator	Study Stage
Type 1 Diabetes Prevention	University of Queensland, Australia Yale University Funding provided by JDRF	Pre-clinical (animal models)

Azeliragon – Extensive preclinical and clinical development program



Azeliragon (TTP488) is a novel, oral small molecule RAGE antagonist that inhibits RAGE interactions with its natural ligands such as AGEs, A β peptides, S100 proteins and HMGB1



Extensive demonstration of pre-clinical effects in several animal models of diverse medical conditions



Major components to support an NDA completed such as long-term toxicology studies, carcinogenicity studies, clinical pharmacology and others



Integrated clinical safety database that could be used to support NDA (over 1,200 individuals dosed)






Multiple GMP batches of product produced to meet registration requirements prepared in support of Alzheimer's development program

Partnered Development Programs



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)	 NEWSQARA 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

Thank you

