

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

## **Forward looking statements**

The statements made in this presentation may include forward-looking statements regarding the type 1 diabetes, Alzheimer's disease, 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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- We are focused on treating **metabolic and inflammatory disorders** to minimize their longterm 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

#### **Company Overview**

## **Our People**



Jeff Kindler, JD Chairman of the Board

CEO, Centrexion Therapeutics Fmr. Chairman and CEO, Pfizer Fmr. EVP, General Counsel for McDonald's Corporation Fmr. Partner of William & Connelly



**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

#### Company Overview

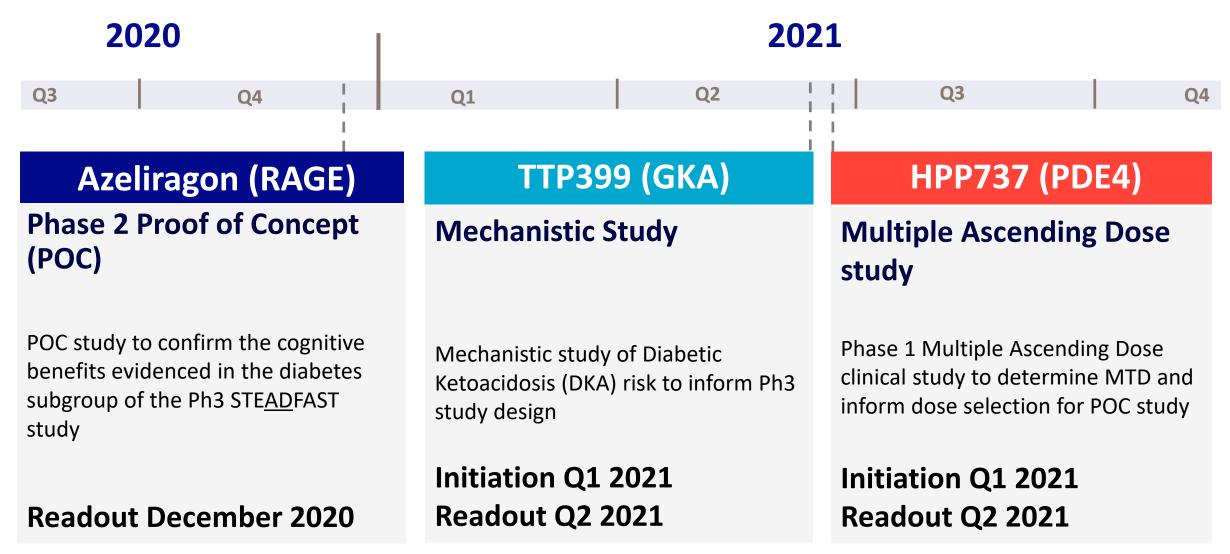
## Pipeline

Indication	Preclinical Phase I	Phase II	Phase III	<b>Biological Rational</b>
Type 1 Diabetes (T1D)	ТТРЗ99 (GKA)			Liver-selective GKA; no disruption of GKRP
Dementia with Diabetes	Azeliragon (RAGE)			Small molecule antagonist of RAGE
Psoriasis	HPP737 (PDE4)			Small molecule oral PDE4 inhibitor
Cystic Fibrosis Related Diabetes (CFRD)	TTP273 (Oral GLP1-R)			Small molecule oral GLP1-R agonist

#### **Partnered Programs**

	Preclinical Phase I	Phase II	Phase III	Partner / Te	erritory
Type 2 Diabetes (T2D)	TTP273 (Oral GLP1-R)				China and other Pacific Rim Countries (excl. Japan)
Primary Mitochondrial Myopathy	HPP593 (PPAR-d)			Reneo	Worldwide
COPD/Atopic Derm/Psoriasis	HPP737 (PDE4)			NEWSOARA 恒翼生物医药	China and other Pacific Rim Countries (excl. Japan)
5					vTv Therapeutics 2020

## Multiple Data Readouts Expected Across Pipeline in 2020/2021



# Diabetes

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

## Type 1 Diabetes / TTP399 T1D is a Burdensome Disease

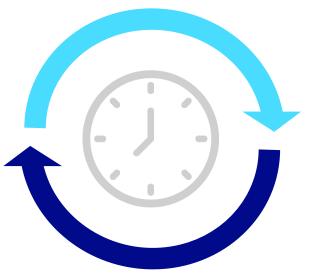
People with T1D never get a day off from managing it

It requires constant monitoring of blood glucose levels

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







Risk of nighttime hypoglycemia and seizures



It requires constant management, 24 hours a day



Must count the carbs and account for everything they eat



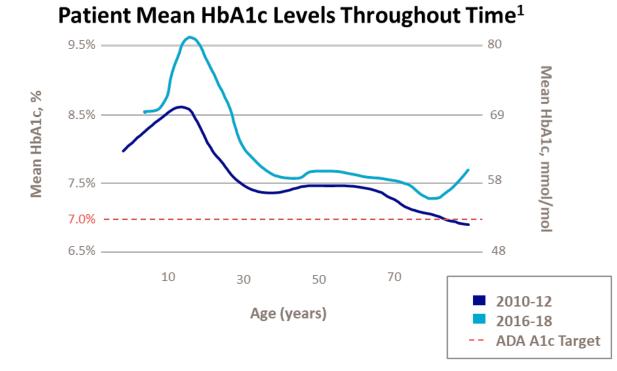
It is exhausting and has long-term dangerous complications



## Type 1 Diabetes / TTP399 Insulin Alone is Not Enough

#### Nearly 80% of people with type 1 diabetes fail to achieve ADA target A1c levels<sup>1</sup>

Despite improved and more widely adopted diabetes technology, clinical outcomes continue to decline<sup>2</sup>



# 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 diabetesrelated fatalities<sup>3</sup>

1. <u>Diabetes Technol Ther</u>. 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) <u>21</u>:66-72; DOI: 10.1089/dia.2018.0384

3. Osama Hamdy, et al. Medscape May 31, 2019, Diabetic Ketoacidosis (DKA)

Type 1 Diabetes / TTP399

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

**~7.4 Million** Americans with diabetes (T1D and T2D) take insulin, including 1.5M T1D patients<sup>1</sup>

**36%** of US diabetic patients (T1D and T2D) had  $\geq$ 1 episode of severe hypoglycemia in the last year <sup>2</sup>

**245,000 Emergency Room visits** due to severe hypoglycemia by adults with diabetes (2014)<sup>3</sup>

**\$1.8 Billion** in total direct medical costs of hypoglycemic events (2009)<sup>4</sup>

(1) <u>https://care.diabetesjournals.org/content/41/6/1299</u>

(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 <a href="https://www.uwo.ca/diabetesalliance/img/iNPHORM\_posters\_full\_sized/EASDposter\_Sept%2023-Large.jpg">https://www.uwo.ca/diabetesalliance/img/iNPHORM\_posters\_full\_sized/EASDposter\_Sept%2023-Large.jpg</a>

(3) CDC National Diabetes Statistics Report 2017

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

## **Limited Treatment Options for a Significant Patient Population**

have limited potential in T1D<sup>(4)</sup>

## Large commercial opportunity with significant unmet need

- <u>**30 million**</u> people suffer from T1D globally<sup>(1)</sup>
- In the US, 1.5 million adult and pediatric T1D patients<sup>(2)</sup>; ~77k new T1D adults diagnosed annually
- <u>Nearly 80%</u> of people with T1D <u>fail to achieve ADA</u> <u>target A1c levels</u><sup>(3)</sup>
- Limited historical innovation for current standard of care
  - Requires constant management and monitoring
- No oral adjunct therapies approved in the US
- Potential >\$1 billion market for oral adjunctive treatments to insulin in T1D

	Insulin						
	Pramlintide						
	SGLT-i					Type 1 Diabetes	
	Alpha glucos	sidase				Treatment	
	GLP-1 mime	tics					
	Sulfonylurea	as					
	DPP4-i						
	Metformin						
				GIS	Incre (EU/ patie	<b>ty risks</b> eased DKA Japan approvals only fc ents with BMI ≥ 27 kg/r	
NO	effect in T1D		Limited effe		ulin se	cretion	

No approved oral therapies for T1D in the US, and available T2D treatments

#### TTP399 GKA

#### **Product attributes:**

- Oral treatment
- Reduce hypoglycemia
- Improve time-in-range
- Reduce insulin dose

#### Without:

- Diabetic ketoacidosis ("DKA")
- Weight gain

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<sup>(1)</sup> IDF Diabetes ATLAS 8<sup>th</sup> edition.

<sup>(2)</sup> Global data, 2019.

 <sup>(3)</sup> 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

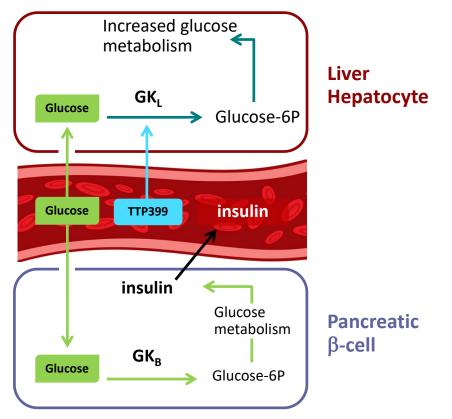
#### Type 1 Diabetes / TTP399

## **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 Activator<sup>1</sup>



#### TTP399 activates GK in the liver



TTP399 does not activate GK in the pancreas

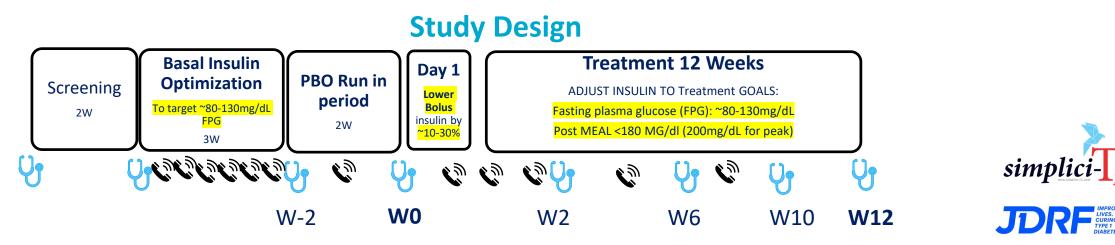


TTP399 does not interrupt the interaction between GK and its regulatory protein

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

#### Type 1 Diabetes / TTP399 Simplici-T1 — Adaptive Phase 1b/2 Study Trial Design

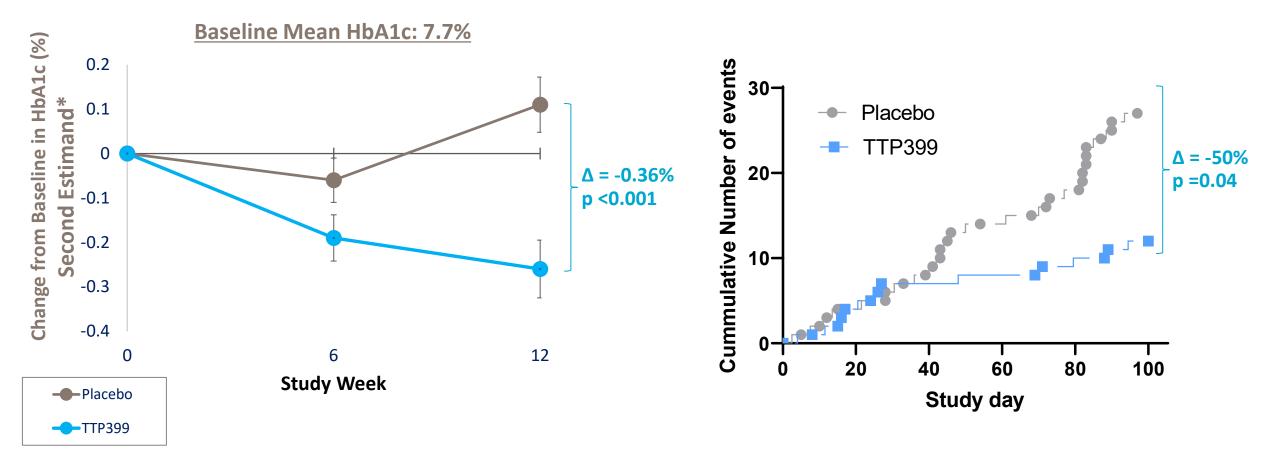
- Simplici-T1 study designed to explore the safety and efficacy of TTP399, as an oral adjunctive therapy for T1D
- Double-blind Placebo controlled 12 weeks of dosing, 800mg QD or placebo (1:1) in 104 patients with T1D
- Treat-to-target design allowed changes in insulin dose <u>after the insulin-optimization period in all</u> <u>participants via frequent PI follow-up</u> to achieve and maintain the pre-specified targets (FPG: ~80-130mg/dL; post meal glucose: <180-200 mg/dL)</li>



- 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

#### Type 1 Diabetes / TTP399 Simplici-T1: TTP399 Treated Subjects Achieved Better Glycemic Control while Reducing Hypoglycemic Events

#### Change in HbA1c



\*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).

**Hypoglycemic Events** 

Type 1 Diabetes / TTP399

### **Pivotal Study Development Plan\***

Advice Received	<ul> <li>Received guidance from FDA regarding development via Type C meeting</li> <li>Guidance on Ph3 primary endpoints of HbA1c and/or reduced hypoglycemia</li> <li>Mechanistic study supporting reduced risk of DKA encouraged by FDA to inform Ph3 design</li> </ul>				
2021	Conduct DKA mechanistic study				
2021	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)					

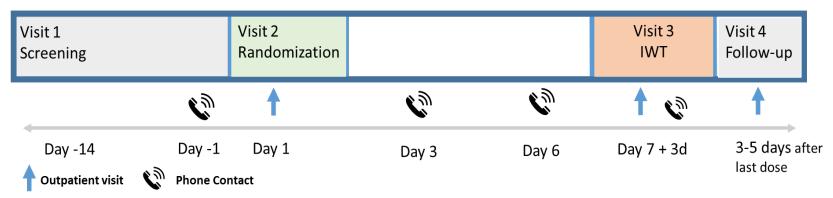
\*Current development plan may change based on continued dialogue with FDA and other stakeholders and capital availability.

## Proposed 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 (βhydroxybutyrate) will be collected for 10h



Initiation: Q1 2021 Readout: Q2 2021

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

Herring et al, Diabetes Care 2020 <u>https://doi.org/10.2337/dc19-2579</u>
 Patel et al. Diabetes Technology & Therapeutics <u>19</u>,618-622, 2017) <u>https://</u>doi/10.1089/dia.2017.0267
 <u>https://vtvtherapeutics.com/wp-content/uploads/2020/08/GKA-Poster-Keystone-2017\_01182017\_final-minipigs.pdf</u> TTP355: liver-selective GKA (first generation)

# Dementia

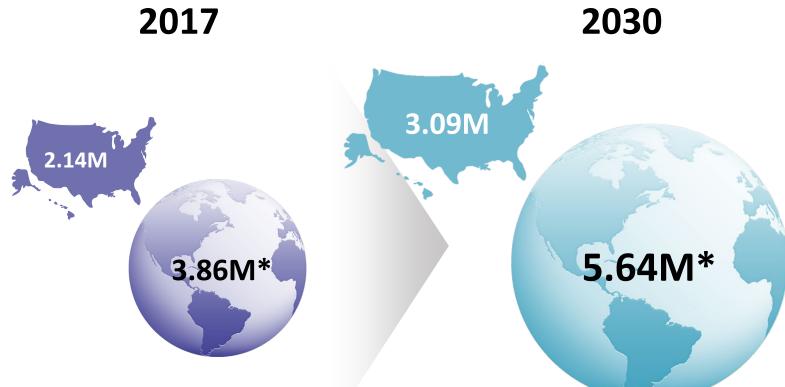
Azeliragon RAGE antagonist for Dementia with Diabetes



#### **Prevalence of Dementia (Alzheimer's) with Diabetes**

#### **Market Size**

Market for Dementia with diabetes expected to reach **\$2.04B by 2030** in 7MM\* from \$1.18B in 2017



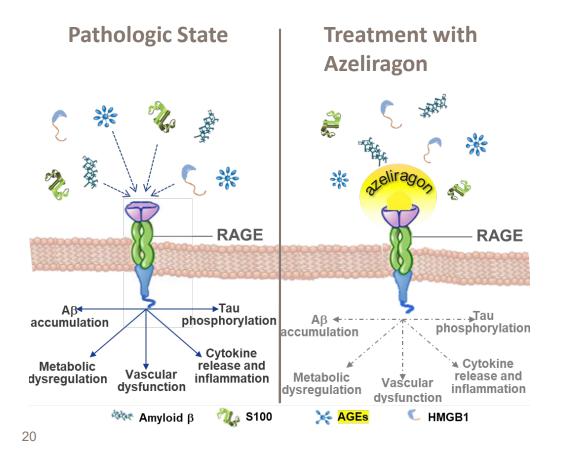
\*7 Major Markets: US, Germany, France, Italy, Spain, UK and Japan

Source: Delveinsight, Dementia with Diabetes, Market Insights, Epidemiology and Market Forecast – 2030, March 2020

#### Brain / Azeliragon (RAGE)

## **Targeting RAGE for Treatment of Dementia with Diabetes**

Azeliragon antagonizes the Receptor for Advanced Glycation Endproducts (RAGE), blocking ligands from binding to the receptor and blunting resultant downstream pathologic events



## Well established associations between AGEs / RAGE and diabetic complications

- Advanced glycation endproduct (AGE) accumulation is increased in patients with diabetes and parallels the development of cognitive impairment and dementia
- Increases in AGEs:
  - promote increased expression of RAGE
  - are linked to development of end-organ complications such as retinopathy, neuropathy and nephropathy



## Potential benefits of RAGE antagonism for dementia in diabetes

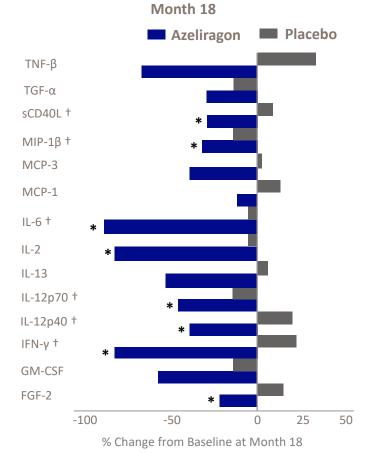
- Blockade of, and reduction in, microglia activation
- Less brain atrophy
- Less dysregulation of brain glucose metabolism
- Reduction in inflammation
- Preservation of cognition and functional activities

#### **STEADFAST:** Potential Beneficial Effect on Cognition in Patients with Elevated HbA1c

#### STEADFAST A-Study Type 2 Diabetes Subgroup (FAS) ADAS-cog11 -3--2-Improvement Change from Baseline **∆=4.9** P<0.001\* **∆=5.5** 2-Worsening p=0.006\* 3-5 6-7-12 15 3 9 18 0 6 Month Azeliragon (n=26) Placebo (n=21) No. of Patients azeliragon 26 25 24 22 19 24 25 20 18 17 21 21 18 18 placebo

Type 2 Diabetes: Patients with diabetes (HbA1c  $\geq$  6.5% at anytime during the study) Results are LSMeans  $\pm$  SE based on MMRM model. \*All p values are nominal. FAS =Full Analysis Set

#### **Reduction in Plasma Inflammatory Biomarkers**



Results are Medians

\* Nominal p<0.05 Wilcoxon test

+ Biomarkers with direct relationship to RAGE

21 Data presented on March 30, 2019 at the 14<sup>th</sup> International Conference on Alzheimer's & Parkinson's Diseases held in Lisbon, Portugal <sup>1</sup>Thomas et al. Alzheimer's & Dementia 2016:12;598-603.

## Elevage Study: Phase 2 Study Topline Readout in December 2020

#### **Study Objective:**

- Proof of concept study to confirm the cognitive benefits evidenced in the diabetes subgroup (n=47) of the STE<u>AD</u>FAST study
- Powered to demonstrate treatment difference between azeliragon and placebo on the ADAS-cog

#### **Study Design:**

- 6 months of dosing 5mg Azeliragon or Placebo
- 43 patients enrolled
- Primary Endpoint: ADAS-cog14
- Secondary Endpoints: Amsterdam IADL, CDR-sb, FAQ

## **Readout December 2020**

Seek FDA guidance Prior to Initiating Registration Trial

Initiate Registration Trial



vTv Therapeutics 2020

# Inflammation

HPP737 PDE4 Inhibitor as an oral treatment of Psoriasis



## Inflammation / HPP737 (PDE4) **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 in US, Japan, 5EU (France, Germany, Italy, Spain, and UK ). <sub>24</sub> Source: Global Data, Plaque Psoriasis Global Drug Forecast and Market Analysis to 2027. Published Dec 2018



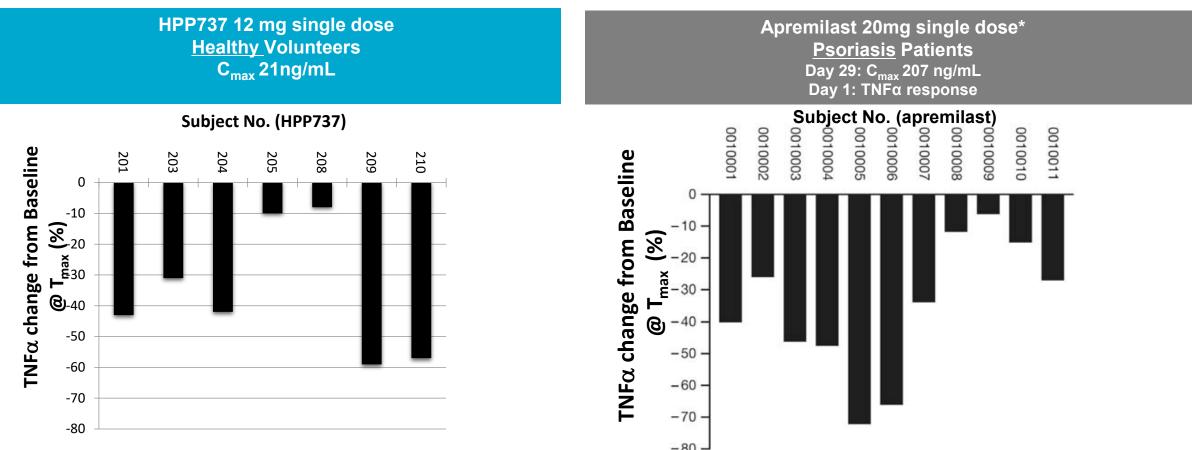
\$12.2B 2017

\$19.2B 2027

## Inflammation / HPP737 (PDE4) HPP737 Shows Differentiated Profile from other PDE4 Inhibitors in Phase 1 Studies in Healthy Volunteers

#### 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 TNFα similar to published data with Apremilast\* but at ~10x lower drug concentrations



\* 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

**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

# Partnered Development Programs



## **Creating Value Through Partnerships**

Asset	Partner	Territory	<b>Target Indications</b>	Economics for vTv
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
PPAR-δ Agonist Program	Reneo	Worldwide	Primary Mitochondrial Myopathy, Fatty Acid Oxidation Disorder, McArdle Disease	Equity interest in Reneo Milestones and Royalties
TTP273 (Oral GLP-1r)		China and other Pacific Rim Countries (excl. Japan)	Type 2 Diabetes	Milestones and Royalties Utilization of data to advance development in ROW

# Thank you

