



Corporate Presentation

**Committed to Improve the Quality of Life
for People with Diabetes**

January 2022

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Committed to Improve the Quality of Life for People with Diabetes



- vTv Therapeutics is a clinical-stage biotech with a pipeline of drug candidates.
- vTv's lead product TTP399, an oral glucokinase activator, is being developed as a **transformative treatment for the reduction in hypoglycemic episodes** for the global diabetes population.
- TTP399 received **Breakthrough Therapy Designation** by the FDA in 2021.
- vTv owns worldwide rights and is planning to enter **Phase 3 pivotal studies in 2022.**

Our Executives



Deepa Prasad
President, Chief Executive Officer







- >20 years healthcare experience across operations, venture capital, investment banking
- Board Member, Design Therapeutics (NSDQ: DSGN)
- Previously General Partner, WestRiver Group (Healthcare VC)
- Recipient of Falk Marques/Deloitte General Partner Award
- Previously VP, Financial Strategy and Business Development, Coherus Biosciences (NSDQ: CHRS)
- ~10 years in investment banking across biotech private placements, buy-side/sell-side and cross-border M&A
- B.S. at University of California, Berkeley, MBA from the Kellogg School of Management at Northwestern University



Carmen Valcarce, Ph.D.
EVP, Chief Scientific Officer

- >30 years of pharmaceutical research and development experience focused on the metabolic space
- Instrumental in TTP399 from idea -> development
- At Novo Nordisk for 7 years as a Project Leader for its glucokinase project
- Managed 12 INDs and run clinical studies across diabetes
- Inventor of more >20 patents and patent applications and author on numerous peer-reviewed scientific publications
- Obtained Ph.D. at the Universidad Autonoma de Madrid, Spain, in the field of metabolic diseases and mitochondrial development

Pipeline

PRODUCT	PRECLIN	PHASE I	PHASE II	PHASE III	PARTNER	TERRITORY
TTP399 GK Activator	Type 1 Diabetes					
TTP273 Oral GLP-1R Antagonist	CFRD	Type 2 Diabetes			 	China and Pac Rim (excl. Japan)
HPP737 PDE4 Inhibitor	SAD/MAD Completed	Psoriasis				China and Pac Rim (excl. Japan)
HPP593 PPAR- δ Agonist	Primary Mitochondrial Myopathy					Worldwide
Azeliragon RAGE Antagonist	Pancreatic Cancer					Worldwide
HPP971 Nrf2 Activator	Renal Diseases					Worldwide
HPP3033 Nrf2/Bach1 Modulator	Undisclosed					
Azeliragon RAGE Antagonist	T1D Prevention					

TTP399 Highlights

Novel Product with Unique Mechanism of Action

- Only liver-selective glucokinase activator known to be in clinical development
- Once-daily oral pill as an adjunctive treatment to insulin
- Granted Breakthrough Therapy Designation by FDA April 2021

Significant Unmet Need

- Nearly 80% of people with Type 1 Diabetes (T1D) fail to achieve target A1c levels
- Hypoglycemia is a major barrier to achieving glycemic control
- No oral adjunctive therapies for T1D are currently FDA approved in the U.S.

Attractive Efficacy Profile and Well-Tolerated

- 13 clinical trials (including 3 Phase 2 trials in T1D and T2D) with ~600 patients dosed to date
- Statistically and clinically significant reduction in hypoglycemia and HbA1c in T1D
- No evidence of increased risk of diabetic ketoacidosis. Common AEs included headache and GI issues, similar to placebo

Massive Market Opportunity for an Oral Adjunctive Therapy in a \$16B Market

- Potential for expansion into Type 2 Diabetes patients
- Dominated by 3 large players: Novo Nordisk, Lilly, Sanofi
- Global pivotal trials anticipated in 1H 2022; vTv has worldwide rights

TTP399

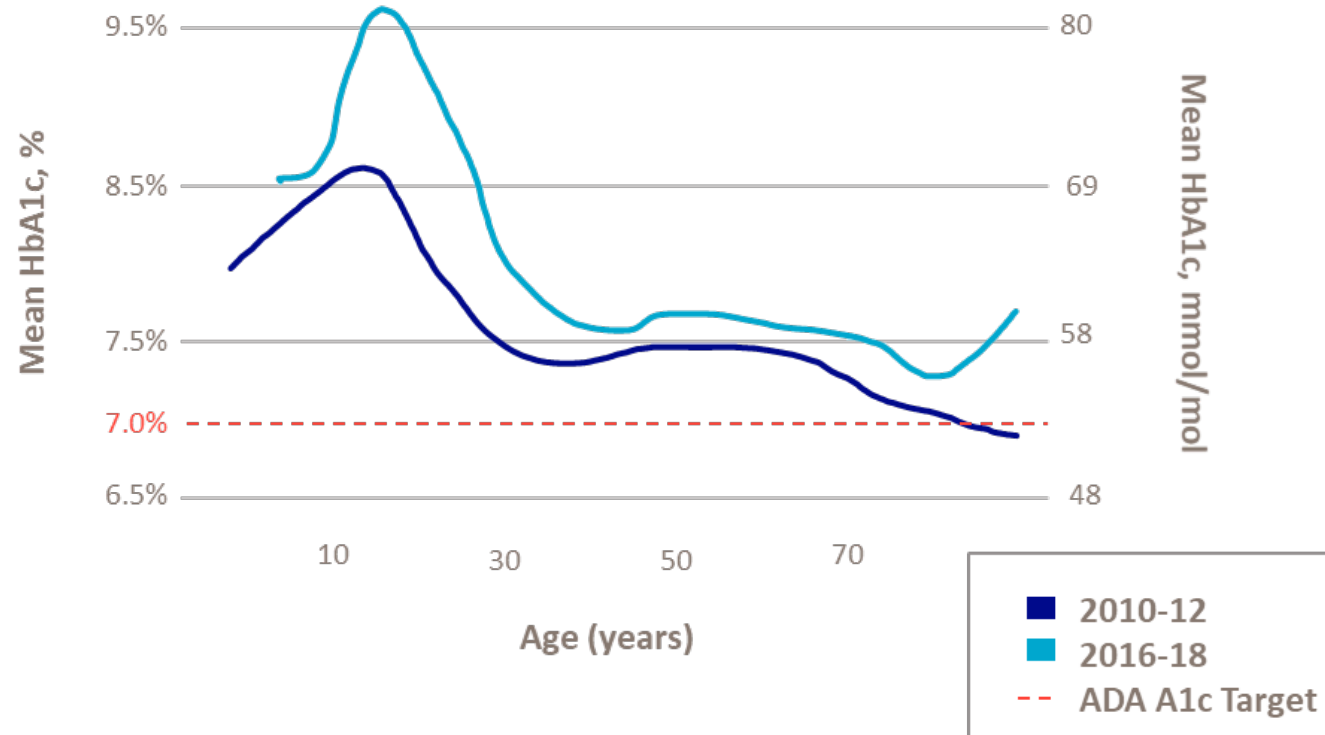
**Liver-Selective Glucokinase Activator (GKA) as an
Adjunctive Treatment to Insulin**



Subcutaneous Insulin Alone is Not Enough

Life-threatening, Short-term Complications Still Unsolved

Patient Mean HbA1c Levels Throughout Time¹



Nearly **80% of people** with Type 1 diabetes fail to achieve ADA target A1c levels

Severe **hypoglycemia** is a major barrier to achieving glycemic control

Diabetic Ketoacidosis (DKA) accounts for **14% of all hospital admissions** of patients with diabetes and **16% of all diabetes-related fatalities**

Sources:

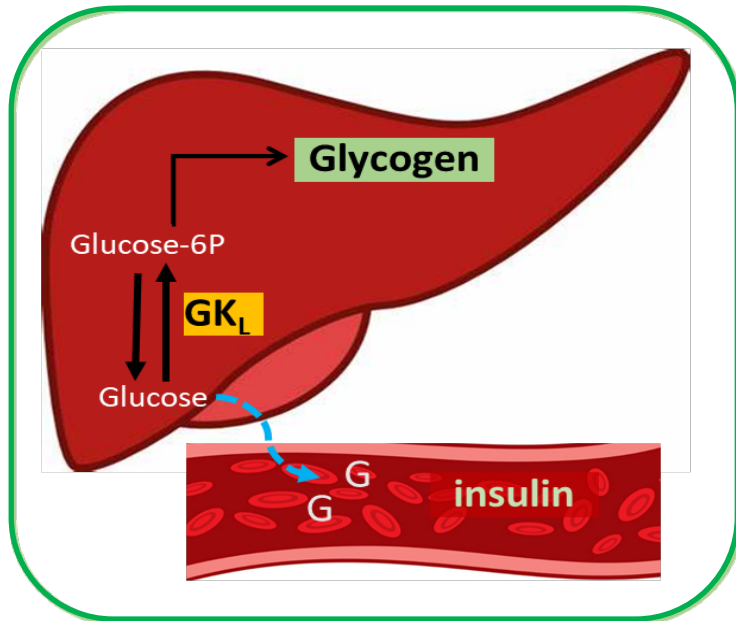
1. [Diabetes Technol Ther](#). 2019 Feb;21(2):66-72. doi: 10.1089/dia.2018.0384. Epub 2019 Jan 18.
2. Foster et al. [Diabetes Technology and Therapeutics](#) (2019) 21:66-72; DOI: 10.1089/dia.2018.0384
3. Osama Hamdy, et al. [Medscape May 31, 2019, Diabetic Ketoacidosis \(DKA\)](#)
4. Meneghini et al 2017 DOI: 10.1111/dom.13208

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

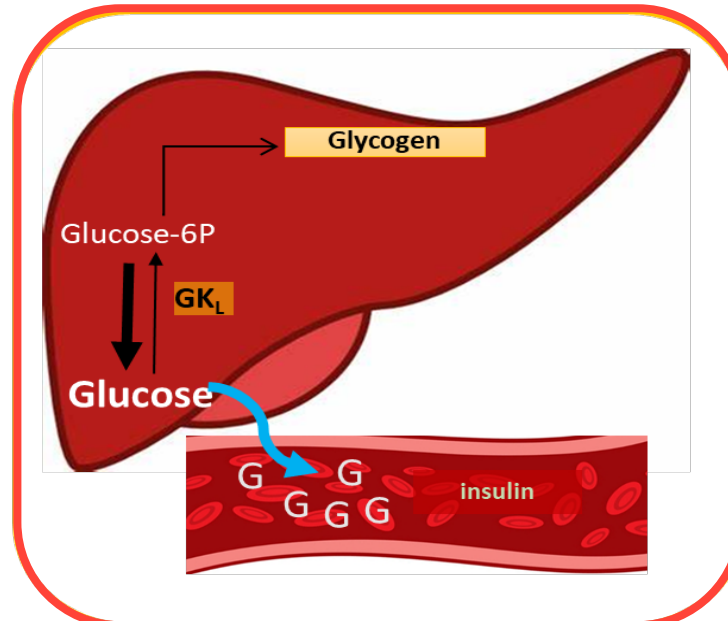
Healthy (Non-Diabetic)



Normal Glucose metabolism:

- GK activity
- Glycogen storage

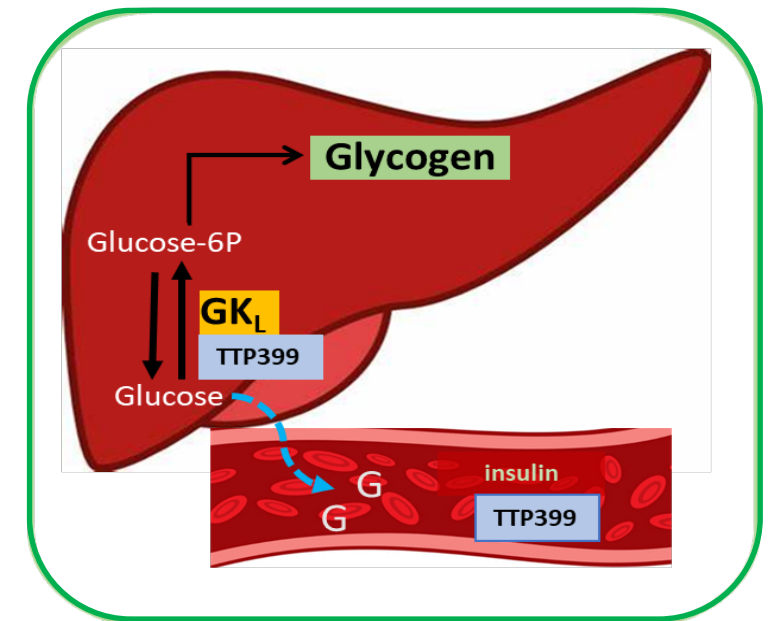
Type 1 Diabetes



Abnormal Glucose metabolism:

- Lower GK activity
- Lower Glycogen storage

Type 1 Diabetes + TTP399



Normalization of Glucose metabolism:

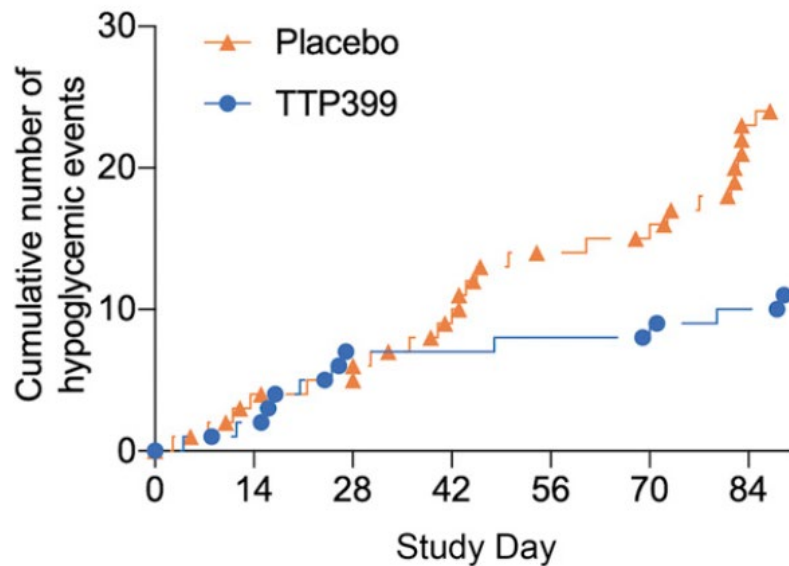
- GK activation
- Normalization of Glycogen storage

Simplici-T1 — Adaptive Phase 1b/2 Study

Study Design:

- **Part 1:** 20 participants using continuous glucose monitors and continuous subcutaneous insulin infusion via insulin pumps
- **Part 2:** 85 participants receive multiple daily injections of insulin or CSII.
- **Dosing:** TTP399 800mg or placebo once daily for 12 weeks (randomized 1:1) **Treat to target, optimized insulin dose for each patient**

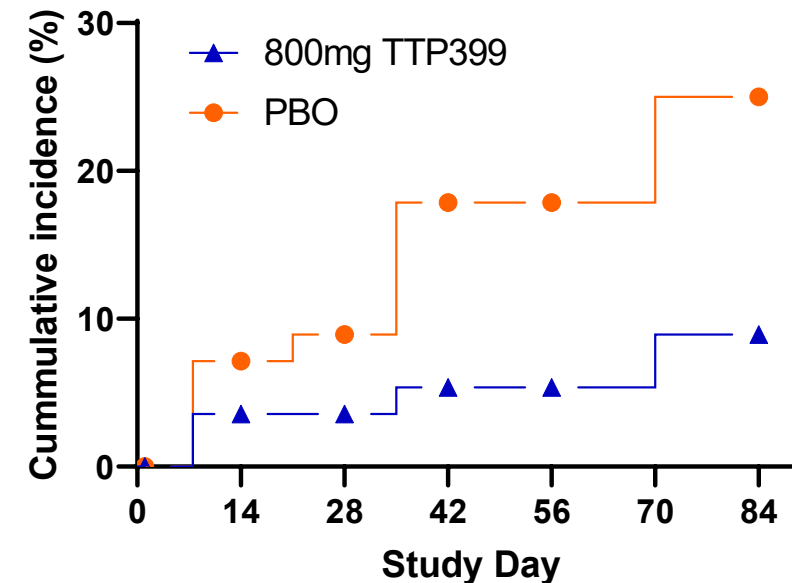
Hypoglycemic Events



40% REDUCTION in hypoglycemic episodes relative to placebo

“Keto” Events

Central lab ketone values
>0.4mmol/L

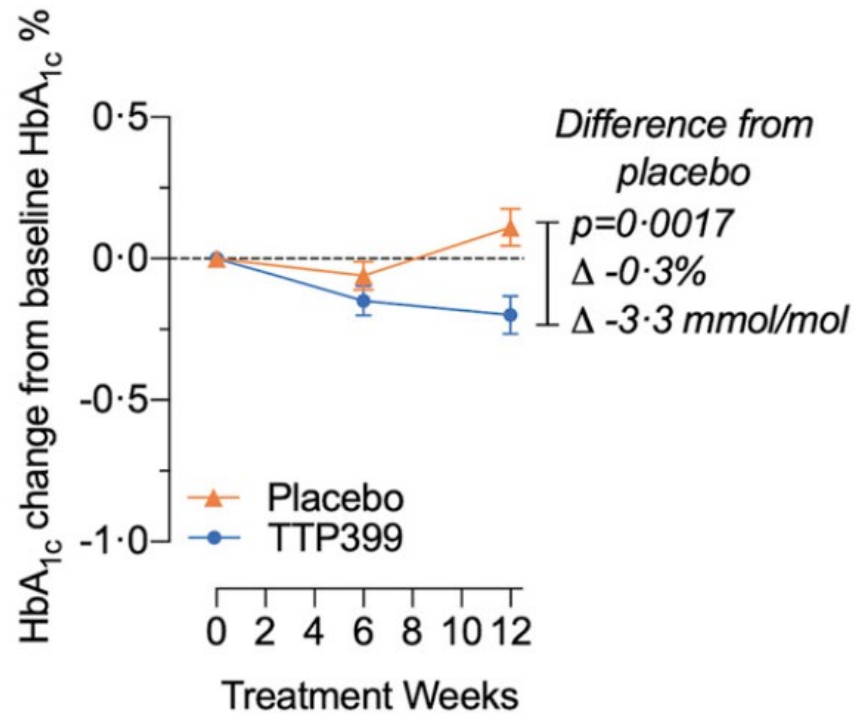


Plasma β -hydroxybutyrate and urinary ketones were **LOWER** during treatment with TTP399 than placebo

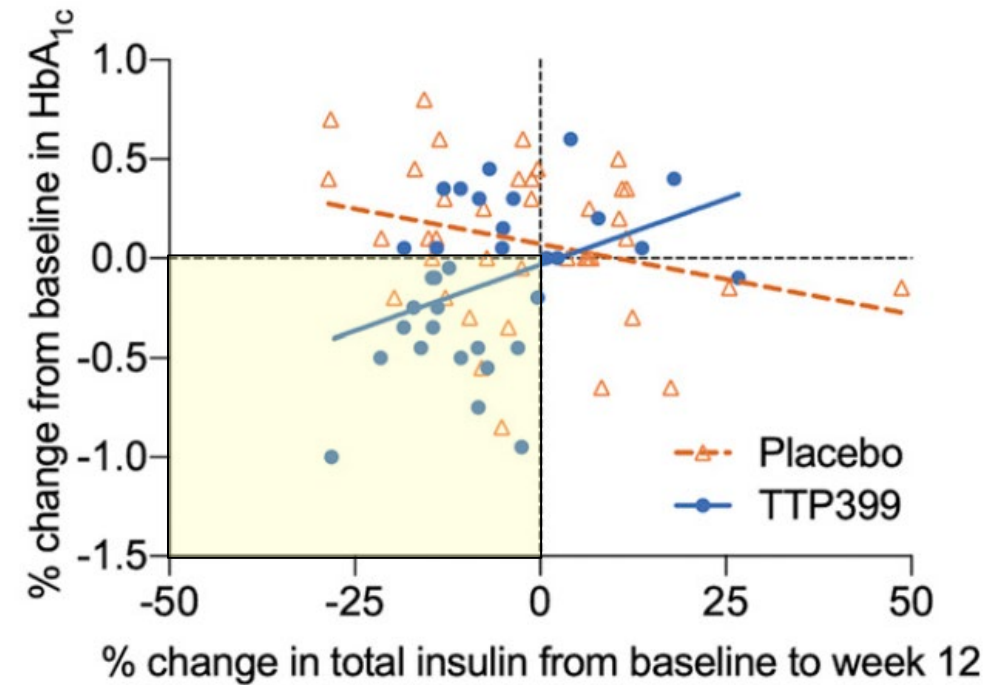
Simplici-T1 — Adaptive Phase 1b/2 Study

TTP399 Treated Subjects Achieved Better Glycemic Control while Decreasing their Insulin Dose

Change in HbA1c



$\Delta A1c$ vs Δ Total Insulin

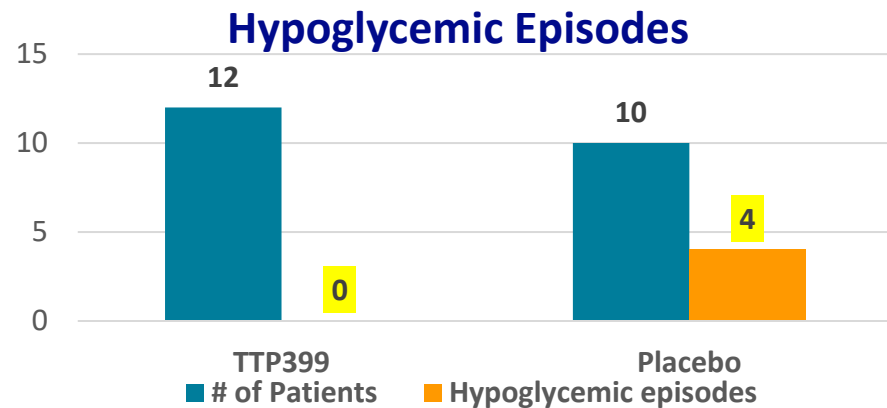


*The pre-specified second estimand analysis evaluated the effect on HbA_{1c} for patients without evidence of noncompliance with prescribed treatment who did not administer notable increases of bolus insulin of three or more units. This second estimand analysis was conducted consistent with current regulatory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

Mechanistic Study of Diabetic Ketoacidosis Risk (TTP399-118)

Study Design:

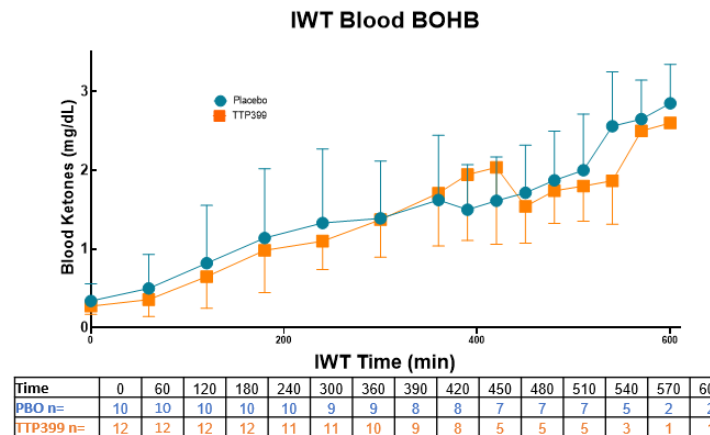
- Patients:** 23 adults with T1D on insulin pumps (~ 80% using closed loop systems); 1 pt on placebo discontinued prior to measurement per patient request
- Dosing:** TTP399 800mg or placebo once daily for 7 days (randomized 1:1)
- Insulin withdrawal test (IWT):** on day 7, insulin delivery stopped in AM and serial measurements of plasma glucose and ketones (β -hydroxybutyrate, BOHB) collected for 10h or until stopping criteria were achieved



Zero hypoglycemic episodes during treatment

- Reduction in fasting plasma glucose of ~30mg/dL ($p=0.03$)
- 0 hypoglycemic episodes in TTP399 group, 4 in placebo
- Good safety profile comparable to placebo

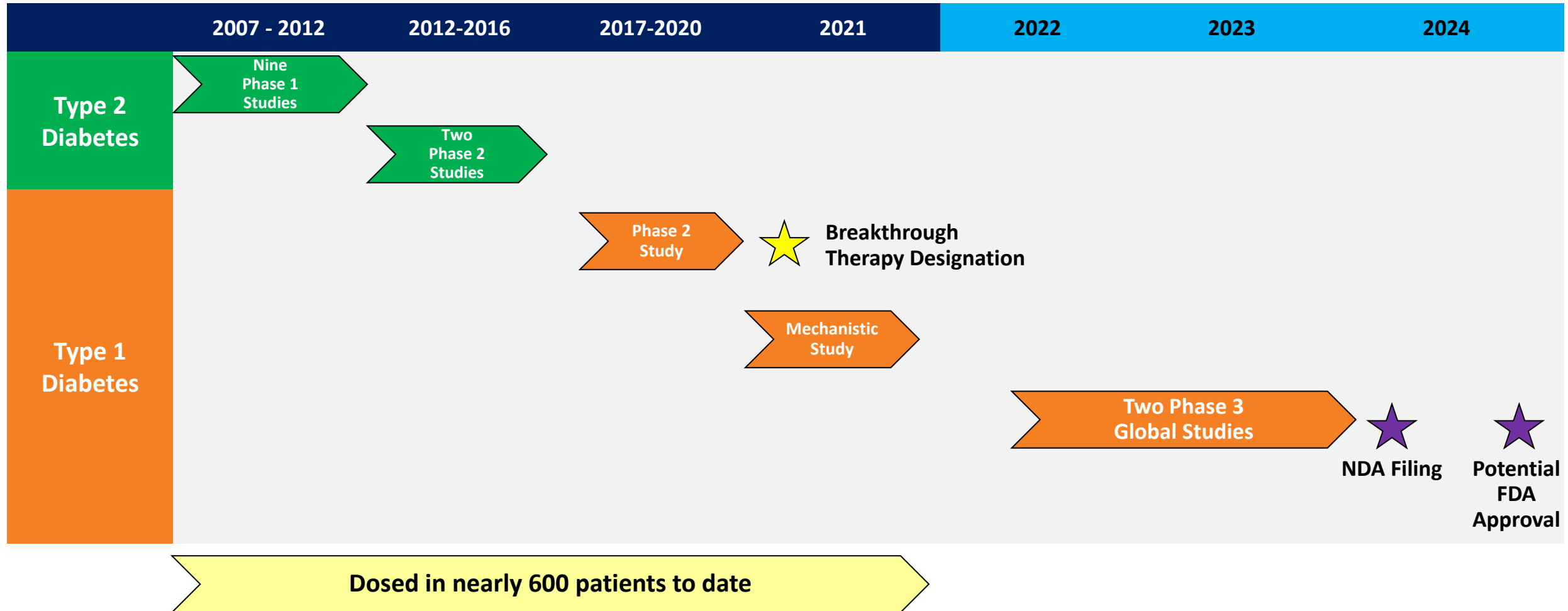
Insulin Withdrawal Test (10 hour maximum duration)



No increased risk of ketoacidosis relative to placebo during conditions of insulin deficiency (IWT)

- No significant differences between the arms in blood ketone or glucose profiles
- Fewer subjects in TTP399 group reach bedside BOHB >3mM (25% in TTP399 vs 50% in placebo)
- Only one subject (1/12) in the TTP399 group presented bicarbonate <18mEq/L at the end of the IWT. Four subjects (4/7) in the placebo group.

TTP399 Development Plan



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

TTP399

Competitive Landscape



Except for Insulin, Available Approved Diabetes Treatments have Limited Potential

Mechanism of Action	Administration	Adverse Events	Regulatory Approvals
Insulin	Subcutaneous	Hypoglycemia Weight gain	Approved worldwide
Amylin Analogue	Subcutaneous	Hypoglycemia	Approved in U.S and EU
SGLT1/2 inhibitor	Oral	Increased risk of DKA Mycotic infections	Not approved in US for T1D. Received CRL. Approved in EU for improved glycemic control for T1D pts with BMI \geq 27 kg/m ²
SGLT2 Inhibitors	Oral	Increased risk of DKA Mycotic infections	None approved in the US; Approvals only in EU and Japan None approved in hypoglycemia Multiple CRLs received for T1D-related indications
GLP-1 Mimetics	Subcutaneous	Hypo/hyper glycemia associated with ketosis	Not moving towards Regulatory Approval
Glucagon	Injectable Nasal spray	Multiple side effects (e.g., seizures, shakiness, vomiting)	Approved in U.S / EU as a rescue therapy for hypoglycemic episodes
Liver-selective glucokinase activator (TTP399)	Oral	No evidence of increased risk of diabetic ketoacidosis Common AEs included headache and GI issues, similar to placebo	Granted Breakthrough Therapy Designation by FDA April 2021 Planning to enter Phase 3 Pivotal trials in 2022 for reduction in hypoglycemic episodes

Sources:

American Diabetes Association: Diabetes Care 2019; 42 (Supplement 1):S90-S92, <https://doi.org/10.2337/dc19-S009>.
Curr Opin Endocrinol Diabetes Obes. 2021 Feb 1;28(1):8-13.

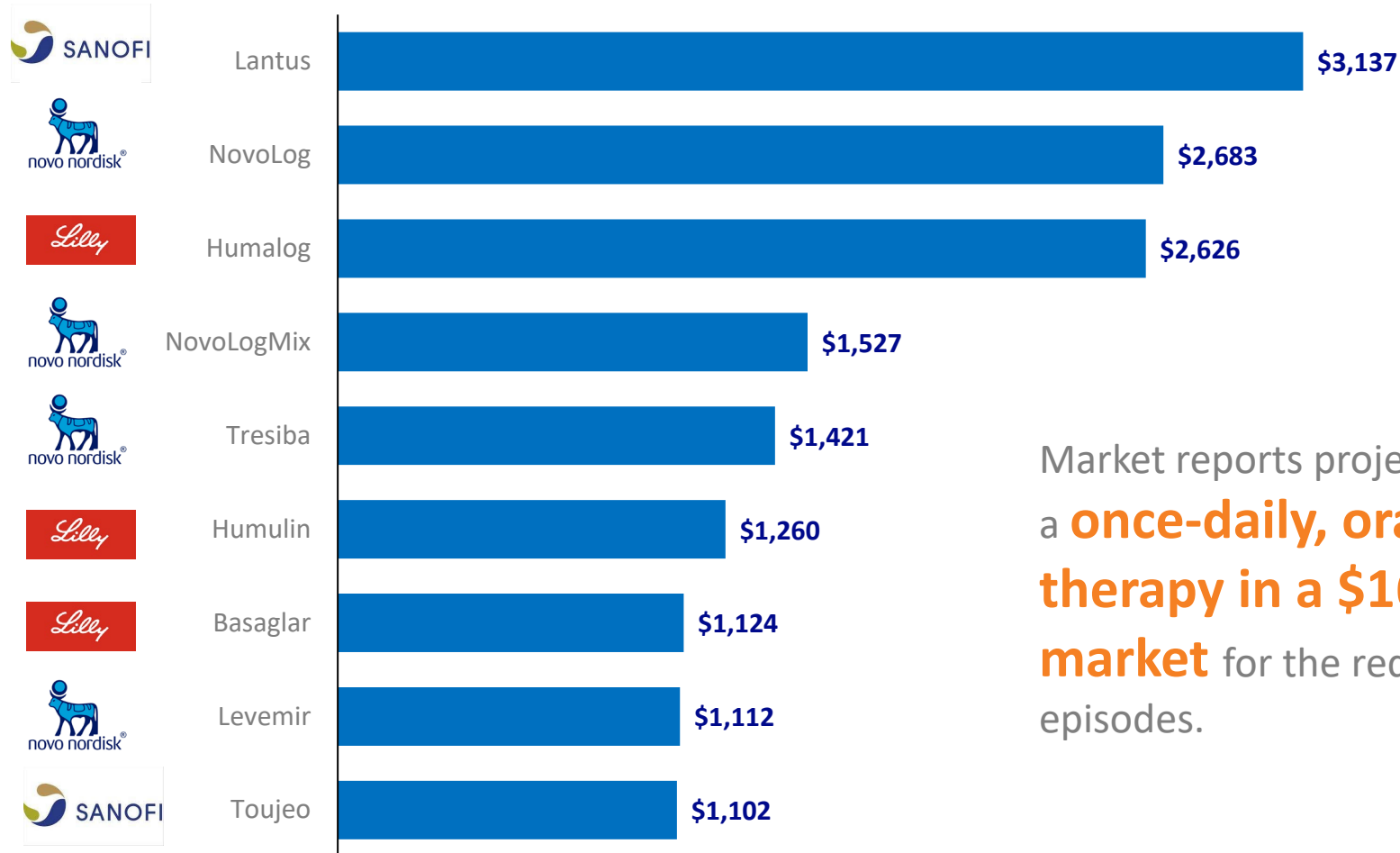
TTP399

Market Opportunity



\$16B Global Insulin Market Comprised of 3 Major Players

Top 2020 Global Insulin Sales (\$m)



Market reports project TTP399 may be used as a **once-daily, oral adjunctive therapy in a \$16B global insulin market** for the reduction of hypoglycemic episodes.

Hypoglycemia is the Most Common Acute Complication of Diabetes

- Hypoglycemia occurs when **blood sugar levels <70 mg/dL**.
- **Happens quickly** with symptoms ranging from sweating, nausea, coordination problems, headaches to seizures
- **Hypoglycemia is more common** in people with type 1 diabetes. Most people with T1D experience **at least 1 or 2 episodes of mild hypoglycemia per week**.
- **“Hypoglycemia unawareness”** occurs when patients have blood sugar readings below <70mg/dL and feel no symptoms
- In 2019 - the Endocrine Society made **reducing hypoglycemia a strategic priority**

Hypoglycemia Increases with Age in a Global Aging Population



REUTERS

World Business Markets Breakingviews Video More

HEALTHCARE NOVEMBER 4, 2021 / 4:00 AM / UPDATED 15 HOURS AGO

SPECIAL REPORT-Drugmakers pushed aggressive diabetes therapy. Patients paid the price.

By Robin Respaut, Chad Terhune, Deborah J. Nelson

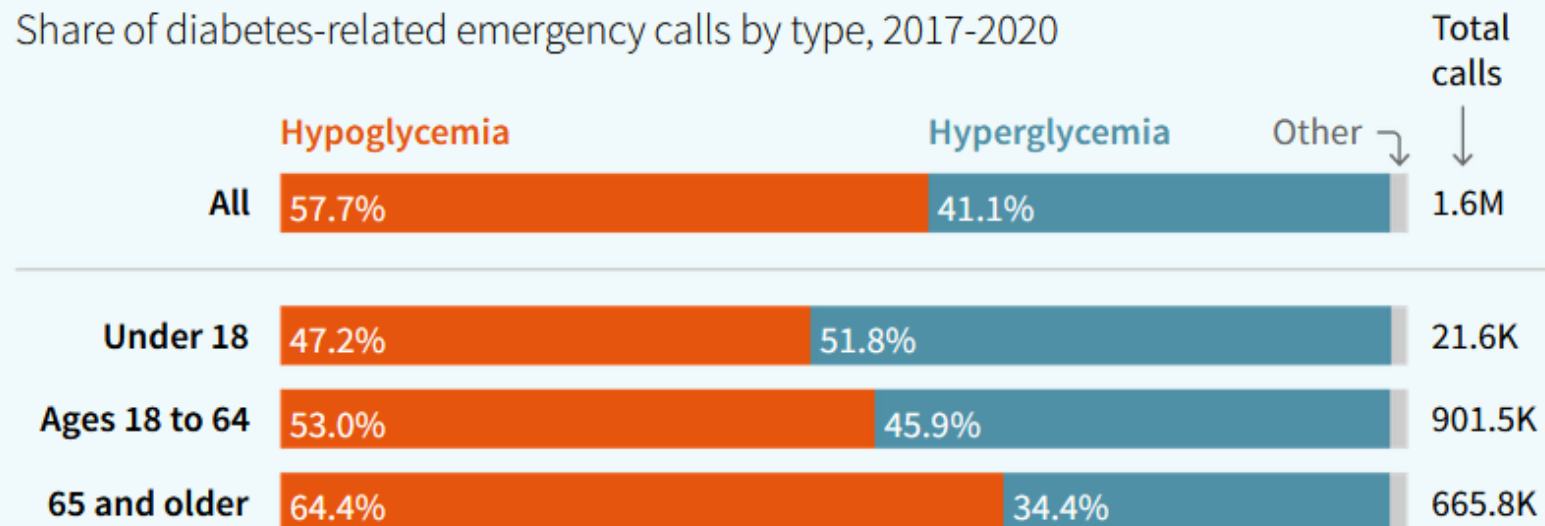
33 MIN READ



State of emergencies

The risk of hypoglycemic crisis increases with age, accounting for two-thirds of diabetes-related 911 calls among the elderly in recent years.

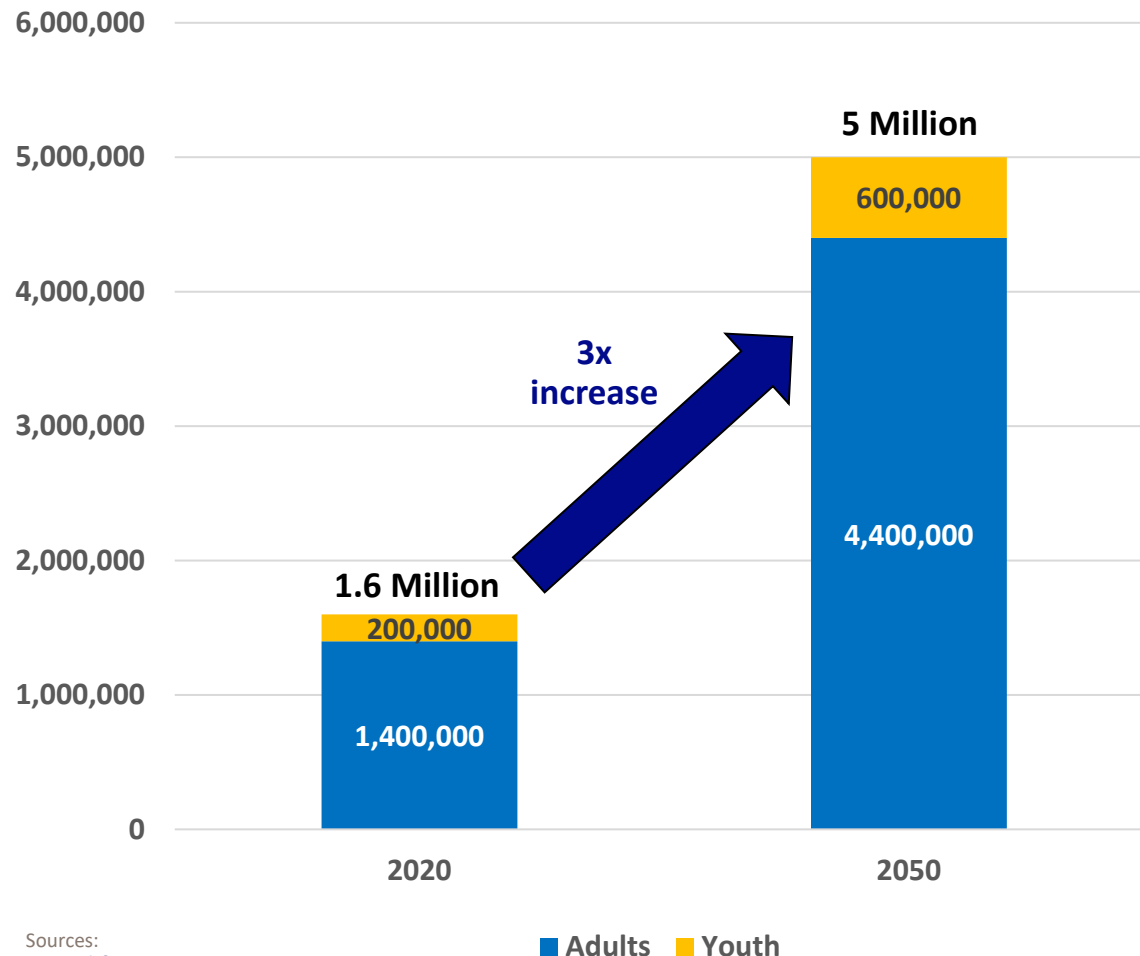
Share of diabetes-related emergency calls by type, 2017-2020



Source: Reuters analysis of 911 calls and emergency events in the National Emergency Medical Services Information System database in which a diabetic problem was the primary or secondary issue triggering the event.

Growing Patient Population

U.S. Type 1 Diabetes Population



Market reports project

U.S. Type 1 Diabetes Patient Population to triple by 2050 with

worldwide growth being fastest in the Middle East and Africa.

In 2020, the **U.S. market** accounted for **96%** of worldwide short-acting insulin revenue share.

Recent epidemiological data have shown that **more than half of all new cases** of type 1 diabetes occur in adults.

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Thank you

