Hua Medicine
华领医药

Hua Medicine Company Presentation

2021 Q1

Disclaimer

This document may contain statements that constitute “forward-looking statements”, including, but not limited to, statements relating to the implementation of strategic initiatives, and other statements relating to our future business development.

While these forward-looking statements represent our judgments and future expectations concerning the development of our business, a number of risks, uncertainties and other statutory requirements may render actual developments and results to differ materially from our expectations.

These factors include, but are not limited to, (1) general market, macro-economy, governmental and regulatory trends, (2) movements in local and international securities markets, currency exchange rates and interest rates, (3) competitive pressures, (4) technological developments, (5) changes in the financial position or creditworthiness of our customers, obligors and counterparts, and changes in the developments in the markets in which they operate, (6) legislative developments, (7) management changes and changes to our business group structure and (8) other key factors that may adversely affect our business and financial model.

We are not under any obligation to (and expressly disclaim any such obligations to) update or alter forward-looking statements whether as a result of new information, future events, or otherwise.

This material may not be reproduced, distributed or transmitted to any other person or incorporated in any way into another document or other material without the prior written consent of us.

This document is not:

(a) an offer of securities for sale in Hong Kong or elsewhere; or

(b) an invitation to enter into an agreement to acquire, dispose of, subscribe for or underwrite securities; or related to the issue of any securities.

This document (and the information contained herein) is not for publication or distribution to any person(s) except as written permitted by us.

Hua Medicine – A Global First-in-Class Biotech Diabetes Care Innovation

Hua Medicine

Li Chen
CEO & CSO

Bob Nelsen
Chairman

Roche

Arch Ventures

JUNO THERAPEUTICS
DENALI THERAPEUTICS
GRAIL
VIR
gossamerbio

Founding Investors

Arch Ventures
Fidelity INVESTMENTS
venrock
SAIL
WuXi AppTec
J Baldwin

China-Based First-In-Class

- **Global rights** to dorzagliatin composition of matter, chemical process, formulation and multiple products in FDC with OADs
- **China strategic partner selected – Bayer**
- **Met Primary Endpoint** in both pivotal Phase III monotherapy and combination with metformin trials for China regulatory approval purposes
- **First-in-Class (GKA) drug** to significantly and sustainably reduce HbA1c safely over 52 week as a glucose sensitizer
- **First Novel Concept** addressing impaired glucose sensor function - the underlying cause of T2D
- Broad indications diabetes care
  - Demonstrated viability in combination with DPP-4 inhibitor & SGLT-2 inhibitor
  - Suitable for DKD patients
- **RMB 949.6mn cash** as of June 30, 2020

Copyright © Hua Medicine 2021

Hua Medicine – *Advancing the Treatment Paradigm for Type 2 Diabetes Globally – Launching in China First*

Hua Medicine owns global rights to dorzagliatin, a global first-in-class oral glucokinase activator (GKA), for the treatment of Type 2 diabetes

- 2 Phase III registration trials successfully completed in Chinese Type 2 diabetes patients
- 14 clinical studies completed in China and USA supporting China NDA filing
- Product sale and promotion partnership with Bayer China established
- Manufacturing and commercial supply on track to meet expected blockbuster sales status

Enriched pipeline with "Dorzagliatin +" products to treat broad spectrum of T2D patients

- Fixed dose combinations of dorzagliatin with OADs: metformin, sitagliptin, empagliflozin, dapagliflozin
- New patient in late stage T2D: add on to Insulin
- New indication with add on to PPAR for NASH
- New indication with add on to GLP-1 for NASH and obesity
- New indication in Alzheimer in combination with DPPIV inhibitors

Personalized diabetes care in development

- Diabetes population, new classification based on AI-machine driven learning
- Diabetes prevention

Copyright © Hua Medicine 2021

Key Takeaways from this Presentation

Why does the world need another T2D drug?

- Diabetes is a global pandemic that currently progresses to additional costly complications despite introduction of new classes of drugs
- Current drugs only treat the symptoms of T2D, namely glucose reduction – they are not designed to address the underlying cause of T2D

How is dorzagliatin different?

- Dorzagliatin is specifically designed to address the underlying cause of T2D by restoring the loss of glucose sensitivity in patients
- Dorzagliatin targets and restores the glucose sensor in β-cells, gluocokinase, specifically – potential to change the progressive degenerative nature of the disease – a new hope for a cure in select sub-population of T2D patients
- Dorzagliatin can be used as combination therapy with the top-selling oral anti-diabetic drugs (e.g., metformin, SGLT-2 inhibitors and DPP-IV inhibitors)
- Dorzagliatin has potential to be used to treat moderate to end stage renal kidney disease patients with T2D in controlling blood glucose levels

Accordingly, dorzagliatin has the strong potential to be positioned early, and as a cornerstone therapy in the standard of care treatment paradigm for T2D globally

Copyright © Hua Medicine 2021

Why does the world need another T2D drug?

Type 2 Diabetes is a Worldwide Epidemic!

Type 2 diabetes is a worldwide epidemic fueled by the increasing prevalence of obesity, sedentary lifestyles and poor nutrition. Diabetes is characterized by hyperglycemia, which chronic sustained exposure to is associated with long-term damage, dysfunction, and failure of various organs leading to microvascular complications (e.g., retinopathy, nephropathy and neuropathy), as well as macrovascular complications (e.g., stroke, myocardial infarction and peripheral arterial disease). As a result, diabetes is an expensive disease leading to progressively higher medical costs.

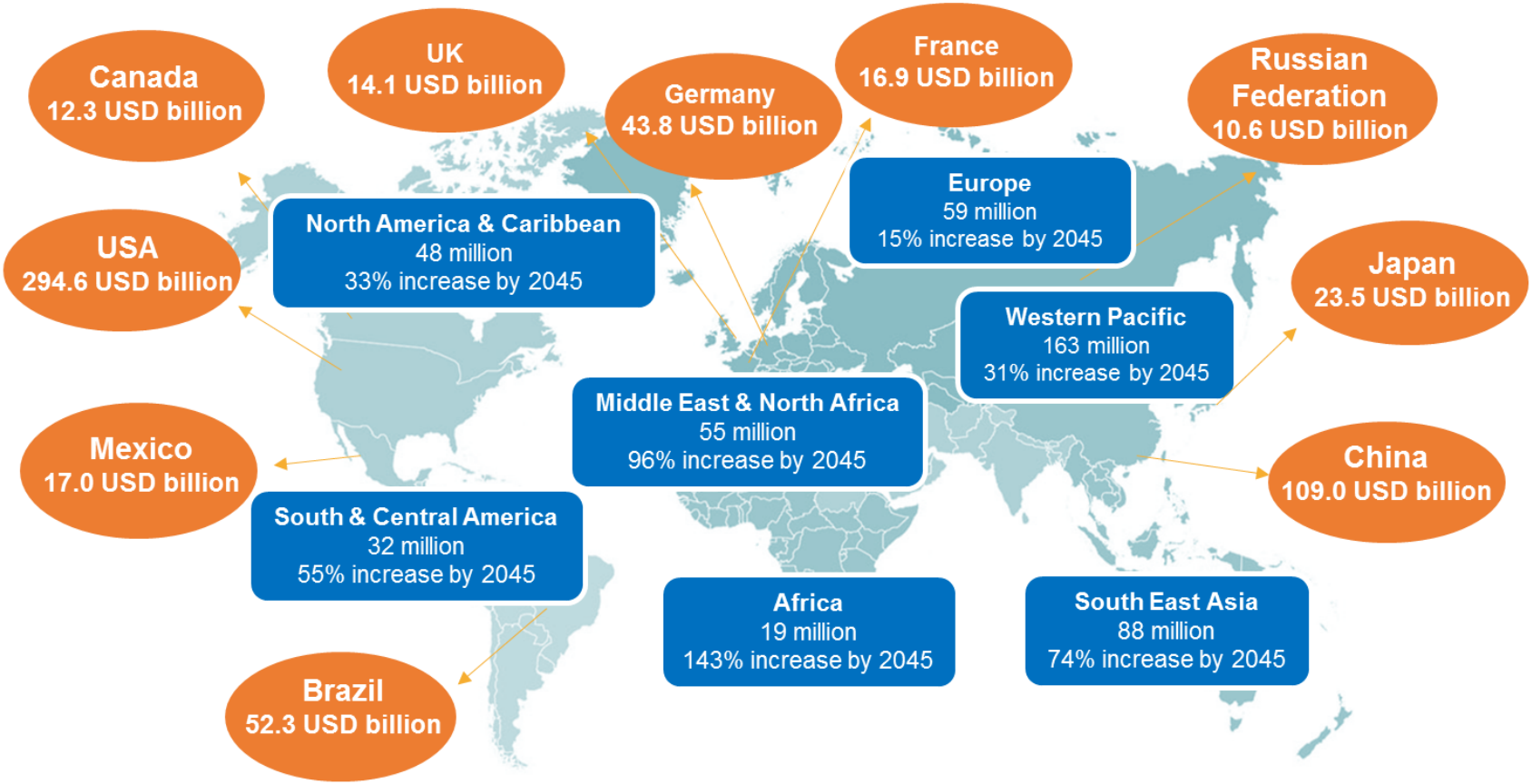
"Confounding the diabetes epidemic and high costs, ***therapeutic targets are not being met.*** *There is a lack of improvement in reaching clinical targets since 2005 despite advancements in medication and technology treatment modalities.* ***Indeed, between 2010 and 2016 improved outcomes stalled or reversed."***[1]

Source 1: Consensus Report, Diabetes Self-management Education and Support in Adults with Type 2 Diabetes, published in Diabetes Care in July 2020, the American Diabetes Association, the Association of Diabetes Care & Education Specialists, the Academy of Nutrition and Dietetics, the American Academy of Family Physicians, the American Academy of PAs, the American Association of Nurse Practitioners, and the American Pharmacists Association.

Copyright © Hua Medicine 2021

Despite multi-billion global spending on diabetes treatment, diabetes is still not being treated properly

- **~463 million** people live with diabetes across the world.
- Currently **no approved therapeutics** targets to repair of **the underlying cause of T2D**.
- In 2019, IDF estimates that total diabetes-related health expenditure will reach USD 760 billion. It is projected that the expenditure will reach **USD 825 billion** by 2030 and **USD 845 billion** by 2045.



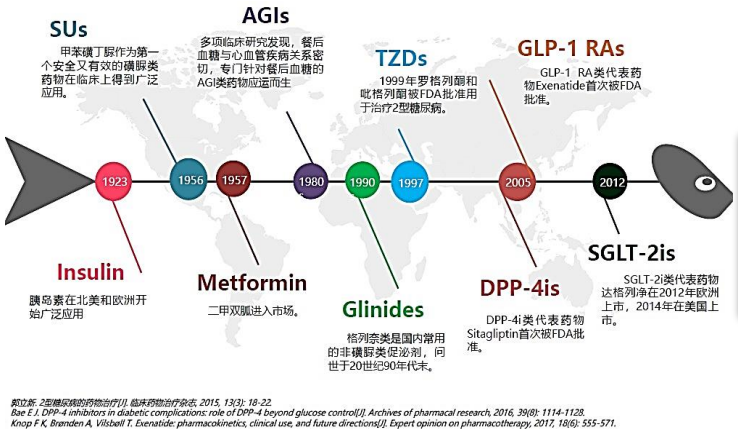
Source: IDF DIABETES ATLAS Ninth edition 2019

Note: Diabetes-related health expenditure refers to the direct costs. Direct costs are the health expenditures due to diabetes – regardless of whether this expenditure is born by patients themselves or by private or public payers or by government.

Copyright © Hua Medicine 2021

Global Unmet Medical Needs in Glycemic Control

9 Classes of Drugs

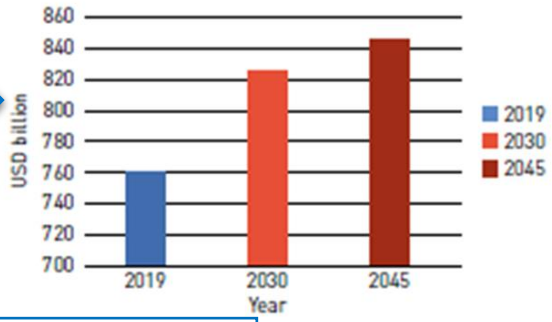


US $760 bn

450 Mn Diabetes
Many
Complications

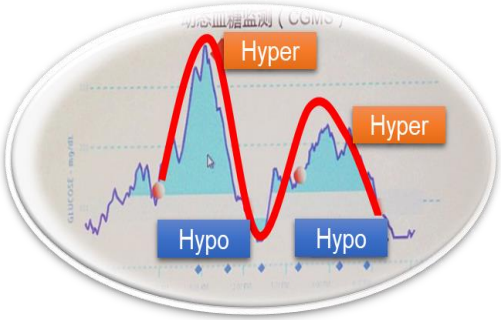
IDF 2019

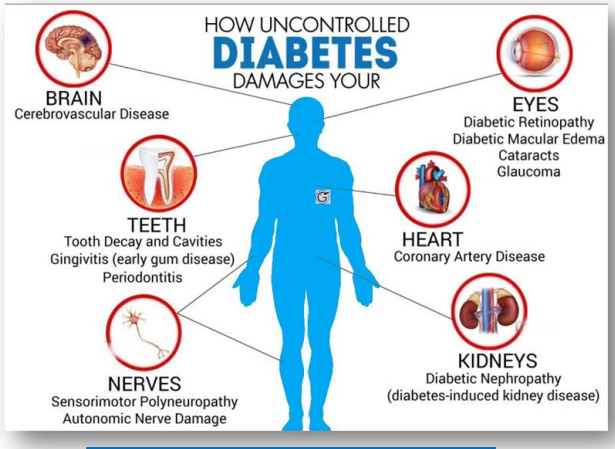
Total diabetes-related health expenditure for adults (20–79 years) with diabetes in 2019, 2030 and 2045



Top 10 Nations

Rank	Country or territory	Total diabetes-related health expenditure in 2019 (USD billion) (20-79 years)
1	United States of America	294.6
2	China	109.0
3	Brazil	52.3
4	Germany	43.8
5	Japan	23.5
6	Mexico	17.0
7	France	16.9
8	United Kingdom	14.1
9	Canada	12.3
10	Russian Federation	10.6





Blood glucose fluctuation

Diabetes Complications

Economic Burden

Source: Cheng YY, Chen L. Global J Obesity, Diabetes and Metabolic Syndrome 2020, 7：018-023
Source: Foos Wang et al Value in Health Regional Issues, 2019, 18: 36-46

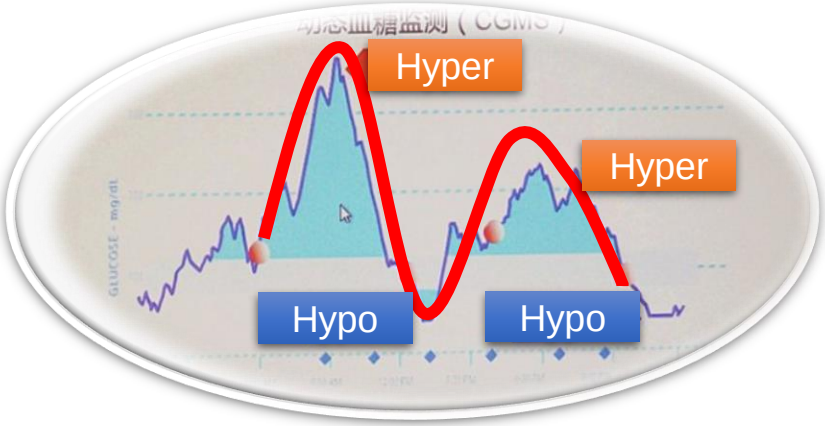
Copyright © Hua Medicine 2021

How Do We Stop Type 2 Diabetes?

Goal in treating diabetes:

To maintain blood glucose levels within a healthy range, achieving ***glucose homeostasis*** (4-6.5mM)

Lowering blood glucose levels alone will not stop the progressive degenerative nature of diabetes, leading to complications



Copyright © Hua Medicine 2021

The current treatment paradigm for Type 2 diabetes is beginning to shift

ADA Guideline
2020

- New recommendations are added on use of the ambulatory glucose profile (AGP) report and **time in range (TIR)** for assessment of glycemic management.
- New evidence and a recommendation were added on early combination therapy for Type 2 Diabetes
- SGLT-2 inhibitors or GLP-1 receptor agonists are introduced in strategy in patients with cardiovascular disease meeting A1C goals for cardiovascular benefit.

CDS Guideline
2020

- **HbA1c** is incorporated into the diagnostic criteria for diabetes
- **Time in Range (TIR)** added to blood sugar control goals
- The guideline clarifies that lifestyle intervention and metformin are the first-line treatments for hyperglycemia in patients with T2D.
- For patients with T2D with ASCVD or high risk of cardiovascular risk, GLP-1RA or SGLT2i with evidence of ASCVD benefit should be added to metformin treatment.

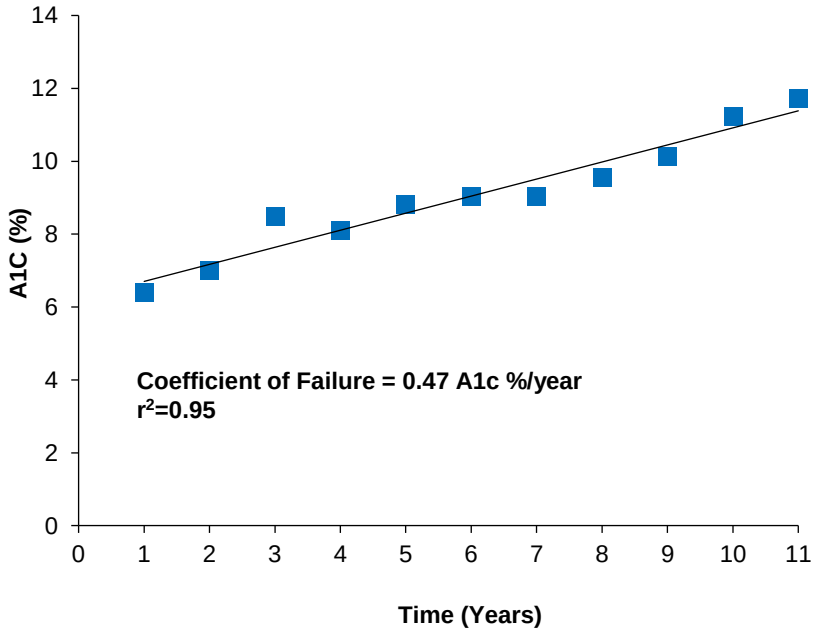
Copyright © Hua Medicine 2021

How is dorzagliatin different?

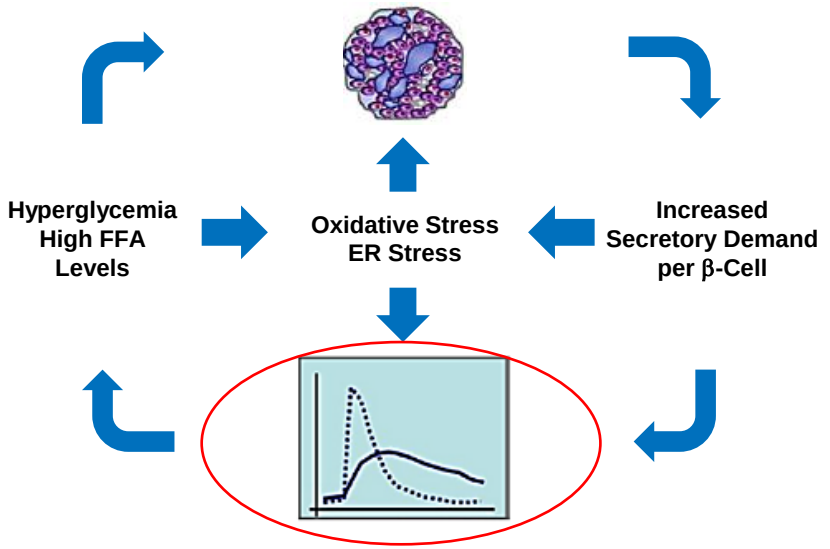
T2D is a Progressive Disease with Degeneration of β Cell Function and Increasing Insulin Resistance

- Type 2 diabetes is a progressive disease with deterioration of β cells function
- Loss of glucose sensitivity in Type 2 diabetes patients is the first step in the progressive destruction of β cells
- Impaired β cells function results in hyperglycemia stress which causes progressive damage of β cells
- Deterioration of the 1st phase insulin secretion is the leading cause of impaired glucose homeostasis

Patients with Monotherapy: HbA1c Increased by 1% Every 2 Years, β-Cell Function Decreased Accordingly[1]



Impaired β-Cell Function Results in Hyperglycemia Stress which Causes Progressive Damage of β Cells



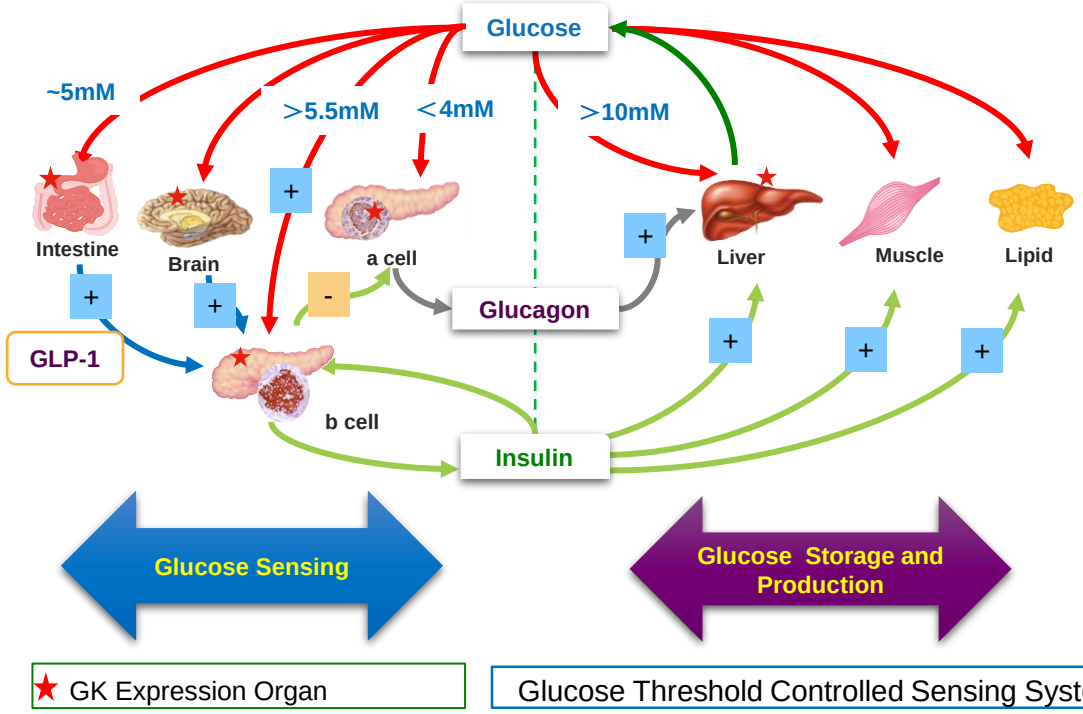
- Deficiency in the ability of glucose to trigger insulin release
- Cells have **lost glucose sensitivity** and early phase insulin release is reduced
- Reduction in glucose sensitivity is the key culprit behind Type 2 Diabetes

Source: Vivian Fonseca, Diabetes Care, 2009, Vol 32, S2; Source: J Merier, R Bonadonna Diabetes Care (2013) 36, S113
[1] Retrospective survey.

Copyright © Hua Medicine 2021

Glucose Regulates whole Body Glucose Homeostasis via glucokinase GK a Glucose Sensor Protein

- Glucose sensitivity is a measure of how well glucose controls Glucose Homeostasis
- Glucokinase GK is a glucose sensor and plays a central role in glucose homeostasis
- **Glucose augments release of glucose controlling hormones, Insulin-GLP1-Glucagon, through glucokinase in GK expressing endocrine organs: pancreas and intestine**
- Glucose regulates glucose storage and hepatic glycogen dynamic via GK/GKRP in the liver



Glucose Homeostasis

Glucose Controls Blood Glucose in a Narrow Range:
4- 6.5 mM

Set Point:
5 mM

Glucokinase GK expression and function are impaired in T2D patients

Data Source: Li Chen，2016《药物进展》modified based on Franz Matschinsky publication

Copyright © Hua Medicine 2021

Glucokinase is a Glucose Sensor in Glucose Homeostasis

Thermostat in a Building

- Primary Messenger: air temperature
- Set Point: 22^{o} Celsius
- Threshold: 21-23^{o} Celsius
- Controller: Thermo Sensor (thermostat)
- 2nd Messenger: Electronic signal
- Operator: Heater, Cooler, Ventilator

Glucose Homeostasis in Human Body

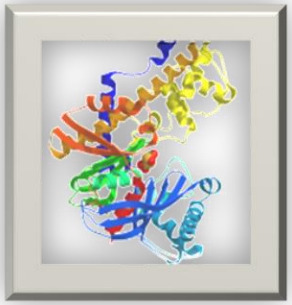
- Primary Messenger: glucose level
- Set Point: 5 mmol/liter[1]
- Threshold: 4-6 mmol/liter[1]
- Controller: Glucokinase in the pancreas and small intestine-Glucose Sensor
- 2nd Messenger: insulin, glucagon, GLP-1
- Operator: Glucose uptake, utilization, storage and production organs

Operation

Cooler

Heater

Ventilator



Operation

Insulin / GLP-1

Glucagon

Liver GK

When the sensor GK malfunctions or is impaired, automatic control is lost
This will cause insulin resistance and reduction of beta cell function that lead to T2D

Source: Franz Matschinsky, Mol. and Cell Biology of Type 2 Diabetes and Its Complications, 1998, vol 4, pp 14-29

[1] A common measure of blood glucose levels is hemoglobin A1c, or HbA1c, which measures average glycated blood glucose levels for the 3 months prior to testing. HbA1c levels for people without diabetes is between 4% and 5.6% (equivalent to 4-5.6 mmol/liter), for people with impaired glucose tolerance (IGT), or pre-diabetics, is between 5.74% and 6.4% (equivalent to 5.74 -6.4 mmol/liter) and for people with diabetes is 6.5% or higher (equivalent to 6.5 mmol/liter or higher).

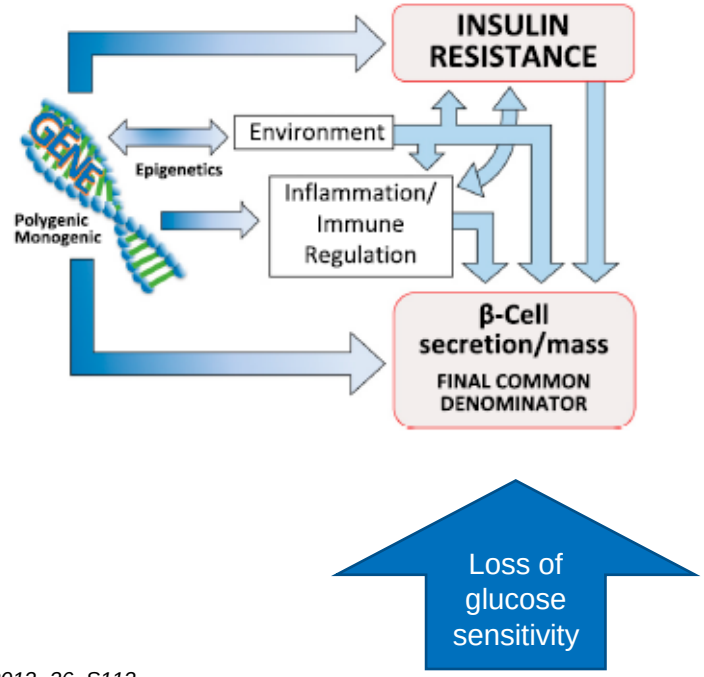
[2] In addition to GK (also referred to as hexokinase type 4), Hexokinase types 1-3 play a role in the glucose homeostasis process. Unlike a properly functioning GK, which is only active at blood glucose levels over 5.5 mmol/liter, hexokinase types 1-3 are active in the presence of even small amounts of glucose in the bloodstream – providing as a bodily survival mechanism needed energy to the brain, muscles and other core bodily functions.

Copyright © Hua Medicine 2021

A New Class of Antidiabetic Medicine – Glucose Sensitizer: Dorzagliatin

- The **root cause of the failure** in managing diabetes is the **inability to address the loss of glucose and insulin sensitivity** in T2D patients
- Dorzagliatin is a **novel glucokinase activator** ("GKA") that improves glucose sensitivity in T2D patients

- Rescue the beta cell mass and hepatic GK function in animal model
- Acts on: glucose sensing in pancreas, liver and intestine
- Regulates glucose dependent insulin, glucagon and GLP-1 release
- Improve 24hr glycemic control, early insulin secretion and beta cell function
- Completed 14 clinical trials including 2 pivotal Phase III trials in China and USA with excellent glycemic control with minimum hypoglycemia risk, accompanied with improve beta cell function and insulin sensitivity
- Dorzagliatin + existing antidiabetics = systematic diabetes care

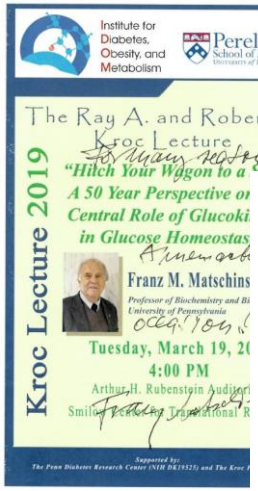


Source: Vivian Fonseca, Diabetes Care, 2009, Vol 32, S2; Source: J Merier, R Bonadonna Diabetes Care 2013, 36, S113
Source: Sharan Edelstein, Diabetes Care 2019, Vol 42, 1742, Source: Stanley Schwartz Diabetes Care 2016, 39(2): 179-186

Copyright © Hua Medicine 2021

Key Recognitions of Glucokinase

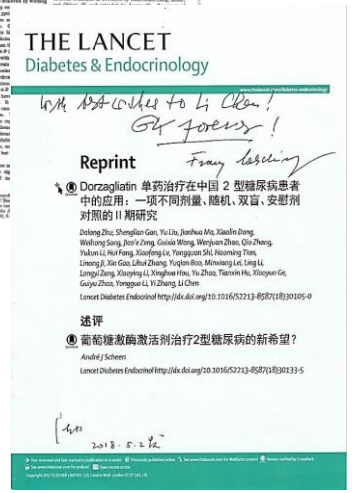
- ✓ Discovered in the 1960s by Dr. Franz Matschinsky, "Godfather of Glucokinase"
- ✓ The 1st GKA Published in Science Magazine in 2003, Roche
- ✓ Dorzagliatin completed POC in 2016, Lancet DE 2018
- ✓ Winner of Rolf Luft Award 2020



Science 2003:

Allosteric Activators of Glucokinase: Potential Role in Diabetes Therapy

"In several rodent models of type 2 diabetes mellitus, GKAs lowered blood glucose levels, improved the results of glucose tolerance tests, and increased hepatic glucose uptake. ***These findings may lead to the development of new drug therapies for diabetes****."*



Lancet 2018: Dailong Zhu and Li Chen

Dorzagliatin Ph II results

A New Hope for Glucokinase Activator for T2D

Rolf Luft Award 2020 awarded to Dr. Franz Matschinsky by Karolinska Institutet

For the discovery that ***glucokinase (GK) is the sensor controlling glucose-stimulated insulin secretion*** *in the pancreatic β-cell. And culminating in the discovery of novel* ***allosteric GK activators*** *currently being assessed in* ***phase III clinical trials****. Speech at the Nobel Forum (Stockholm, Sweden) awards ceremony in the spring of 2021*

Source: Franz Matschinsky et al . Science: Vol 301, Issue 5631, 18 July 2003

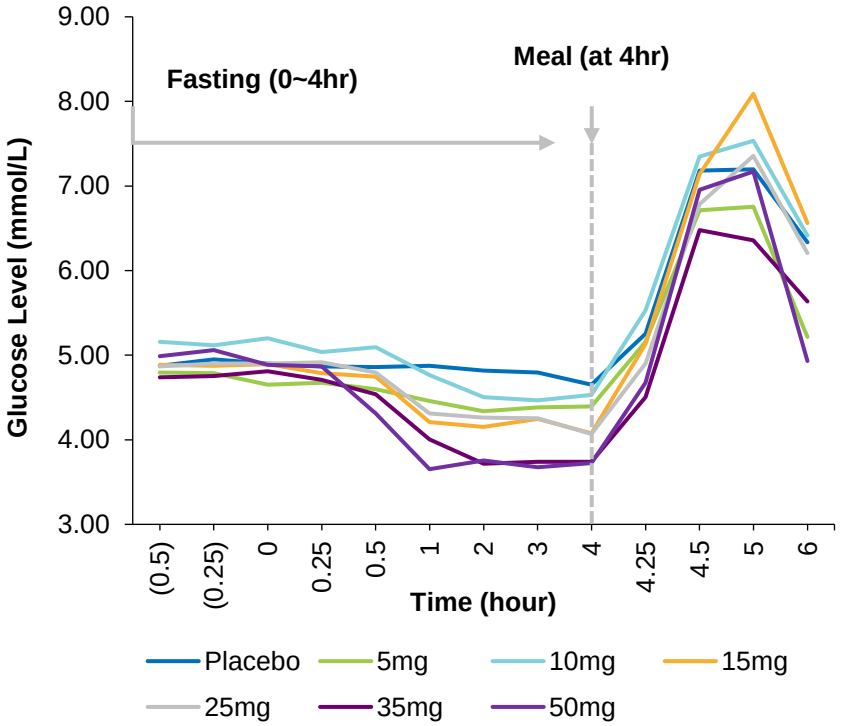
Copyright © Hua Medicine 2021

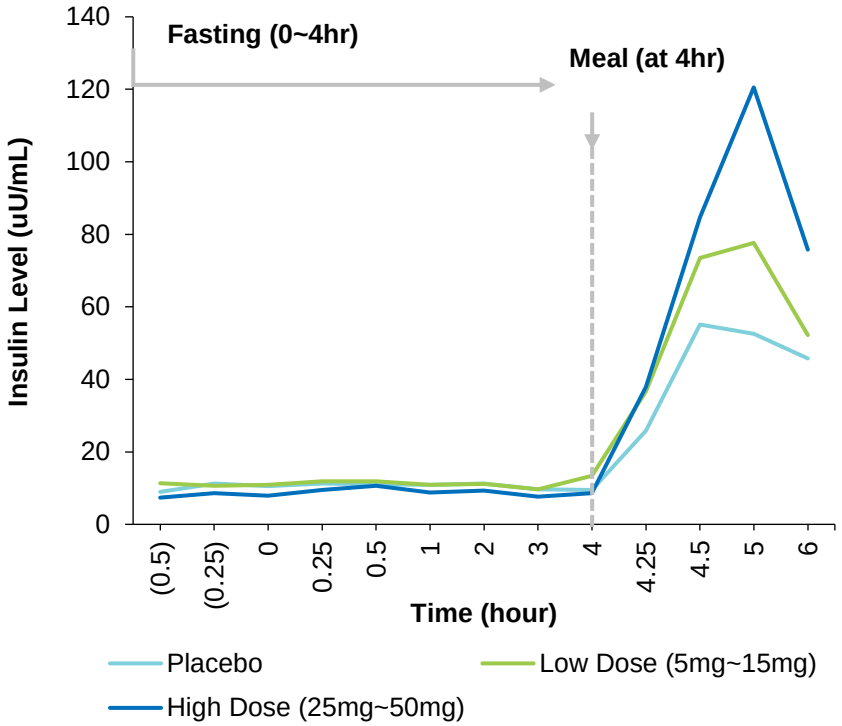
Extensive Supporting Data for Dorzagliatin

Dorzagliatin Modulates GK Glucose Sensor Function as a Glucose Sensitizer

HMM0101

- Phase Ia trial targeted healthy adults in China with a single ascending dose (SAD)
- Patients were fasted over night and having HMS5552 next morning at time hr 0, continued fasting till hr 4 when meal is given



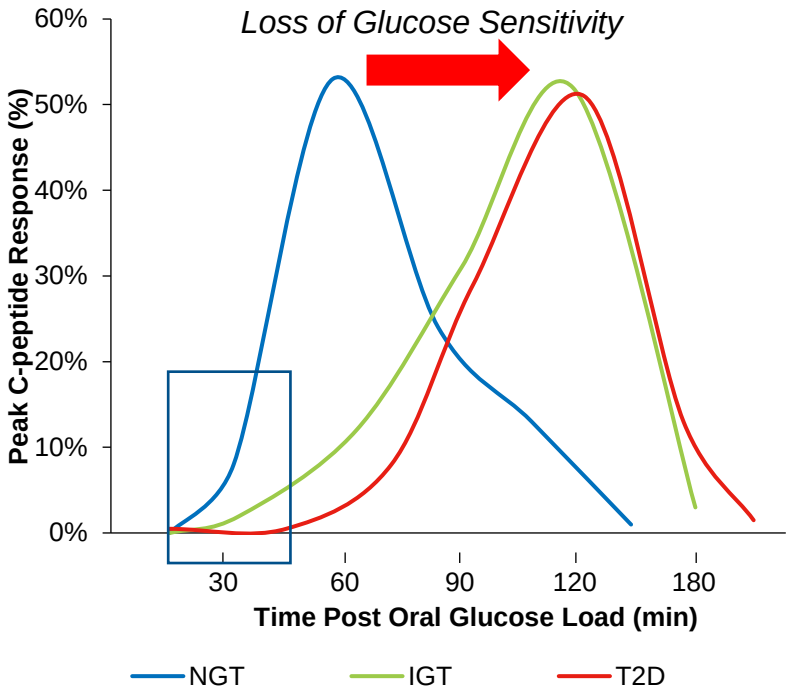


- **Dose dependent reductions in fasting plasma glucose without increases in insulin secretion**
- **Reduce hepatic glucose output by Dorzagliatin**
- **Glucose stimulated Insulin release (GSIR) is enhanced by Dorzagliatin**

Source: H Xu, X Li, Y Zhang, L Chen etal Drug Design, Development and Therapy 2016, 10, 1-8

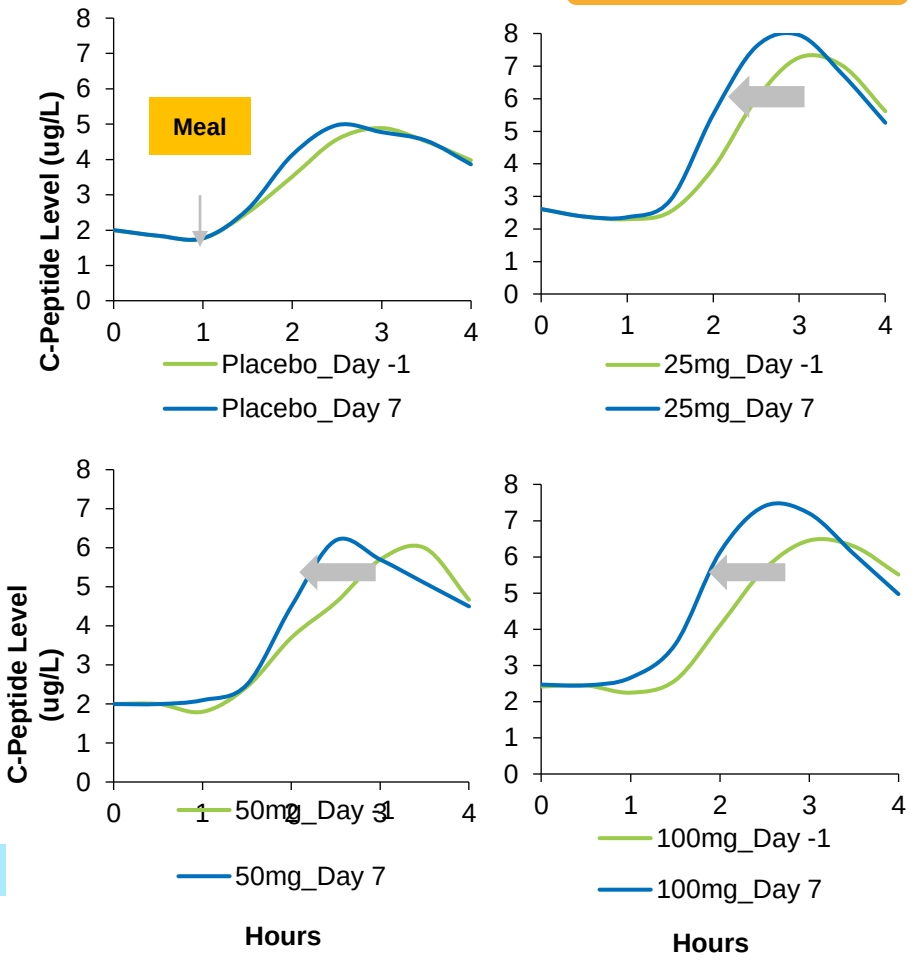
Copyright © Hua Medicine 2021

Dorzagliatin Resets the Thresholds in T2D Patients with Improved Glucose Sensitivity



- **Impaired threshold of GSIR in IGT and T2D patients**

HMM0102



- **Dorzagliatin improves glucose sensitivity in T2D patients**

Source: R.W.Bergstrom J. Clin. Endocrinol. Metab. (1990), 71(6):1447-53
Source: DL Zhu, Y. Zhang, L Chen et al ADA 75th Scientific Session, June 5-9, 2015, Boston

Copyright © Hua Medicine 2021

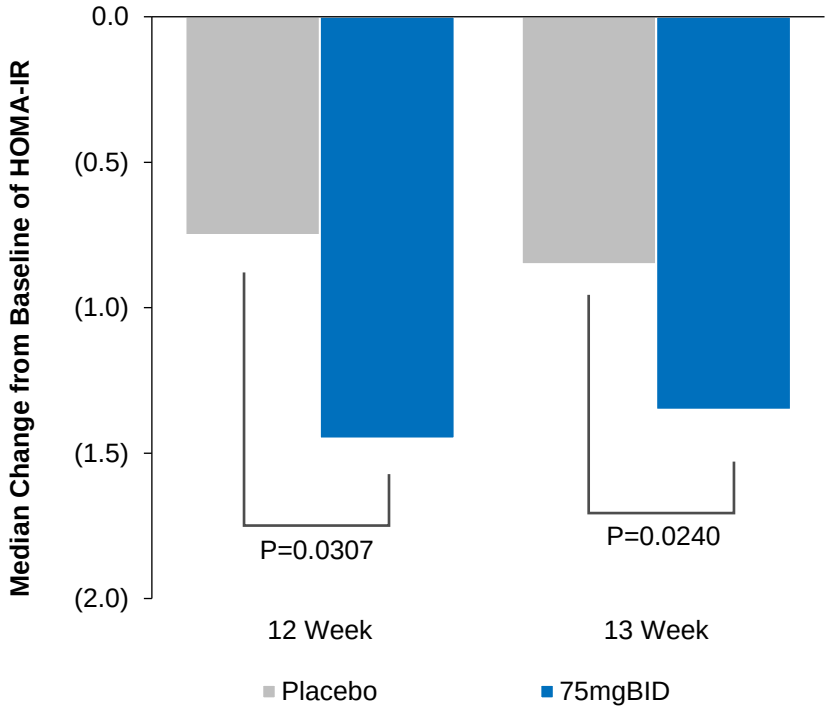
Dorzagliatin Improved β-cell Function and Reduced Insulin Resistance – Phase II Trial

HMM0201

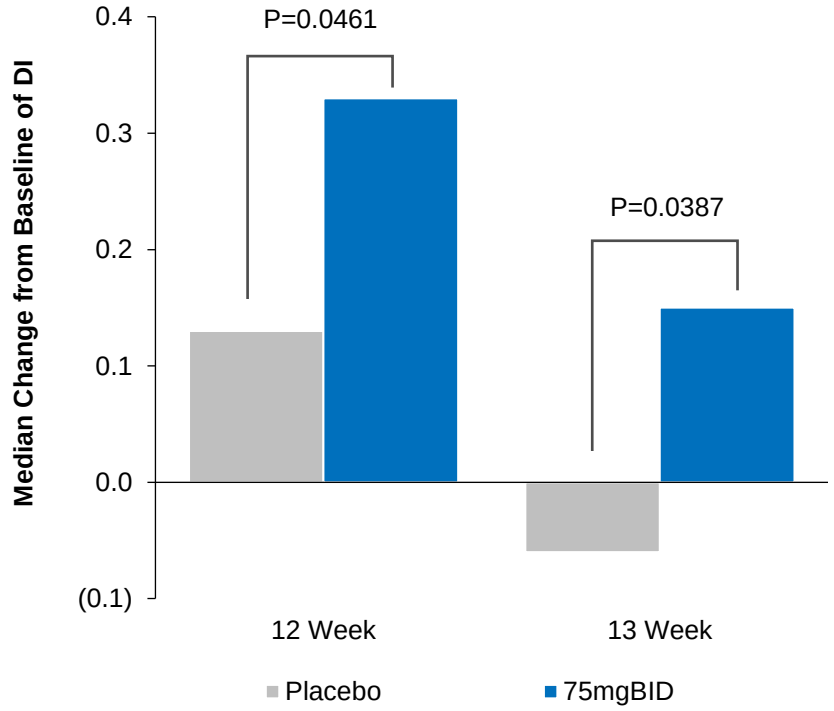
Chinese drug naive Type 2 diabetes patients 3 month treatment

Improves pancreatic β-cell function
Reduces insulin resistance

Reduced Insulin Resistance



Improved β-cell Function



One week after the conclusion of the trial, patients continue to see sustained effect in the HOMA-IR and Disposition Index

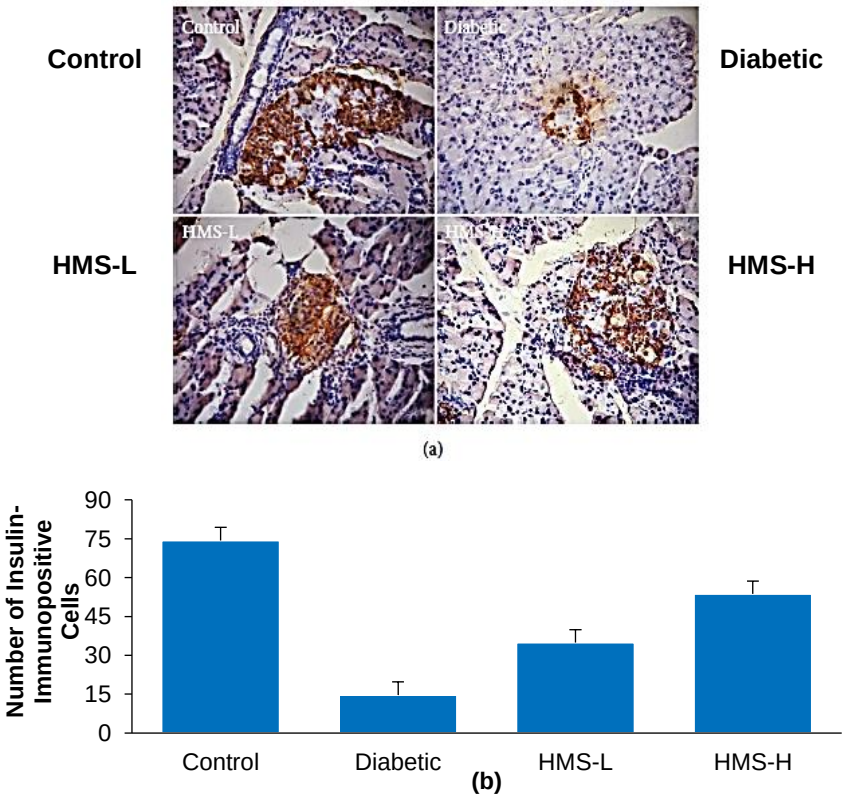
Source: Dalong Zhu Lancet Diabetes and Endocrinology 2018 May 4
Note: HOMA-IR represents homeostatic model assessment – insulin resistance, while DI measures β-cell function

Copyright © Hua Medicine 2021

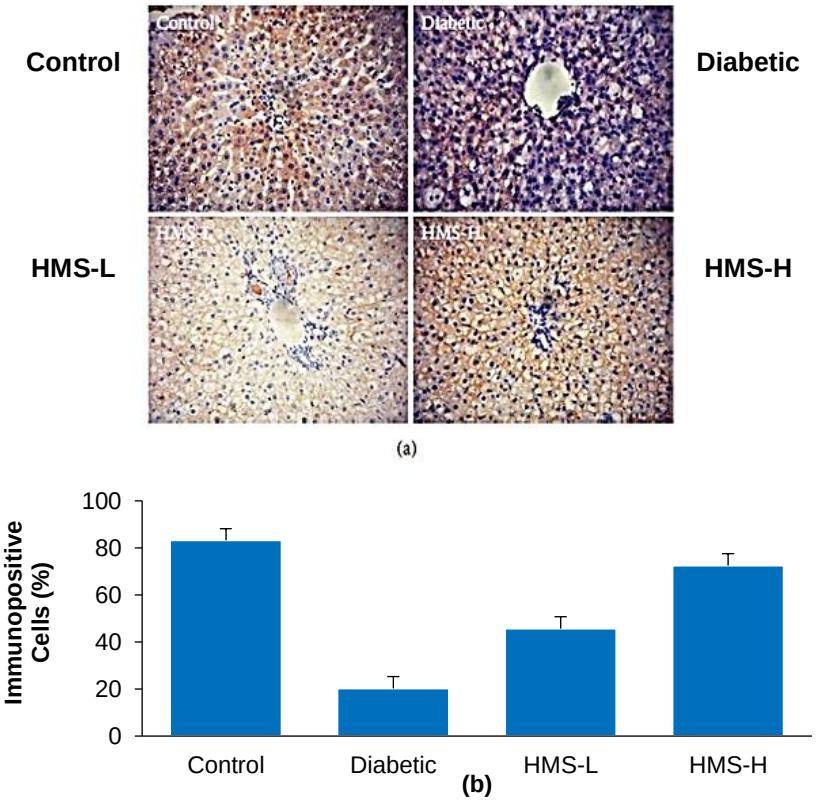
Dorzagliatin Improved β-cell Mass and Increased Hepatic GK Expression in Diabetes Rats

- Hua conducted several non-clinical studies in rats, mice and dogs. It showed that Dorzagliatin rescued glucose sensor function in pancreas and liver, and it improved glucose and insulin sensitivity
- Study results showed that number of insulin-immunopositive cells in pancreas and GK-immunopositive cells in liver increased significantly after the administration of low-dose and high-dose Dorzagliatin

Type 2 Diabetes Rat Pancreas



Type 2 Diabetes Rat Liver

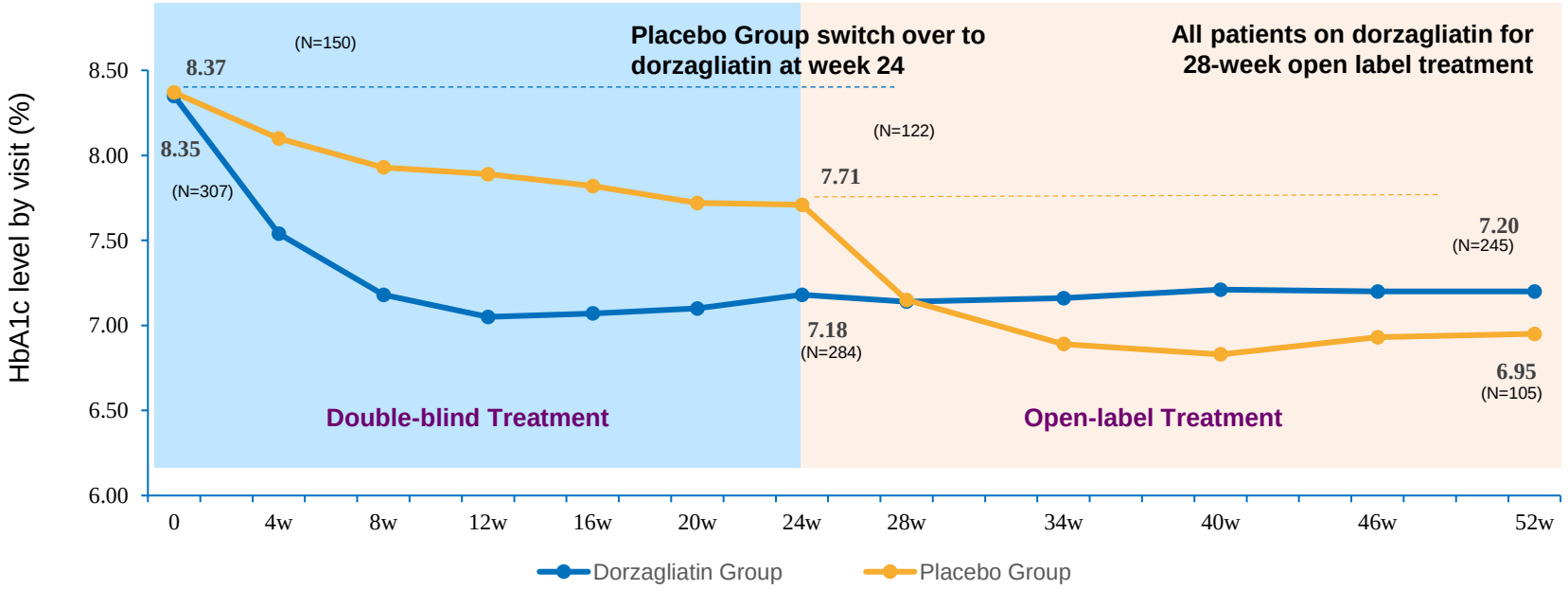


Source: R Wang, H Liu, L Chen, Y Duan, Q Chen, S Xi J. Diabetes Res 2017

Copyright © Hua Medicine 2021

SEED Phase III: Effective & Sustained HbA1c Reduction with monotherapy in drug naïve T2D patients

Change of HbA1c during the 52-week treatment period



Efficacy Endpoints:

- Met primary efficacy endpoint at 24 weeks
- 45.4% of patients in treatment group achieved target HbA1c below 7% at 24 weeks vs. 21.5% of placebo
- Sustained efficacy at 52 weeks

Safety endpoints:

- Dorzagliatin is well tolerated and safe during the 52 week study
- No drug related SAE and severe hypoglycemia
- Hypoglycemia incidence rate (glucose <3.0 mmol/L) is less than 1 percent

Note: Numbers presented in the Figure were computed from descriptive statistical analysis.
**p<0.001 compared with baseline at 52 week.*

Copyright © Hua Medicine 2021

SEED Benchmark 52-Week Data

Study	Drug	MOA	Baseline HbA1c	HbA1c reduction at		HbA1c rebound from 24/26 weeks
				24/26 weeks	52 weeks	
SEED	Dorzagliatin 75mg BID	GKA	8.4	-1.15	-1.11	0.04
Pioneer-4	Oral semaglutide 14mg QD	GLP-1	8.0	-1.3	-1.2	0.1
	Liraglutide 1.8mg QD	GLP-1	8.0	-1.1	-0.9	0.2
Pioneer-2	Empaglifozin 25mg QD	SGLT-2	8.1	-0.9	-0.8	0.1
Award-3	Dulaglutide 1.5mg QD	GLP-1	7.6	-0.78	-0.7	0.08
	Dulaglutide 0.75mg QD	GLP-1	7.6	-0.71	-0.55	0.16
	Metformin	Biguanide	7.6	-0.56	-0.51	0.05
Pioneer-3	Sitagliptin 100mg QD	DPP-4	8.3	-0.8	-0.5	0.3

Figure : Summary of selected anti-diabetes therapy HbA1c reductions from baseline at week 24/26 and week 52

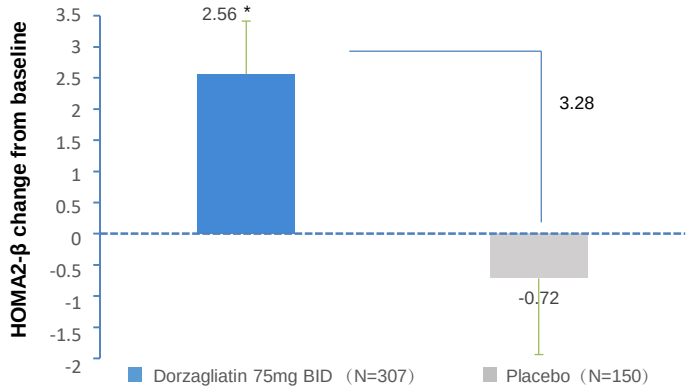
Copyright © Hua Medicine 2021

SEED Phase III 24-WEEK Secondary Results + Safety Results — Presented at ADA

Secondary Results

- Reduction of ***2hPPG*** was observed in Dorzagliatin 75mg BID than placebo (-2.83 vs -0.50mmol/L, p<0.001)
- Significant ***Beta-cell Function Improvement*** (HOMA2-β)

HOMA2-β Change from Baseline to week 24 (FAS)



Data are least squares means. *p<0.05 vs placebo.

Safety Results

During the period of 24 weeks double blinded treatment, dorzagliatin (75 mg, BID) was well tolerated and had a good safety profile

- The incidence of AE was similar between the treatment and placebo groups
- Majority of the AEs were mild in severity
- No death, no drug-related SAE
- No clinically significant abnormal trends or findings in safety lab tests, ECG, physical examination, and vital signs
- Hypoglycemia occurred in one of 310 patients (0.3%) in dorzagliatin group. No severe hypoglycemia was reported

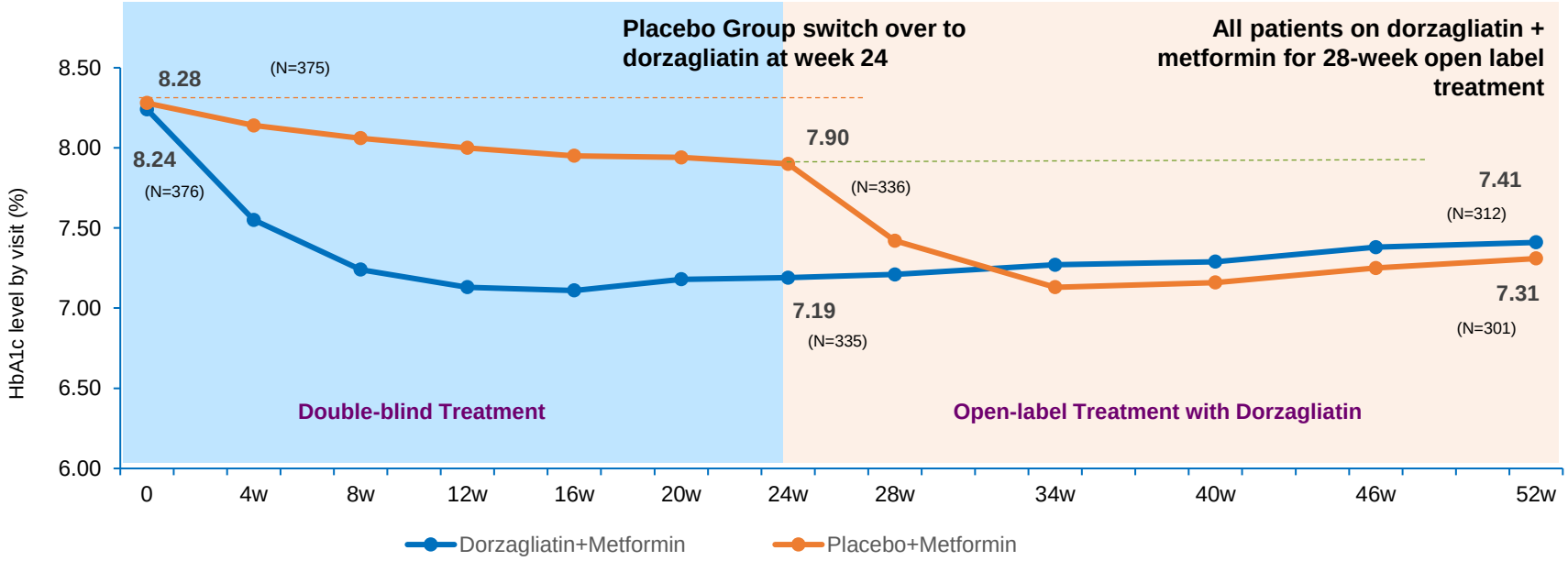
Supports first-line treatment of new-onset Type 2 Diabetes（ADA）

- Quick response, 4 weeks hypoglycemic, 12 weeks β function
- Sustained efficacy
- Address both symptoms and root causes
- Good safety
- Low hypoglycemia risk
- Keep blood glucose in range

Copyright © Hua Medicine 2021

DAWN Phase III: Dorzagliatin as a preferred add-on to Metformin tolerated T2D

Change of HbA1c during the 52-week treatment period



Efficacy Endpoints:

- Met primary efficacy endpoint at 24 weeks
- 44.4% of patients in dorzagliatin treated group achieved target HbA1c below 7% at 24 weeks vs. 10.7% of placebo
- Sustained efficacy at 52 weeks

Safety endpoints

- Dorzagliatin is well tolerated and safe during the 52 week study
- No drug related SAE and severe hypoglycemia
- Hypoglycemia incidence rate (glucose <3.0 mmol/L) is less than 1 percent

Note: Numbers presented in the Figure were computed from descriptive statistical analysis.
**p<0.001 compared with baseline at 52 week.*

Copyright © Hua Medicine 2021

DAWN 24/26 Week Benchmark Data
Combination with metformin

	Drug	MOA	Durations	Randomized number	Dosage(+metformin)	HbA1c Baseline(%)	HbA1c Change(%)	Reach HbA1c<7%
Oral	Dorzagliatin	GKA	24 week	766	75mg BID	8.25	-1.02	44.4%
					Placebo	8.29	-0.36	10.7%
Oral	Dapagliflozin	SGLT-2 Inhibitor	24 week	546	5mg QD	8.20	-0.70	37.5%
					10mg QD	7.90	-0.84	40.6%
					Placebo	8.10	-0.30	25.9%
Oral	Empagliflozin	SGLT-2 Inhibitor	24 week	638	10mg QD	7.94	-0.70	37.7%
					25mg QD	7.86	-0.77	38.7%
					Placebo	7.90	-0.13	12.5%
Oral	Sitagliptin	DPP-4 Inhibitor	24 week	701	100mg QD	7.96	-0.67	47.0%
					Placebo	8.03	-0.02	18.3%
Injection	Liraglutide	GLP-1 RAs	26 week	1091	0.6mg QD	8.40	-0.70	28.0%
					1.2mg QD	8.30	-1.00	35.3%
					1.8mg QD	8.40	-1.00	42.4%
					Glimepiride 4mg QD	8.40	-1.00	36.3%
					Placebo	8.40	0.10	10.8%

Figure : Summary of selected HbA1c change from baseline after 24/26-week metformin combination treatment

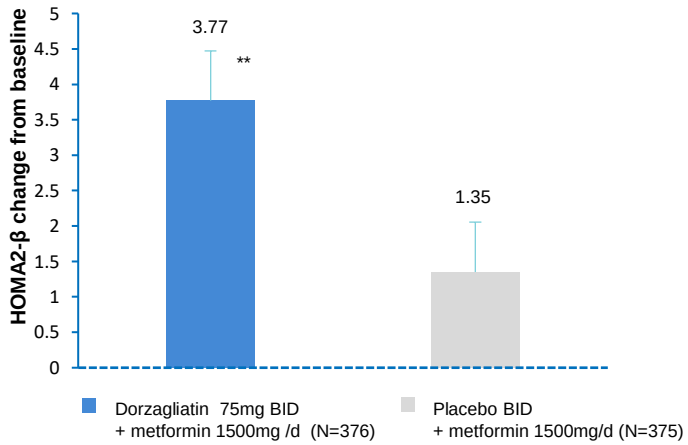
Copyright © Hua Medicine 2021

DAWN/ HMM0302 Phase III 24-WEEK Additional Data — Presented at CDS November 2020

Secondary Results

- Reduction of ***2hPPG*** was observed in Dorzagliatin 75mg BID+ metformin 1500mg/d than Placebo BID + metformin 1500mg/d (-5.45 vs -2.98 mmol/L, p<0.0001)
- Significant ***Beta-cell Function Improvement*** (HOMA2-β)

HOMA2-β Change from Baseline to week 24 (FAS)



Data are least squares means. **p<0.01 vs placebo.

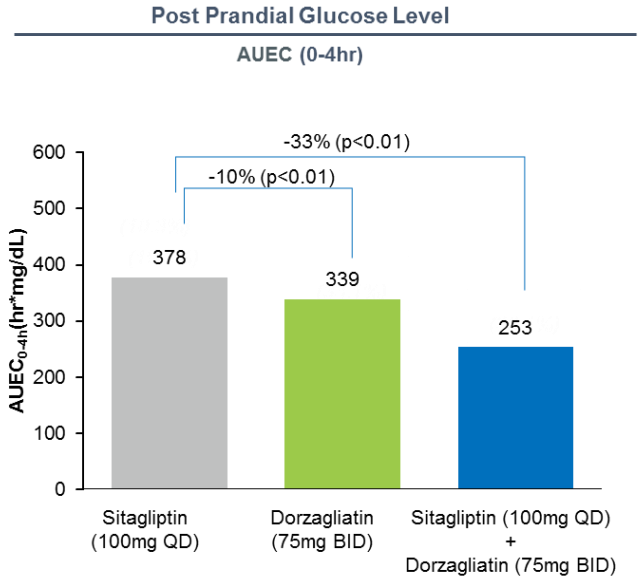
Characteristics of 24-week data

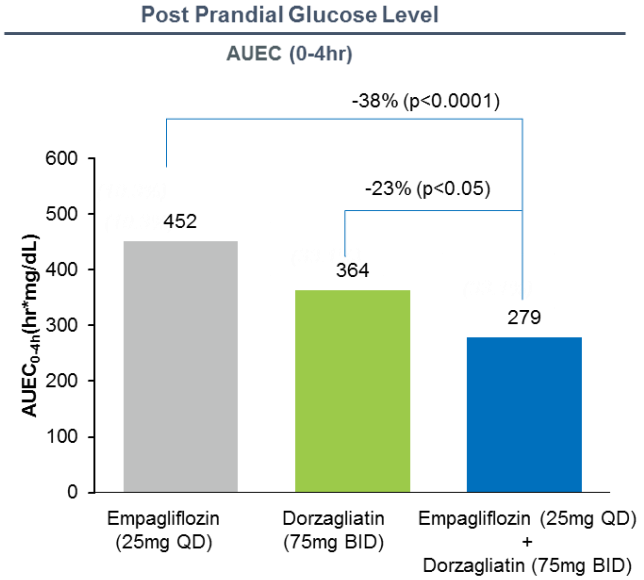
- Fast on-set of action (effective HbA1c reduction in 4 weeks)
- Significant improvement of β-cell function and reduction of insulin resistance in treatment group as compared to the placebo group
- Significant reduction of 2-hour post-prandial glucose reduction was observed in treatment group as compared to the placebo group
- Good safety profile and tolerance of dorzagliatin with limited hypoglycemia (Less than 1% observed during 24-week treatment)
- Sustained efficacy over 24 weeks
- Good response rate

Copyright © Hua Medicine 2021

Dorzagliatin Has Demonstrated Successful Combination Potential with other Global Top Oral Anti-Diabetic Drugs

- No drug-drug interaction observed in 3 Phase I trials in USA for each of metformin, sitagliptin (DPP-4 inhibitor) and empagliflozin (SGLT-2 inhibitor)
- Synergies also demonstrated





DPP-4 inhibitor:

✓ US$ 4B global sales in 2019

SGLT-2 inhibitor:

✓ Fastest growing among OAD with US$ 6B global sales in 2019 and ~24% yoy growth

Note: AUC represents area under the curve, while AUEC represents area under the effect curve.

Copyright © Hua Medicine 2021

Positive Results of HMM0110 – Jan 2020

Jan 2020: Positive Results of HMM0110 Supports the Potential of Dorzagliatin in T2D Patients with Moderate, Severe and End Stage Chronic Kidney Disease (i.e. stages 3-5 of CKD)

Study:

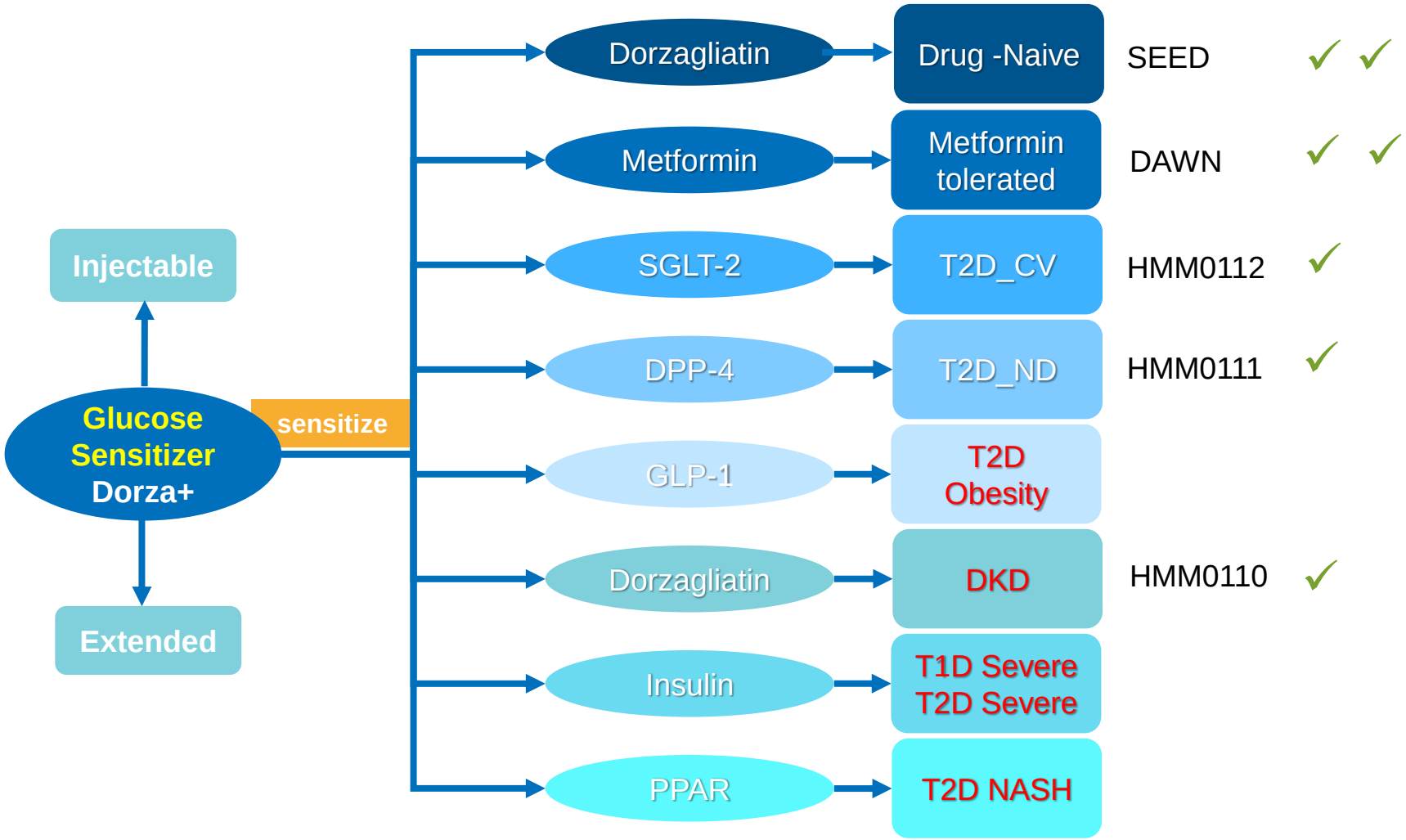
HMM0110 was conducted in China to evaluate whether dorzagliatin can be readily used in Type 2 diabetes (T2D) patients with impaired renal function.

Conclusion:

- In subjects with end stage renal disease and are not on dialysis, **the study indicated no significant impact on PK properties subjects exposed to dorzagliatin.**
- This result **supports dorzagliatin as a promising solution and potential supplementary option for T2D patients with moderate, severe and end stage chronic kidney disease** (i.e., stages 3-5 of CKD) which can **provide satisfactory blood glucose control safely and without dose adjustment**.
- Most of current oral antidiabetic drugs are not readily suitable for patients with renal impairment, especially at moderate, severe and end stages, as current oral treatments either require dose adjustment (e.g., metformin and the top-selling DPP-4 inhibitors) or are contraindicated (e.g., SGLT-2 inhibitors).
- Stage 3-5 CKD patients of T2D patients in China is about 21.9%

Copyright © Hua Medicine 2021

New FIC Product, New Medication, New Opportunity



Fix Sensor, Repair Homeostasis and Treat Root Cause of Diseases

Copyright © Hua Medicine 2021

Commercializing Dorzagliatin

Bayer is the Best Partner for Hua Medicine in China

- ✓ **Established Leadership in Diabetes Care** in China for **20+ years**
  - Leading oral anti-diabetic drug in China 1995-2019: Glucobay® cumulative treated > 30 million patients
  - Industry leading market coverage: Glucobay® listed in 13k+ hospitals / CHCs and 10k+ retail pharmacies
  - RMB 40 billion Glucobay® cumulative net sales reported from 2009 - 2019
- ✓ **Full commitment and dedication of Bayer China** to achieve top-selling results for dorzagliatin's launch - no conflicts
  - Potential synergies in the future with Bayer's WaveForm CGM device for studies relating to optimizing time-in-range (TIR)

- Novel first-in-class drug
- Aspiration to cure diabetes

- Leader in diabetes treatment in China
- Integrated diabetes solutions

Collaborate to Cure

- Hua Medicine: Clinical development, registration, product supply, and distribution
- Bayer: marketing, promotion and medical education activities
- Upfront payment: RMB 300 million
- Milestone payments: Up to RMB 4.18 billion
- Bayer: exclusive rights to commercialize product in China, tiered service fee based on net sales

Copyright © Hua Medicine 2021

Bayer / Hua Medicine *Collaboration to Cure* has launched in China — October 2020

Hua Medicine and Bayer team build strategic consensus to global diabetes care between 21 and 22 October, 2020

Copyright © Hua Medicine 2021

Hua Medicine is Receiving Nationwide Recognition

Hua Medicine selected as only Healthcare Company representative to Pudong Celebration hosted by President Xi Jinping in 12 November, 2020

Copyright © Hua Medicine 2021

World-renowned Advisors and Influential Key Opinion Leaders

Advisors

Franz Matschinsky, M.D.

- Professor of biochemistry and biophysics at the University of Pennsylvania, Perelman School of Medicine
- Founded Penn Diabetes Research Center of the University of Pennsylvania
- Founder of the Islet Cell Biology Core in the University of Pennsylvania
- Received Banting Award (1995), Rolf Luft Award (2020)
- Formulated the glucokinase glucose sensor concept
- *"Glucokinase is a glucose sensor, diabetes gene and drug target"*

Ralph A. DeFronzo, M.D.

- Professor and Division Chief of Diabetes Division at the University of Texas Health Science Center
- Deputy Director of Texas Diabetes Institute
- Led the U.S. development of metformin, and FDA approval in 1995
- Discovered a new approach to diabetes treatment that targets glucose reabsorption in the kidneys, which led to the development and approval of SGLT-2
- Received several prestigious awards, including the Lilly Award (1987) by the American Diabetes Association, Banting Lectureship Award (1988) by the Canadian Diabetes Association, Novartis Award (2003), ADA's Albert Renold Award (2002), the ADA's Banting Award (2008), and the Harold Hamm International Prize (2018)
- Published over 800 articles in peer-reviewed medical journals

Chinese KOLs

Wenying Yang, M.D.

- Director of Endocrinology, Director of Department of Internal Medicine, Vice Chairman of Ethics Committee at China-Japan Friendship Hospital
- Ex President, Chinese Diabetes Society
- Published articles in numerous prestigious journals such as New England Journal of Medicine, Lancet Diabetes and Endocrinology

Dalong Zhu, M.D.

- Director of Endocrinology, Nanjing Drum Tower Hospital
- Current President, Chinese Diabetes Society
- Published articles in numerous prestigious journals such as the Lancet Diabetes and Endocrinology , Diabetes

Xiaoying Li, MD, Ph.D.

- Director of Endocrinology, Zhongshan Hospital
- Vice President, Chinese Diabetes Society
- Published articles in numerous prestigious journals such as the Lancet Diabetes and Endocrinology , Cell Metabolism

Copyright © Hua Medicine 2021

Dorzagliatin presented at multiple sessions at 2020 CDS Scientific Meeting

Dr. Li Chen, CEO and CSO of Hua Medicine, presenting GKA MOA

Professor Zhu Dalong, Chairman of CDS, presenting at 2020 CDS

Dr. Yang Wenying, ex-Chairwoman of CDS, presenting at the 2020 CDS

Dr. Li Xiaoying, Vice President of CDS, presenting at the 2020 CDS

Copyright © Hua Medicine 2021

International Platform of Hua Medicine : ADA TV Program

In the 2019 ADA Conference, the special TV program "Hua Medicine Leads Global Glucokinase R&D" runs through the annual conference ADA TV broadcast schedule

2019 ADA TV Four Steps

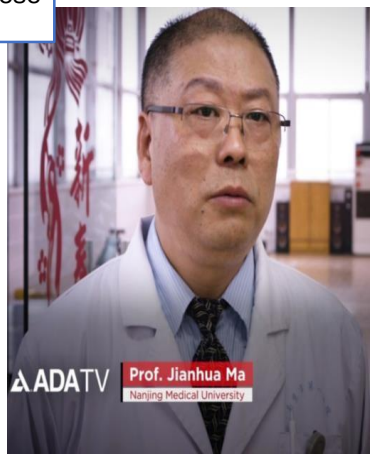
- Glucokinase and glucose homeostasis
- Development of Glucokinase Activator
- Patients in clinical research first
- Global teaming up to end diabetes

The Godfather of Glucokinase

Ex President, Chinese Diabetes Society

Current President, Chinese Diabetes Society

Vice President, Chinese Diabetes Society



Copyright © Hua Medicine 2021

Hua Management Team

Highly Experienced R&D Team with Extensive China and Global Pharmaceutical Experience

Founder & CEO

Li Chen, Ph.D., *Founder & Board Director*

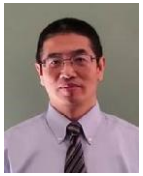
- CSO and Founding Director of Roche R&D Center (China), responsible for development of China's drug discovery strategy, creation of discovery portfolio and management of operations
- Former head of HTC technology at Roche
- Adjunct professor at Tongji University, Ph D advisor
- Over 90 publications and patents in basic research and medical sciences

George Lin
EVP, CFO
Bank of America Merrill Lynch · Credit Suisse

Yi Zhang, Ph.D., MD
SVP, Clinical R&D
Roche

Daniel Du, Ph.D., MD
SVP, RCM
gsk · Pfizer

Jin She, Ph.D.
VP, Chemistry CMC
Roche · MSD



FuxingTang, Ph.D.
VP, CTO, Chemistry CMC
Forest Laboratories, Inc. · Allergan

Yilei Fu, BS, MBA
VP, Quality Assurance
J&J · Boehringer Ingelheim

Wenjie Xu, BS, MBA
VP, Commercial Strategy and Marketing
AstraZeneca · Lilly

Copyright © Hua Medicine 2021

A Blue Chip Board

Chairman
Robert Nelsen

Li Chen

Lian Yong Chen

FIL Capital Management (Hong Kong)

George Lin

Walter Kwauk

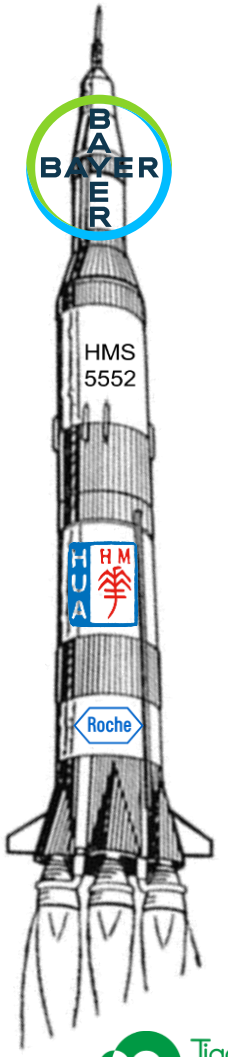
William Keller

Junling Liu

Alec Tsui

Copyright © Hua Medicine 2021

Advancing Global Diabetes Care Forward from China!



Massive unmet medical need in global T2D

- **1 in 10** are T2D patients
- No drug is focused on addressing **underlying cause** of T2D, nor **prevents or delays** complications
- Current approved therapy provide unsatisfactory treatment and control rates

Hua Medicine's dorzagliatin (HMS5552)

- Global **first-in-class** oral anti-diabetic drug: **Glucose Sensitizer**
- Novel mode of action focused on **restoring glucose Sensing** – the underlying cause of T2D
- Profiled for **combination with other approved OADs** that offer systematic diabetes care
- Well tolerated and good safety profile
- Collaborative Innovation: **Leading China diabetes partner** selected
- Launch first in China, global markets next

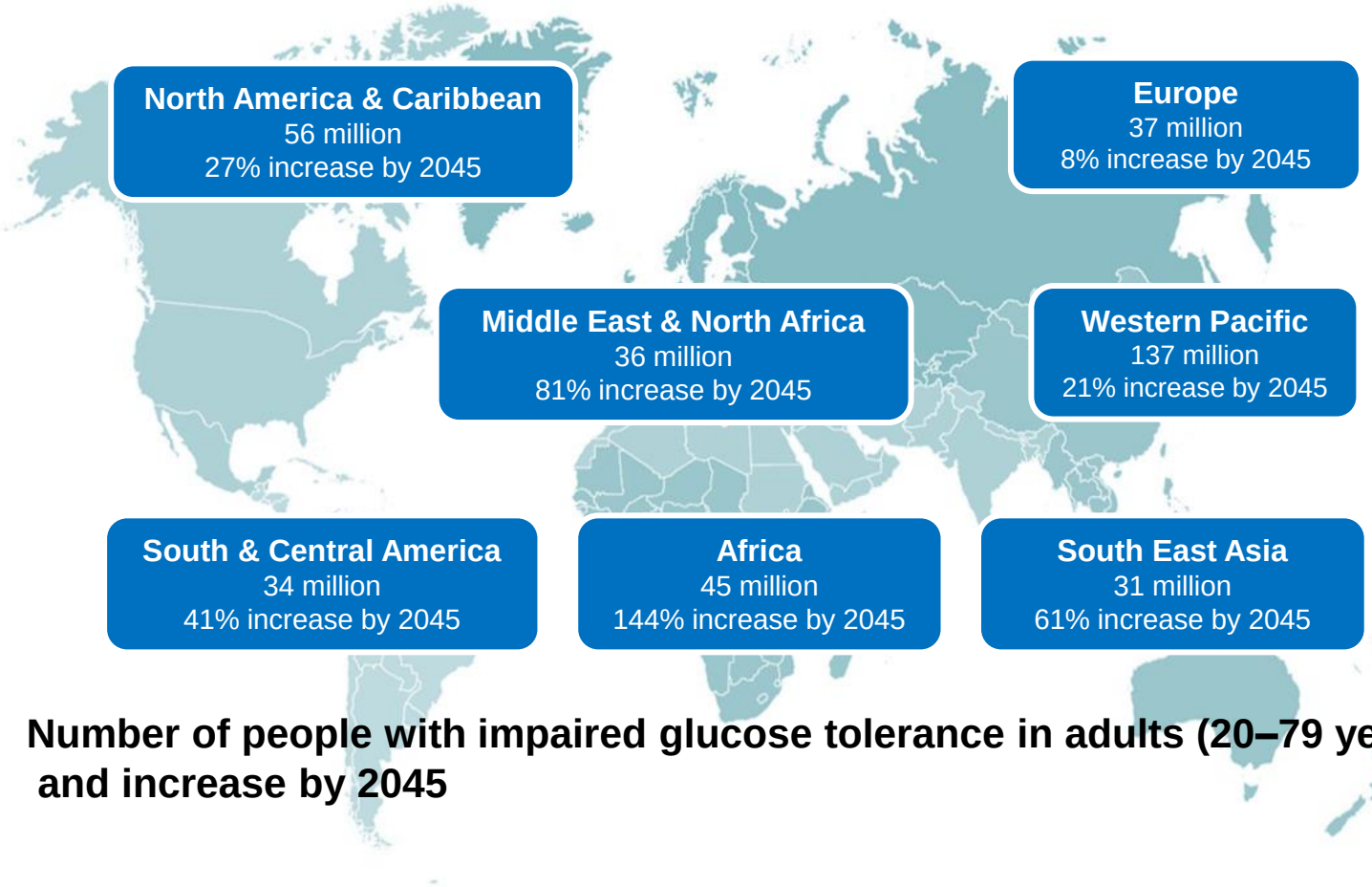
药明康德 WuXi AppTec
Tigermed 泰格医药
DESANO 迪赛诺
COVANCE

Copyright © Hua Medicine 2021

Appendix

Large Unmet Needs within Diabetes

- '**Prediabetes**' is a term increasingly used for people with IGT. It signifies a risk of the future development of T2D and diabetes-related complications.
- ~374 million people live with IGT. This is predicted to rise to 548 million by 2045.



Number of people with impaired glucose tolerance in adults (20–79 years) and increase by 2045

Source: IDF DIABETES ATLAS Ninth edition 2019

Copyright © Hua Medicine 2021

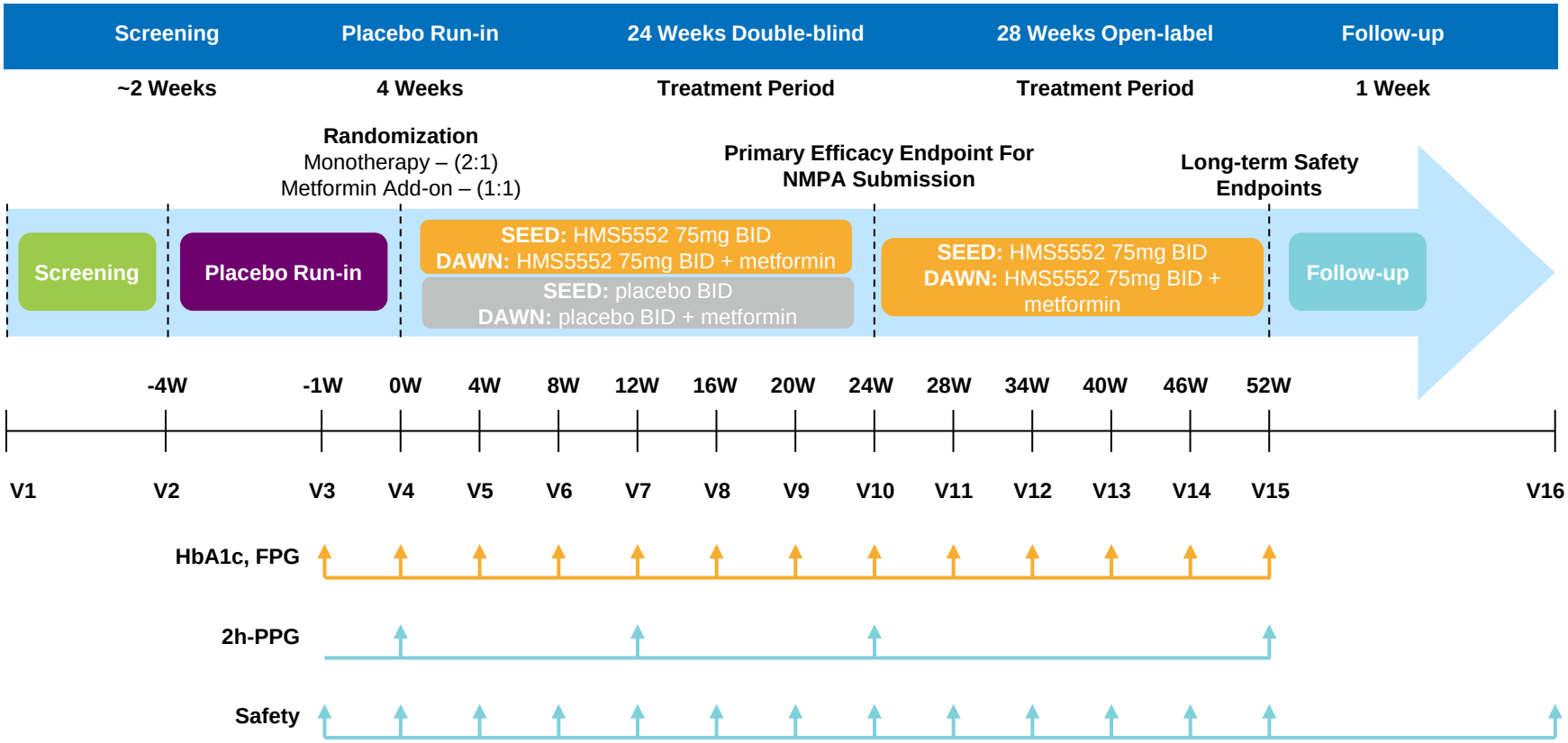
Invention Patents Obtained by Hua Medicine

Copyright © Hua Medicine 2021

Phase III Trials: SEED/ DAWN Study Design

Study Design for:

- SEED: 52-week completed
  Dorzagliatin Mono-therapy Trial for Drug Naïve T2D Patients (463 Patients) ✓
- DAWN: 52-week completed
  Dorzagliatin Metformin Add-on Therapy Trial for Metformin Users (767 Patients) ✓



Primary endpoint of HbA1c reduction of 0.4% over placebo, p-value < 0.05

ACHIEVED FOR BOTH SEED AND DAWN STUDIES AT 24-WEEK

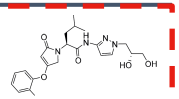
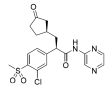
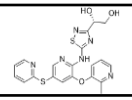
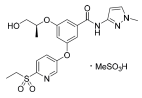
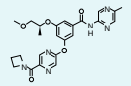
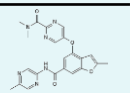
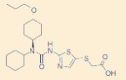
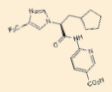
Copyright © Hua Medicine 2021

Not all GKA Candidates are Designed as Glucose Sensitizer

- **Dorzagliatin targets GK both in pancreas and liver**
- **Dual acting with full activation properties fit the profiles of a therapeutic agent to modulate glucose homeostasis in Type 2 diabetes patients**

Glucokinase Activator

- **Dual Acting on GK in Pancreas and Liver**
- **Selective Acting on GK in Liver**

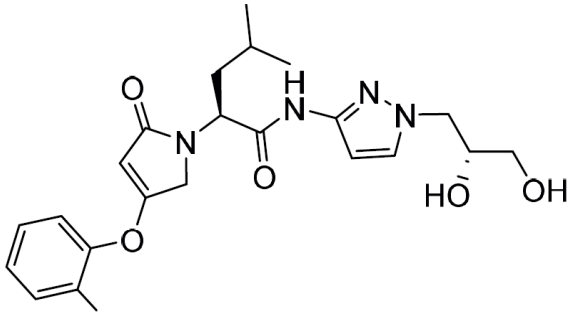
Profile	Compound	Developer	Clinical Stage	Commentary	Chemical Structure
Full GKA (β > 1)	Dorzagliatin	HUA HM	Phase III	Only GKA to have advanced to Phase III	
	RO4389620	Roche		Generated large amounts of unexpected human metabolites	
	AMG 151 / ARRY-403	AMGEN / ARRAY BIOPHARMA		High incidences of hypoglycemia and elevated serum triglycerides	
	MK-0941	MERCK		Lack of sustained glycemic efficacy, increased incidence of hypoglycemia and elevations in triglycerides and blood pressure	
Partial GKA (β < 1)	AZD-1656	AstraZeneca		Reduced Vmax of GK and demonstrated limited efficacies in Type 2 diabetics	
	PF-04937319	Pfizer / PegBio	Phase II completed in US / IND approved in China		
Liver Selective GKA	TTP399	VTV Therapeutics		Sustained efficacy and safety through 24 week; less efficacious than sitagliptin	
	PF-04991532	Pfizer		Reduced Vmax of GK and demonstrated limited efficacies in Type 2 diabetics	

- **Only Hua has advanced GKA to Phase III clinical trials**

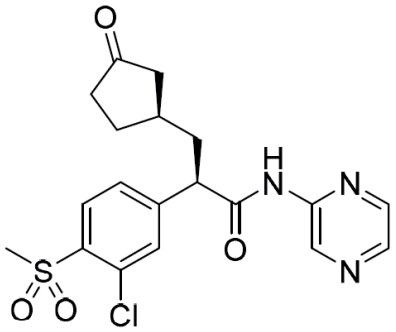
Copyright © Hua Medicine 2021

Dorzagliatin Chemical Structure is Unique To Function as Glucose Sensitizer

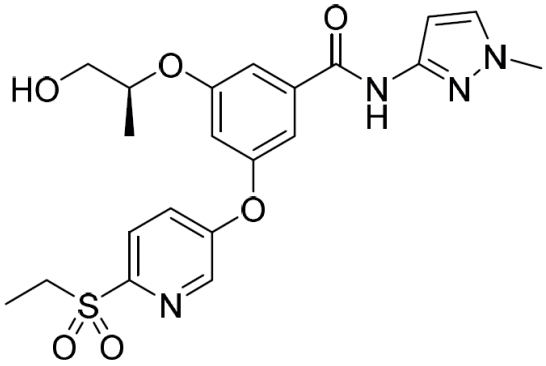
Hua Dorzagliatin



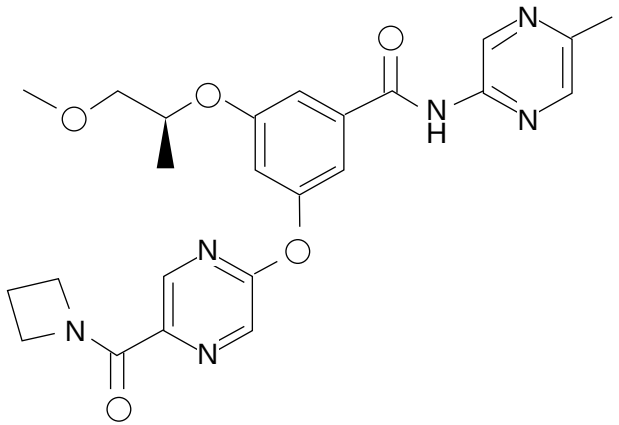
Roche RO4389620



Merck MK-0941

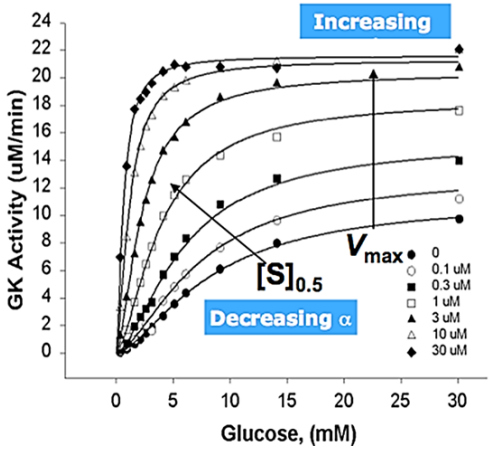


AstraZeneca AZD-1656



Copyright © Hua Medicine 2021

Enzyme Kinetics Profile Defines the Sensitizer Function



$$K_p = \frac{S^n \times V_{max}}{K_s \times \frac{1 + A/K_a}{1 + \frac{\beta \times A}{\alpha \times K_a}} + S^n \times \frac{1 + A/(\alpha \times K_a)}{1 + \frac{\beta \times A}{\alpha \times K_a}}}$$

Influence of GKAs on key parameters of GK enzymatic kinetics.

Variable	Dorzagliatin	Piragliatin	MK-0941	PF-04937319	AZD1656
Vmax-10/Vmax-0	1.464	1.834	1.440	1.014	1.055
Vmax-3.33/Vmax-0	1.448	1.783	1.423	1.004	1.031
β	1.4033	1.7400	1.2267	0.9967	0.9700
α	0.0071	0.0050	0.0055	0.0160	0.0074
S0.5-10/S0.5-0	8.68%	18.21%	4.63%	16.58%	7.14%
S0.5-3.33/S0.5-0	14.64%	32.59%	5.98%	25.74%	10.30%
nH-0	1.833	1.777	1.860	1.870	1.778
nH-1.11	1.677	1.707	1.368	1.747	1.583
nH-3.33	1.563	1.590	1.238	1.717	1.488
nH-10	1.493	1.503	1.208	1.573	1.315
ΔnH (10-0)	-18.55%	-15.38%	-35.08%	-15.86%	-26.02%
ΔnH (3.33-0)	-14.73%	-10.51%	-33.47%	-8.20%	-16.32%
Ka (uM)	15.12	105.93	2.49	17.43	6.23
Ks (mM)	38.69	48.07	53.37	39.87	51.00

Conclusion

- The increase of GK Vmax with a GKA is desirable for developing a therapeutic agent for the treatment of patients with type 2 diabetes who suffered from a down regulation of GK expression.
- The results suggest that large changes of nH over 20% at 10 uM GKA concentration compared with drug free state may lead to clinical hypoglycemia as an indicator for setting the GSIR threshold below 4 mM glucose.

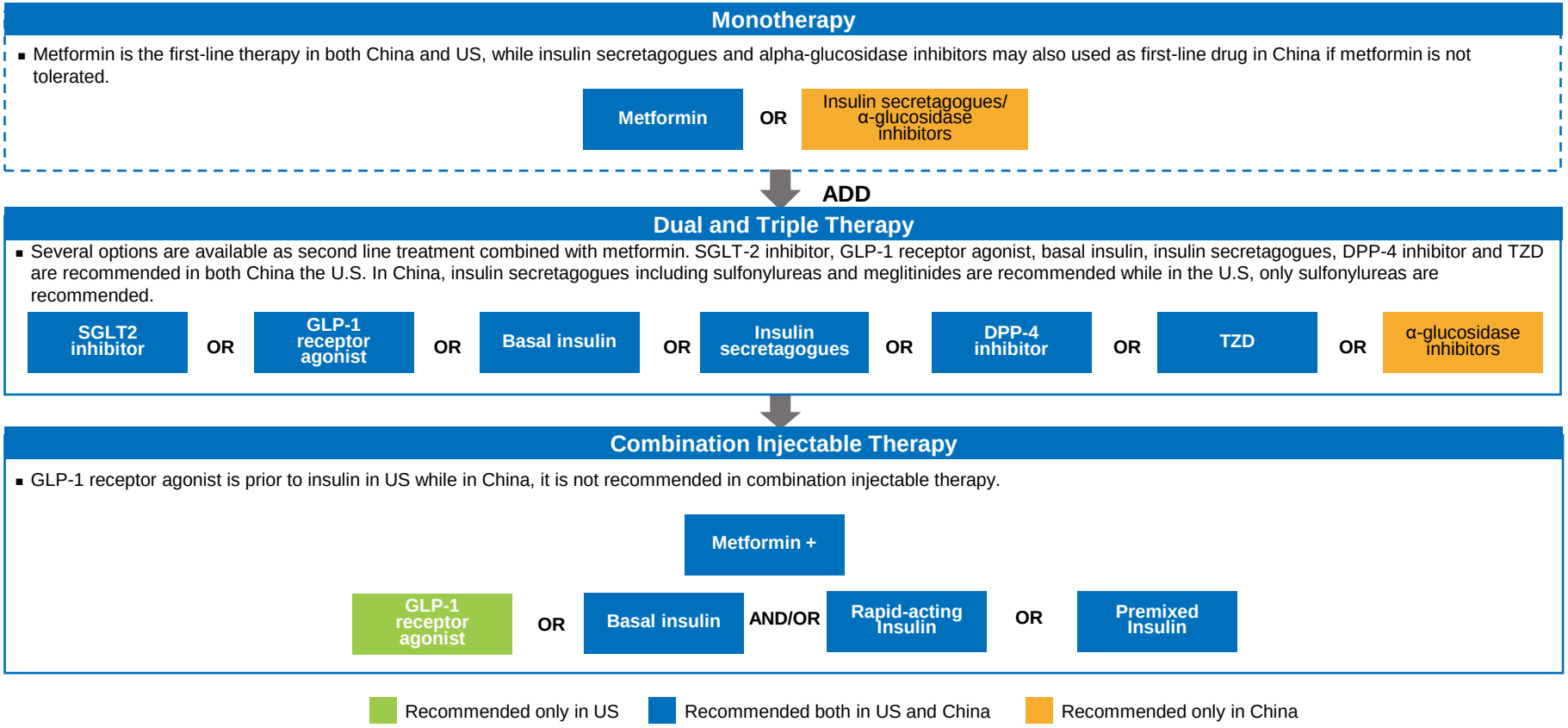
Source: Li Chen, American Diabetes Association (ADA) 79th Scientific Sessions, 7-11 June, 2019, San Francisco, USA

Copyright © Hua Medicine 2021

Comparison of Treatment Analysis of Type 2 Diabetes in China and the United States

Almost all T2D patients will need insulin as they gradually lose most of the β-cells

- Medications comparison of type 2 diabetes in China and US are illustrated below. One major difference is that alpha-glucosidase inhibitors are still used as first line drugs if metformin is not tolerated in China, whereas in US, alpha-glucosidase inhibitors are less popular.
- In US, for most patients who need the greater efficacy of an injectable medication, a GLP-1 receptor agonist should be the first choice, ahead of insulin. However, GLP-1 is not recommended in combination injectable therapy in China.



Source: Frost & Sullivan

Copyright © Hua Medicine 2021

Primary Anti-diabetics in China and United States

Insulin + Older General OAD + Branded Generic

New Injectable Anti-diabetic Reimbursable Drugs in China

New Drug with Novel MOA

Prices and Average Daily Cost of Top Anti-diabetics in China

	Brand Name	Generic Name	Category	Standard Dosage	Drug Sales in 2019 (RMB bn)	Daily Cost (RMB)	Estimated Annual Cost (RMB)
1	Glucobay®	Acarbose	α-glucosidase Inhibitors	3x0.1g/day	7.6	1.1 [1]	396
2	Lantus®	Insulin Glargine	Insulin	200U/week	7.3	17.7	6,372
3	Novomix® 30	Insulin Aspart 30	Insulin	200U/week	6.6	7.1	2,556
4	Ka Bo Ping®	Acarbose	α-glucosidase Inhibitors	3x0.1g/day	5.3	3.8	1.368
5	Chang Xiu Lin®	Recombinant Insulin Glargine	Insulin	200U/week	4.7	14.0	5,040
6	Glucophage®	Metformin	Biguanides	2x0.5g/day	4.6	2.6	936
7	Novolin® 30R	Isophane Protamine Biosynthetic Human Insulin	Insulin	200U/week	3.0	5.4	1,944
8	Novorapid®	Insulin Aspart 30	Insulin	200U/week	2.9	7.2	2,592
9	Januvia®	Sitagliptin	DPP-4 inhibitor	100mg/day	2.6	7.7	2,772
10	Novonorm®	Repaglinide	Glinides	2x1mg/day	2.1	6.2	2,232
11	Amaryl®	Glimepiride	Sulfonylureas	2mg/day	1.9	3.3	1.188
12	Diamicron®	Gliclazide	Sulfonylureas	2x80mg/day	1.8	2.3	828
13	Gan Shu Lin® 30R	Mixture Recombinant Human Insulin Injection	Insulin	200U/week	1.6	4.2	1.512
14	Victoza®	Liraglutide	GLP-1 agonist	1.2mg/day 1.8mg/day	1.6	27.3 41.0	9,828 14,760

Insulin + New Drug with Novel MOA

Prices and Average Daily Cost of Top Anti-diabetics in US

	Brand Name	Generic Name	Category	Standard Dosage	Drug Sales in 2019 (USD bn)	Daily Cost (USD)	Daily Cost (RMB)	Estimated Annual Cost (RMB)
1	Trulicity®	Dulaglutide	GLP-1 agonist	1.5mg/week	3.2	28.6	205.4	73,941
2	Victoza®	Liraglutide	GLP-1 agonist	1.2mg/day 1.8mg/day	2.2	21.7 32.6	155.8 234.1	56,102 84,153
3	Jardiance®	Empagliflozin	SGLT-2	10mg/day	2.0	17.5	125.7	45,243
4	Januvia®	Sitagliptin	DPP-4 inhibitor	100mg/day	1.7	15.3	109.9	39,478
5	Humalog®	Recombinant Insulin Lispro	Insulin	200U/week	1.7	9.1	65.3	23,508
6	Lantus®	Insulin Glargine	Insulin	200U/week	1.3	8.7	62.5	22,492
7	Novorapid®	Insulin Aspart	Insulin	200U/week	1.2	10.5	75.4	27,146
8	Levemir®	Insulin Detemir Injection	Insulin	200U/week	0.8	9.5	68.2	24,552
9	Janumet®	Sitagliptin	DPP-4 inhibitor	2*(50mg:1000mg)/day	0.6	16.0	114.9	41,364
10	Farxiga®	Dapagliflozin	SGLT-2	10mg/day	0.5	18.3	131.4	47,310
11	Invokana®	Canagliflozin	SGLT-2	100mg/day	0.5	17.5	125.7	45,243

Source: IQVIA- China hospital sales data, https://www.yaozh.com , https://www.drugs.com.
Currency exchange rate of USD1: RMB7.1815, USD1:DKK6.7529. Annual cost calculation assumes patients are on drug 360 days a year.
Note： 1 Price of health insurance negotiation

Copyright © Hua Medicine 2021

Hua Medicine
华领医药

Version 03