Hua Medicine
华领医药

全控血糖 稳而有道

2023 Interim Results Presentation

August 2023

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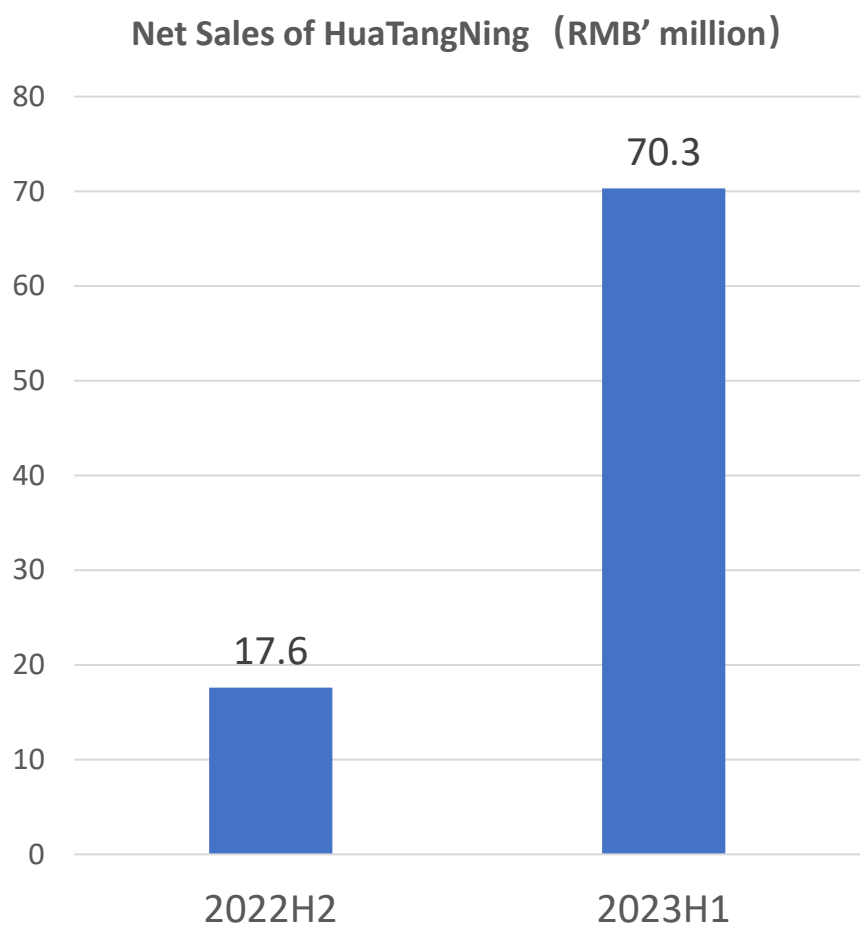
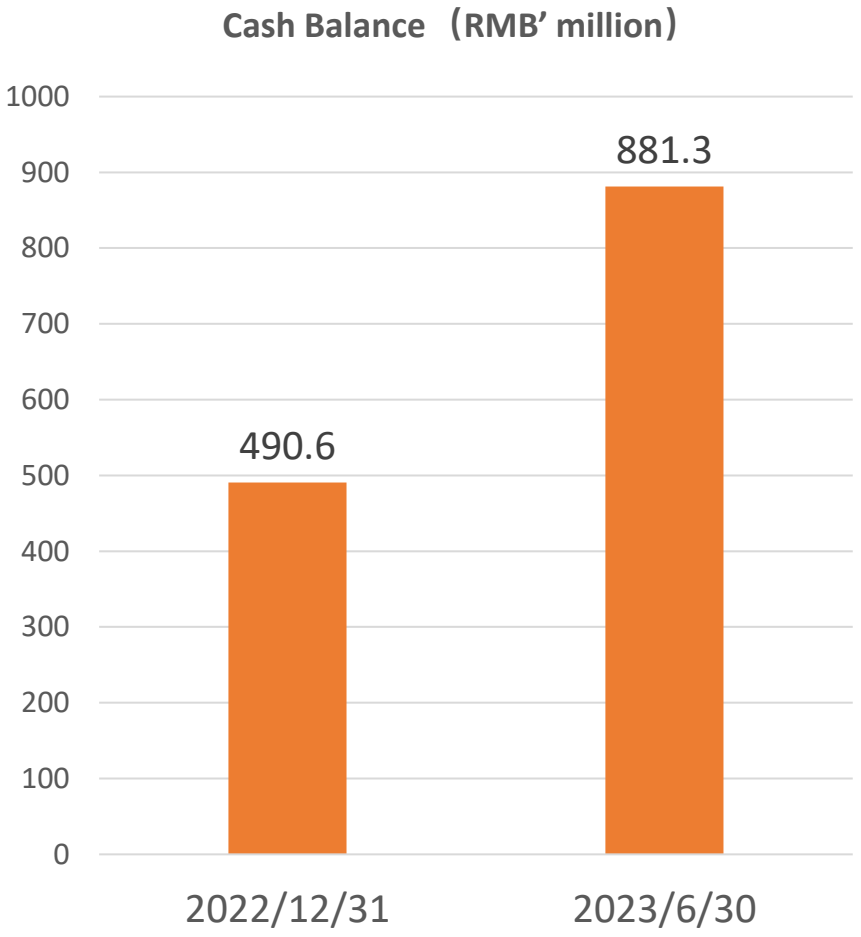
Company Overview

Business Overview

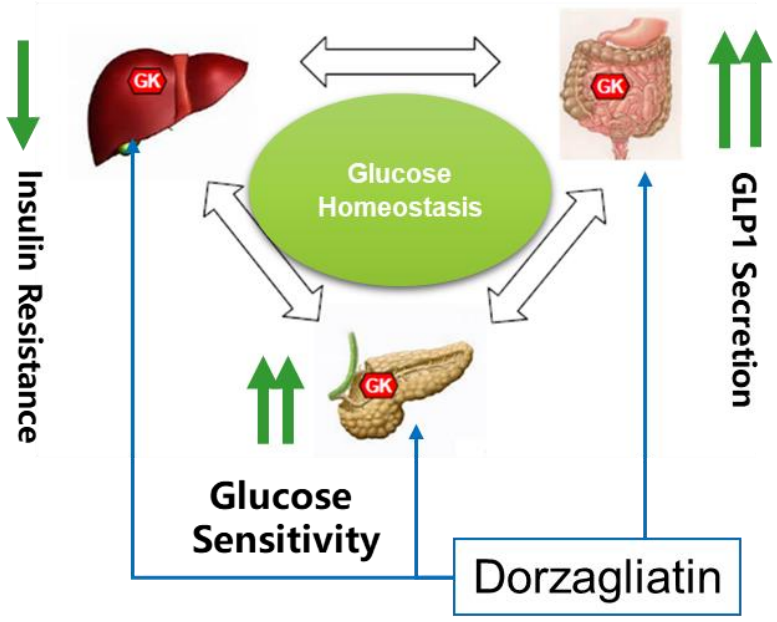


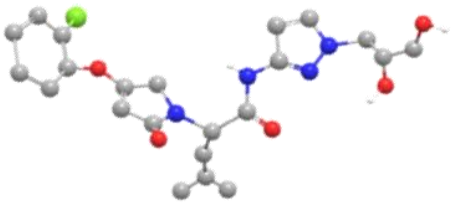


Approximately 212,000 packs of HuaTangNing have been sold, generating net sales of approximately RMB70.3 million, an increase of 299.6% compared to the second half of 2022.

RMB400 million was received as milestone payment of commercialization in Q1. Achievement of a certain milestone RMB800 million relating to the development has been confirmed.

Dorzagliatin –First-In-Class Drug to Restore Glucose Homeostasis





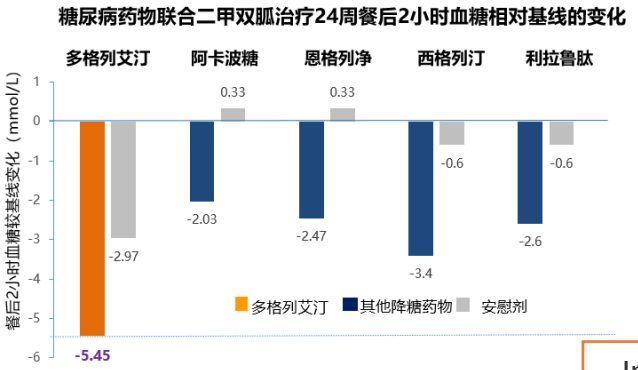
- **Acting on the liver, pancreas and intestines simultaneously, dorzagliatin improves glucose sensitivity and insulin sensitivity to repair glucose homeostasis.**
  - In clinical trials – dorzagliatin improves glucose stimulated GLP-1 secretion in T2D patients with obesity in the United States.
  - The DREAM study demonstrated 65% of T2D patients achieved diabetes remission for 52-weeks without antidiabetic agent after they had experienced good glycemic control in the SEED study with dorzagliatin treatment. In the latest animal studies, sustained improvement in pancreatic islet function in mice for a long time after drug discontinuation was also observed.
  - Animal experiment in GK rats shows that dorzagliatin not only prevent to blood glucose elevation, but also stabilize the expression of glucose transporter protein in hippocampus, which could lead to prevent the cognitive impairment of GK rats.
  - Clinical trial in China illustrated dorzagliatin improves the TIR and pancreas function represented by early phase insulin secretion in T2D patients . Dorzagliatin is expected to help people with IGT to improve islet function and prevent diabetes.
  - Benefiting from its unique mechanism of action, dorzagliatin can bring more benefits to patients and delay the onset of diabetes complications through the further development of fixed-dose combination.

Source: Chen L, Zhang JY et al. Nature Communications , A phase I open-label clinical trial to study drug-drug interactions of Dorzagliatin and Sitagliptin in patients with type 2 diabetes and obesity 2023, 3： 1405.

Dorzagliatin - Fix Three Core Issues of Type 2 Diabetes Simultaneously

- Early phase insulin secretion function impairment is the core cause of diabetes, resulting in insufficient insulin secretion and insulin resistance.
- Impairment of GLP-1 secretion function leads to decreased insulin secretion ability and abnormal diet control.
- Impairment of liver glucokinase function causes insulin resistance and blood glucose fluctuation

Significantly Postprandial Blood Sugar Reduction: "Diabetes in China"



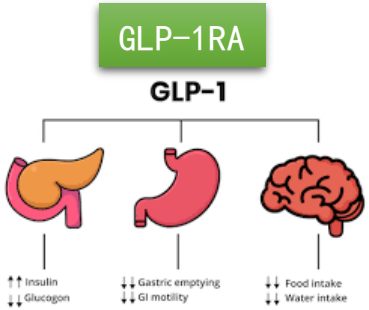
Fix Early Phase Insulin Secretion

Rapid-acting Insulin

Dorzagliatin

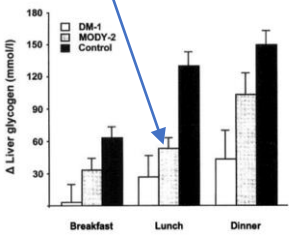
Fix GLP-1 Secretion

GLP-1RA



Improve Glycogen Reserves
Restore liver GK

GK Damage



No Medicine

Technology-led, Innovation-driven, Evidence-based Medicine, High-quality Development

Dorzagliatin monotherapy in Chinese patients with type 2 diabetes: a dose-ranging, randomised, double-blind, placebo-controlled, phase 2 study

Improve Insulin Secretion And Reduce Insulin Resistance

nature medicine ARTICLES

Dorzagliatin in drug-naïve patients with type 2 diabetes: a randomized, double-blind, placebo-controlled phase 3 trial

Phase 3 SEED

news & views

DIABETES

A new class of drug in the diabetes toolbox

The DAWN and SEED trials demonstrate the potential of glucokinase activators for the treatment of type 2 diabetes, but how they fit in the overall treatment algorithm remains to be determined.

Klara R. Klein and John B. Buse

First-In-Class Antidiabetic Drug

nature medicine ARTICLES

Dorzagliatin add-on therapy to metformin in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled phase 3 trial

Phase 3 DAWN

nature communications

Article

A phase I open-label clinical trial to study drug-drug interactions of Dorzagliatin and Sitagliptin in patients with type 2 diabetes and obesity

Improve GLP-1 Secretion

ORIGINAL ARTICLE

WILEY

Diabetes remission in drug-naïve patients with type 2 diabetes after dorzagliatin treatment: A prospective cohort study

DREAM Study Remission of Diabetes

7

TIR Algorithm Thesis

Clinical Expert Consensus

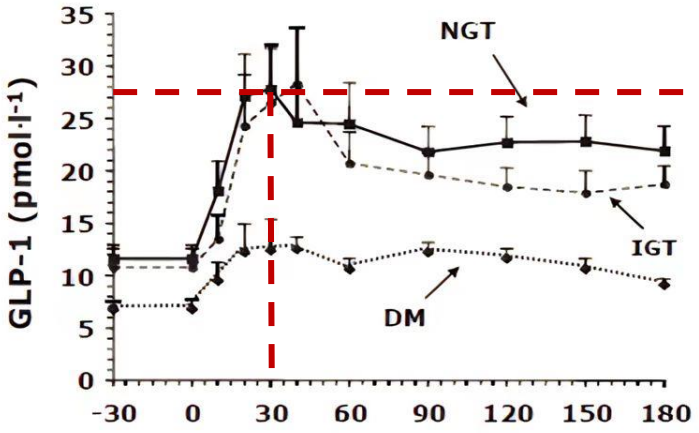
Pharmaceutical Expert Consensus

Dorzagliatin Improve GLP-1 Secretion in T2D Patients with Obesity

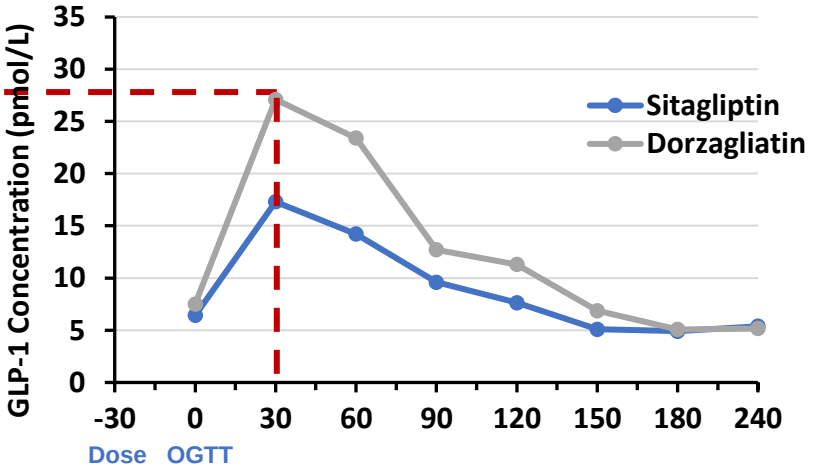
Ferrannini et al. reported that glucose-stimulated GLP-1 secretion was significantly decreased in T2D patients with obesity.

The result of OGTT showed that **dorzagliatin regulated GLP-1 secretion**. At 30 minutes after OGTT, the **GLP-1 level of T2D patients with obesity was close to that of people with normal glucose tolerance**.

GLP-1 Levels of IGT and NGT



GLP-1 levels in T2D Patients with Obesity Treated with Dorzagliatin or Sitagliptin



It was proven for the first time in a clinical trial that dorzagliatin improves GLP-1 secretion in both islets and intestines, thereby increasing glucose-stimulated insulin secretion.

GK: Trigger for Insulin Secretion

As a glucose receptor, it is the first step in intracellular glucose utilization.

GK senses increased glucose concentration, rapidly responds to the release of insulin stored in the vesicles, and increases insulin secretion.**(Phase I is dominant, Phase II is complementary)**

GLP-1: Amplifier of insulin secretion

GLP-1 binds to GLP-1 receptor, activates cAMP pathway and vesicular insulin releases after β-cells perceive the increase of glucose concentration.

It also promotes insulin transcription and replenishes vesicular insulin refilling (Phase II) to improve insulin secretion. **(Phase II is dominant, Phase I is complementary)**

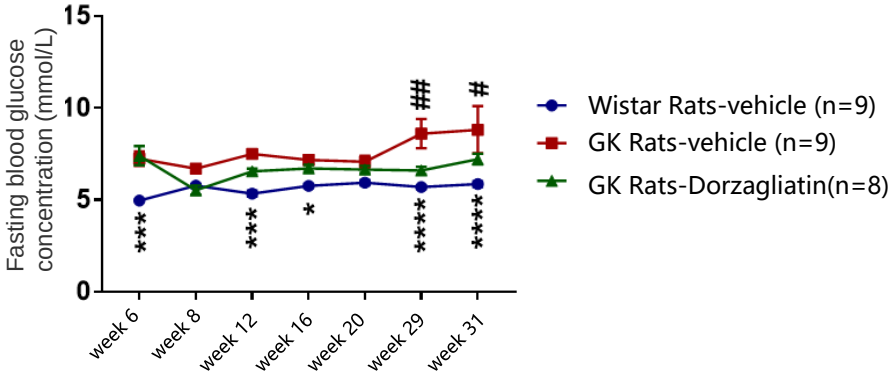
Cooperative Improvement Insulin Secretion

Ferrannini, E. et al, Diabetes, 2008, 57(5), 1340-1348

Dorzagliatin Improves Cognitive Impairment in Rats

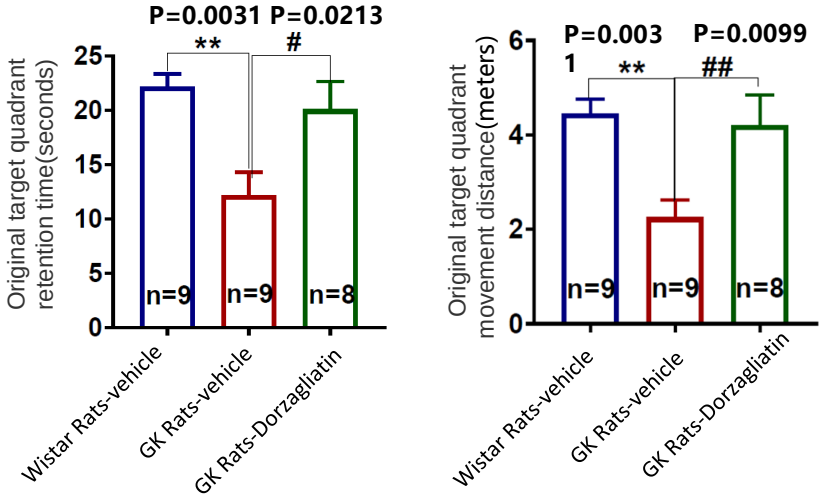
- The spontaneous non-obese diabetic Goto-Kakizaki rats exhibit increase in blood glucose and decreased memory function with age.
- With 26 weeks treatment of low-dose dorzagliatin, **the trend of elevated fasting blood glucose in GK rats was significantly lower than that in the vehicle group, and it had a protective effect against the decline of memory function.**

Changes of Fasting Blood Glucose in Rats with Age



GK-vehicle compared with Wistar group, *P < 0.05, ***P < 0.001, ****P < 0.0001.
GK-vehicle compared with GK-dorzagliatin group, #P < 0.05, ##P < 0.01.

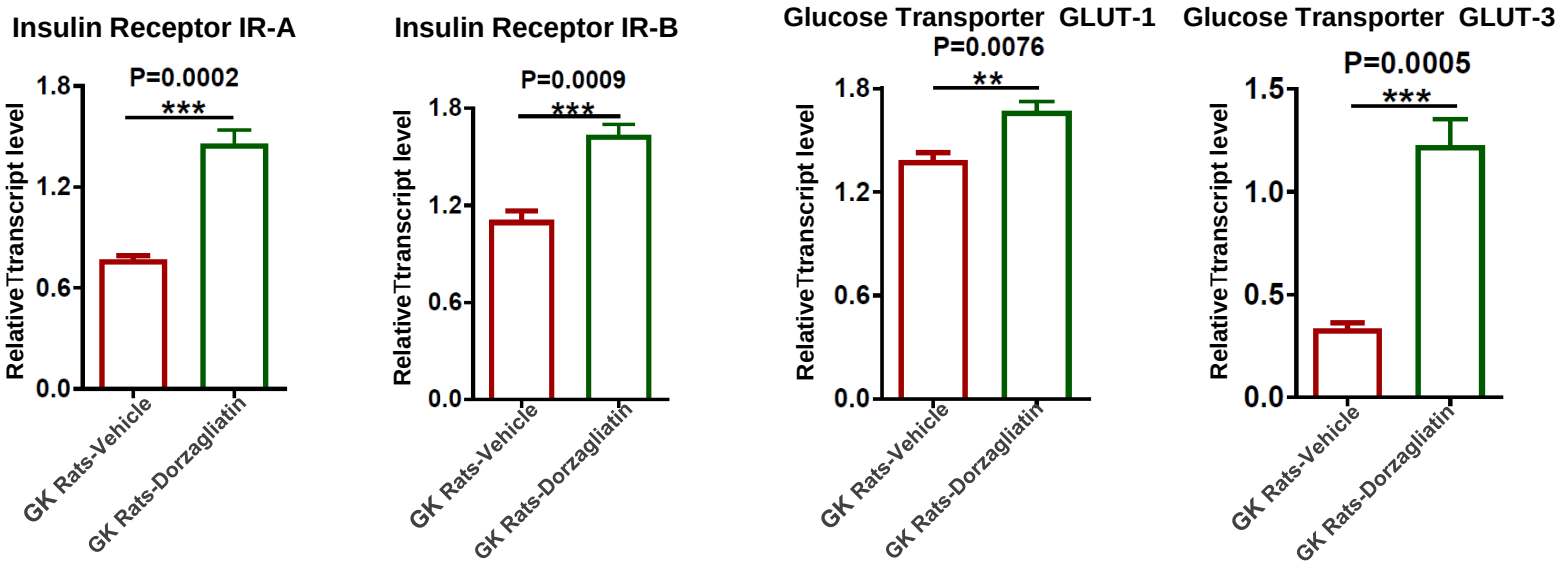
Morris Water Maze Spatial Memory Test at 33 Weeks of Age



2023 ADA Poster, 247-LB

Dorzagliatin Improves Cognitive Impairment in Rats

- Long-term administration of dorzagliatin at low dose prevents the reduction of insulin receptor protein expression and stabilizes the protein expression level of glucose transporters in hippocampus of GK rats.
- Dorzagliatin exerts a protective effect on memory function by protecting the glucose metabolism function in body and inhibiting the decline of glucose metabolism function in the brain of GK rats.



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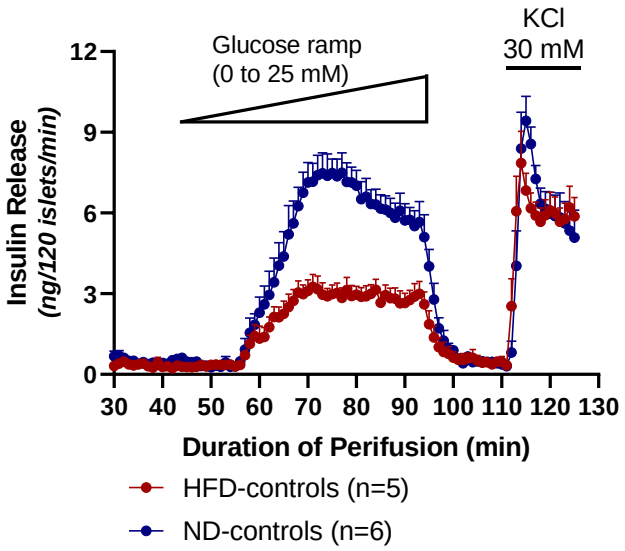
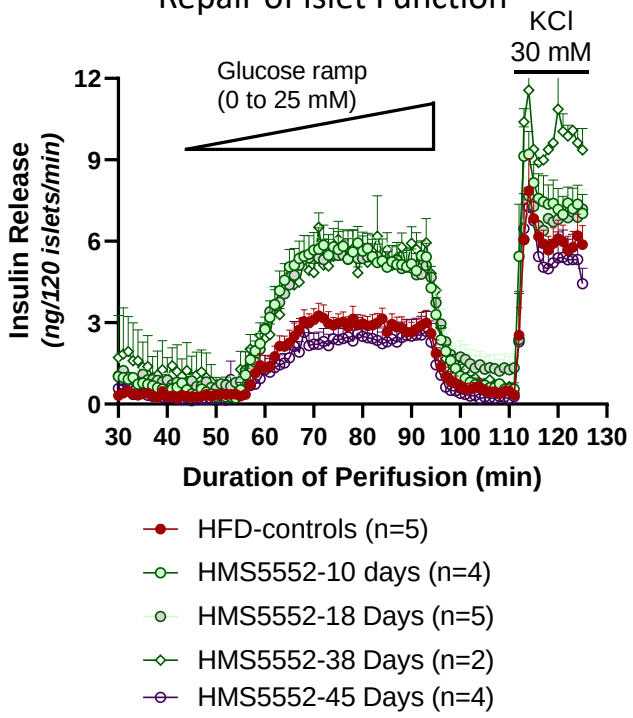
Dorzagliatin Continued to Repair Impaired Islet Function of Diabetic Rats

Impaired Islet Function in Obese/Diabetic Rats Induced by HFD



Dorzagliatin Achieves Long-term Repair of Islet Function

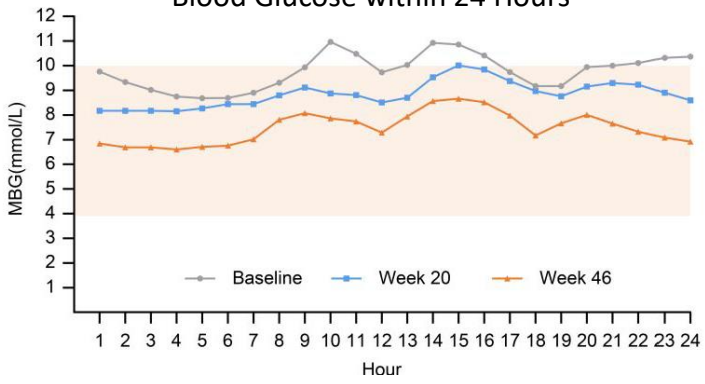


- Dorzagliatin **significantly improved impaired islet function in diabetic rats** during 19 days of administration.
- Islet function **continued to improve on day 10, day 18 , and day 38 in the absence of antidiabetic agents,** until the impairment of islet function reappeared on day 45.

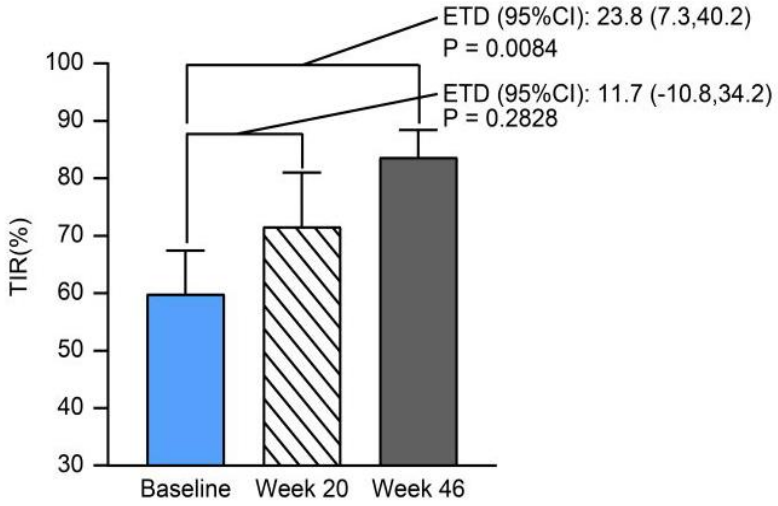
2023 ADA Poster, 247-LB

Dorzagliatin Improved TIR and Repaired Islet Function

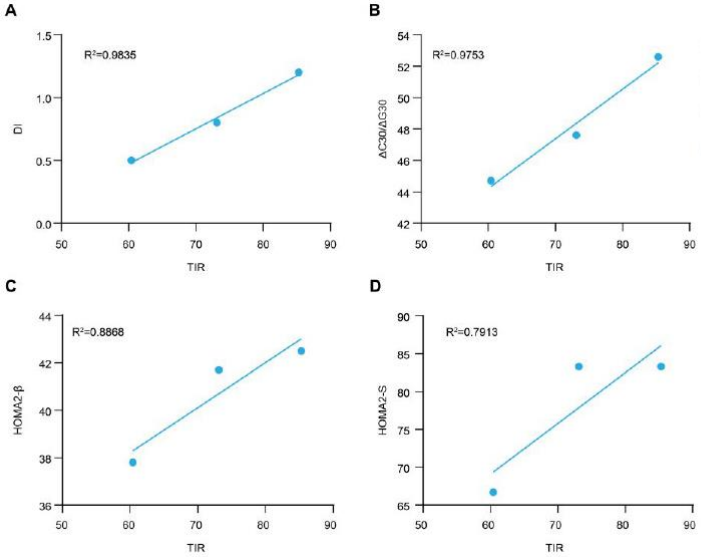
Dorzagliatin Significantly Improved Patients' Blood Glucose within 24 Hours



TIR Increased with the Duration of Treatment, Reaching 83.7% at 46 Weeks



The Islet Function was Improved Synchronously by TIR



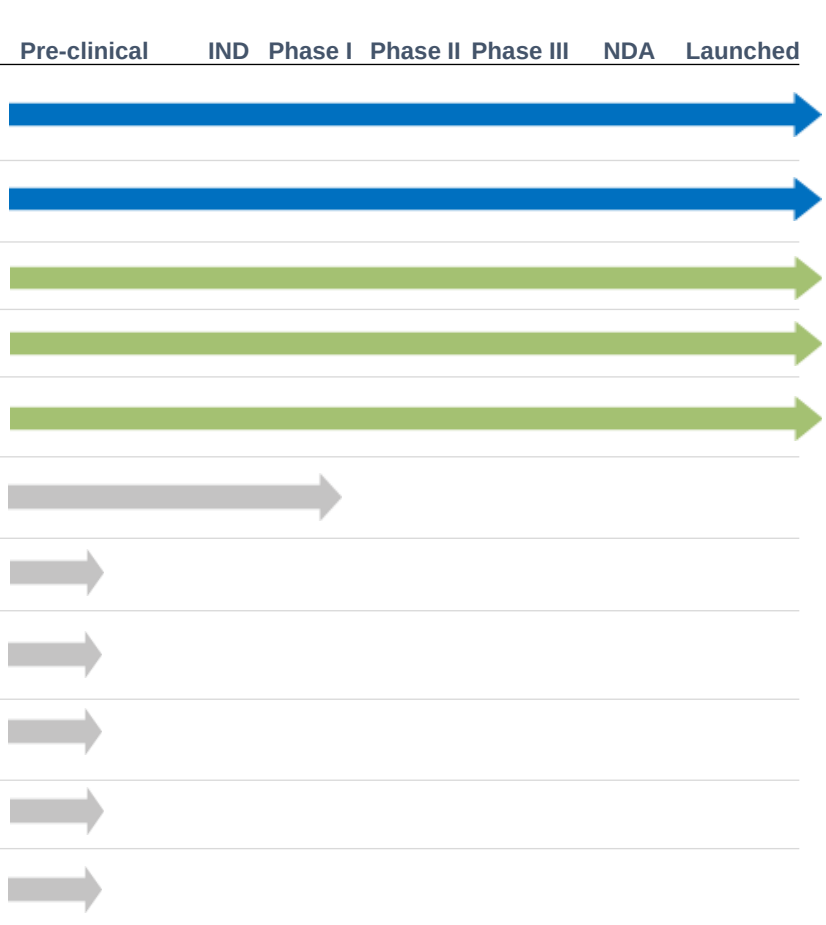
- Dorzagliatin significantly improved daily glucose homeostasis in diabetic patients.
- Long-term use of dorzagliatin brings a steady improvement in TIR.
- The patients' damaged islet function was gradually restored.

Diabetes Obes Metab.2023 Jun 29. doi: 10.1111/dom.15179

Outlook

Hua Medicine R&D Pipeline

Product Name	Indication	Development phase
HuaTangNing (华堂宁®)	T2D –Drug Naïve	Launched (China)
	T2D –Metformin Tolerated	Launched (China)
HuaTangNing (华堂宁®) No dose adjustment in	DKD	Launched (China) - Allowances
	Combination therapy with DPP4i	Launched (China) - Allowances
	Combination therapy with SGLT2i	Launched (China) - Allowances
Fixed dose combinations - dorzagliatin and OADs	T2D	Phase I ready
2nd Generation GKA	Metabolic Diseases	Pre-clinical
Glucokinase regulator	Congenital Hyperinsulinism	Pre-clinical
Fructose Kinase Inhibitor	Metabolic Disease	Pre-clinical
mGLUR5 NAM- CNS	PD-LID	Pre-clinical
Clinical Fructose detection	IVD	Pre-clinical



2nd Generation GKA Ready to IND in US

1st Generation GKA

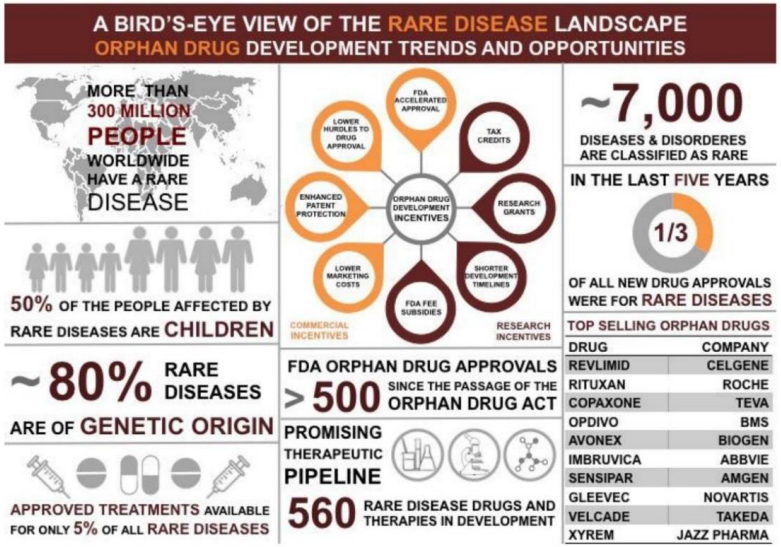
- Chinese market, Chinese patients
- One tablet twice daily
- Restore impaired glucose homeostasis, improve β-cell function
- Cooperate with major pharmaceutical companies in the Chinese market

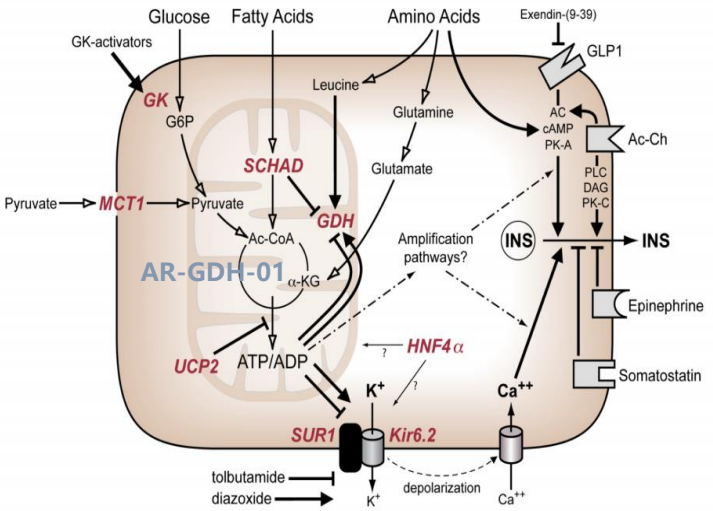
2nd Generation GKA

- Western markets, the majority of patients with obesity
- Rare diseases treatment
- Consistent with western patients' drug usage habits
- Restore impaired glucose homeostasis, improve β-cell function, seek diabetes prevention and remission
- Explore the possibility of breakthrough therapy designation in the field of rare disease

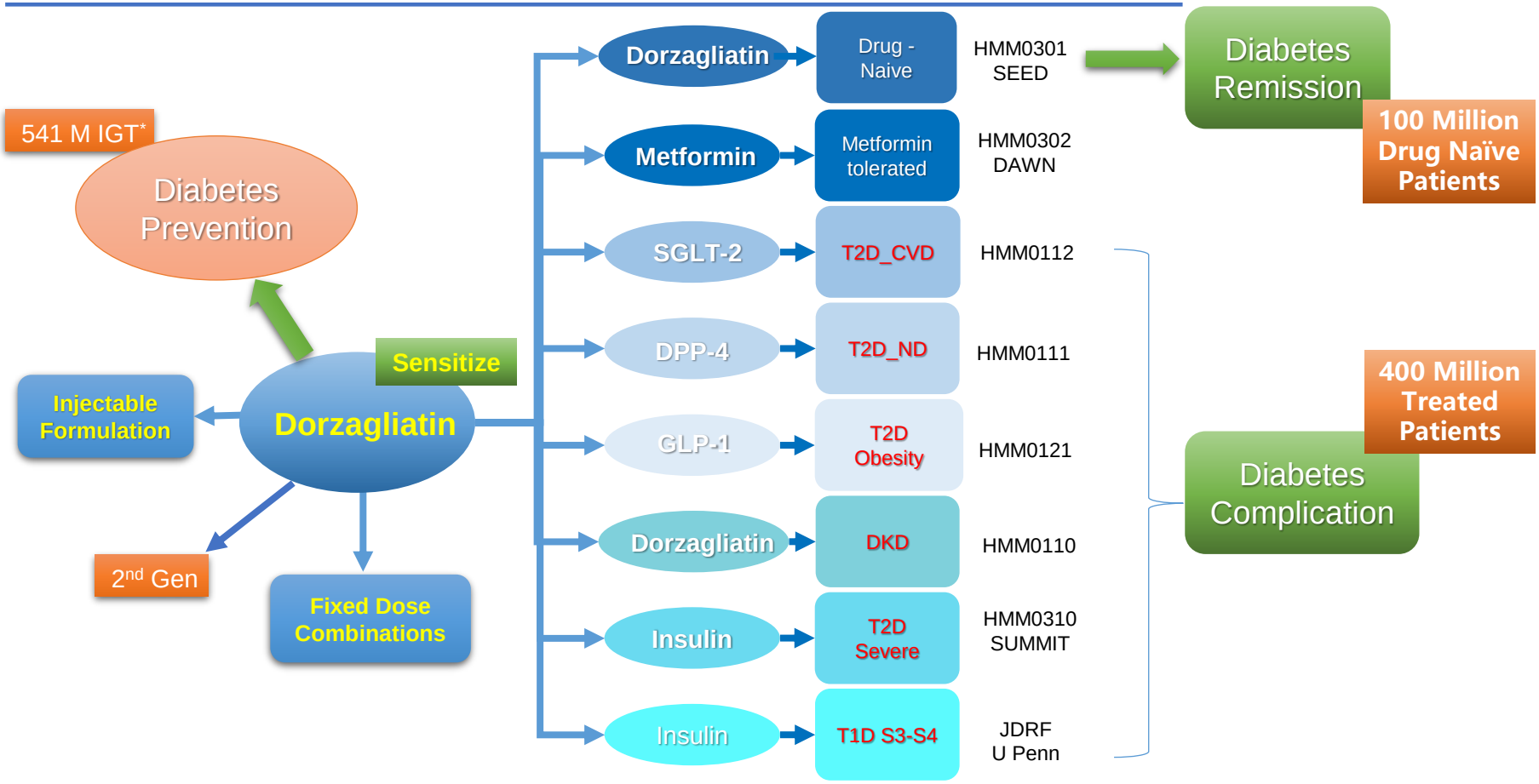
Drug Development of Congenital Hyperinsulinemia

- Congenital hyperinsulinemia is a serious disease threatening the health of newborns, which will cause permanent brain damage and life-long disability, or even life threatening in half of the patients without proper treatment.
- Congenital hyperinsulinemia is a rare disease, which has been listed in the list of rare diseases in China. Effective medical intervention is urgently needed, and the patients also need effective new drugs.
- The number of people with hypoglycemia due to genetic mutations is estimated to be 47,000 in China and nearly 150,000 globally.





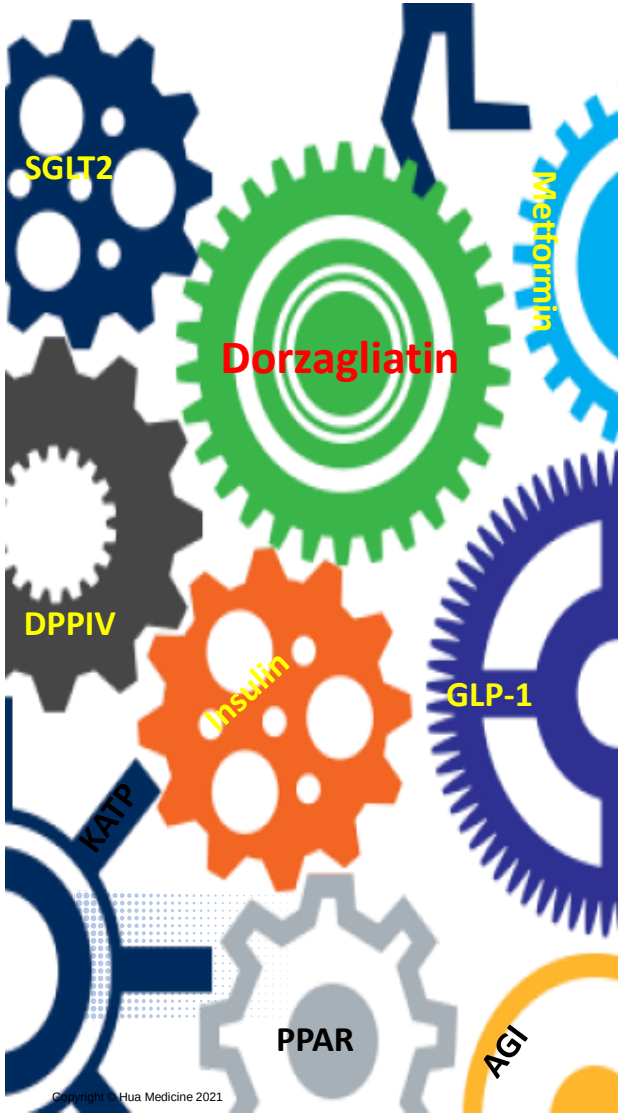
Restore Glucose Homeostasis: New Chance of Diabetes Remission and Ultimately Prevention



- **Diabetes remission** by early intervention of Dorzagliatin: impact about 100 M diabetes patients
- **Diabetes prevention** by Dorzagliatin for IGT subjects: about 541 M IGT patients worldwide
- **Diabetes complication prevention** by early combination of Dorzagliatin: about 440 M T2D patients have one or more comorbidities

*IDF Diabetes Atlas 10th Edit; Leon Litwak *Diabetology & Metabolic Syndrome* 2013, 5: 57; Yuanyuan Cheng, Li Chen *Global J Obesity, Diabetes and Metabolic Syndrome* 2020, 7: 18

Goal 2030—Integrated Interventional Diabetes Management



In the medical community environment, explore the potential benefits, broaden the indication, promote a new model of diabetes treatment, and contribute to Healthy China 2030

- Dorzagliatin in combination with metformin, sitagliptin and empagliflozin in the early stage improves the glucose control rate and remission rate in untreated patients and patients treated with oral hypoglycemic agents
- Dorzagliatin combined with insulin or GLP-1RA leads to disease remission and control of diabetic complications.
- Dorzagliatin prevents diabetes in patients with IGT.

Enhancing the comprehensive value of hospital care: Bayer-Hua Medicine DKD joint team

- Management of diabetic kidney disease patients in chronic kidney disease
- Glucose management in the treatment of cardiovascular disease
- Fixed compound formulations provide better medical value

New era of personalized diabetes care

- Artificial intelligence can help to better define disease and enable the precision treatment of diabetes
- Glucose management in neurodegenerative diseases

Future Action

- **Prepare for NRDL Negotiation**
  - We have submitted materials to the National Healthcare Security Administration. According to the publicity of National Healthcare Security Administration, dorzagliatin has officially passed the formal examination NRDL.
  - Hua will participate the NRDL negotiation at Q4.
- **Expand Production Capacity**
  - We have initiated investment into dorzagliatin manufacturing capability at Changzhou SynTheAll, Zhejiang Raybow and Shanghai Desano.
  - The expanded capacity would better fullfill the enlarged demand expected in the future.
- **More Milestone Payment**
  - We will receive an 800 million milestone payment from Bayer related to product development.
  - Hua is expected to receive milestone payments up to RMB 2.94 billion from Bayer in the future; RMB 1.5 billion of upfront & milestone payments already achieved.
  - We have strong cash balance to accelerate our R&D pipeline.

Financial Section

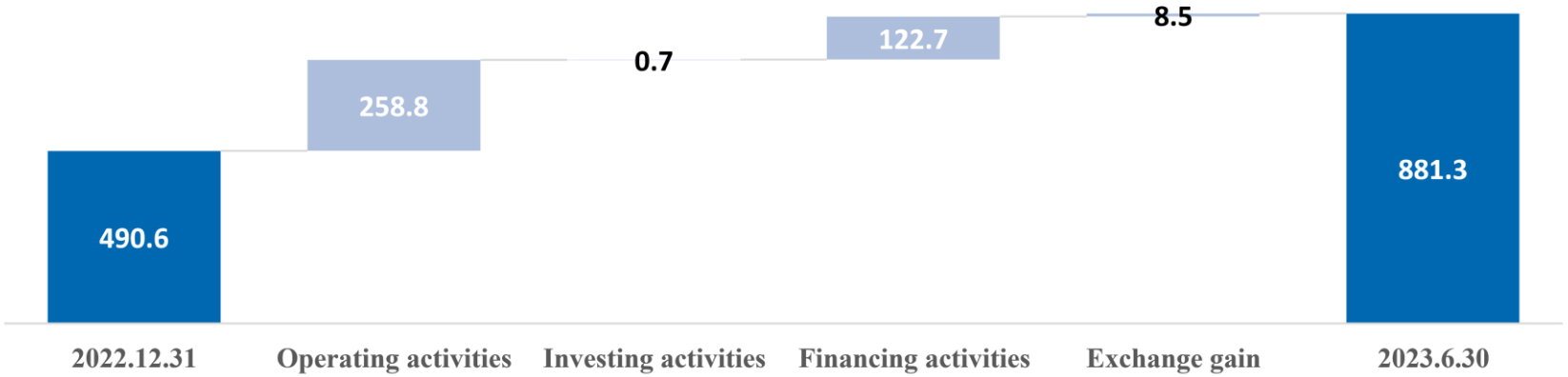
Financial Summary

Cash Balance: RMB881.3million of cash at 6/30/2023 vs. RMB490.6 million at 12/31/2022.

Total cash increase of RMB390.7 million, consisted of

- Net cash from operating activities was RMB258.8 million
- Net cash from investing activities was RMB0.7 million
- Net cash from financing activities was RMB122.7 million
- Net effect of exchange rate changes was RMB8.5 million

Net cash from operating activities of RMB258.8 million consisted mainly of RMB400 million in milestone payments received from Bayer based on the achievement of milestones, RMB76.4 million in sales receipts, and RMB220.4 million in payments for the development of research and development activities, the commercialization of HuaTangNing, production activities and administrative expenses.



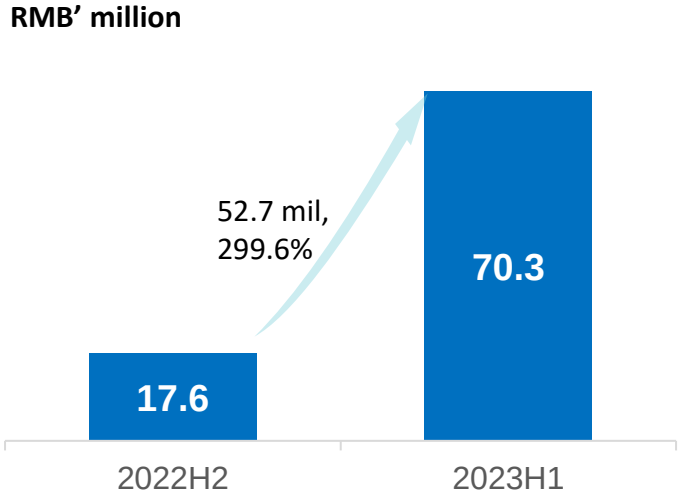
Financial Summary- continued

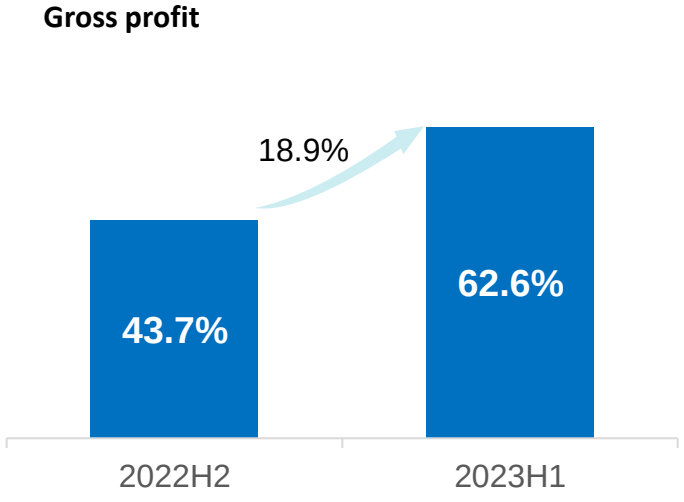
Revenue For the six months ended June 30, 2023, generating sales of approximately RMB70.3 million.

For the six months ended June 30, 2023, approximately 212,000 packs of HuaTangNing (华堂宁®) were sold, generating sales of approximately RMB70.3 million, representing approximately a 299.6% increase in revenue compared with the second half of 2022. From first commercial launch through June 30, 2023, approximately 265,000 packs of HuaTangNing (华堂宁®) were sold, generating sales of approximately RMB87.9 million.

Gross profit For the six months ended June 30, 2023, we recorded a gross profit of approximately RMB44.0 million and a gross margin of 62.6%.

Our gross margin increased by 18.9% as compared to 43.7% for the year ended December 31, 2022, which was primarily due to sufficient supply and increased sales volume, leading to the decreased unit production expense and unit fixed cost. As our commercialization scale increases, the gross margin is expected to continually increase to a more normalized rate.





Financial Summary- continued

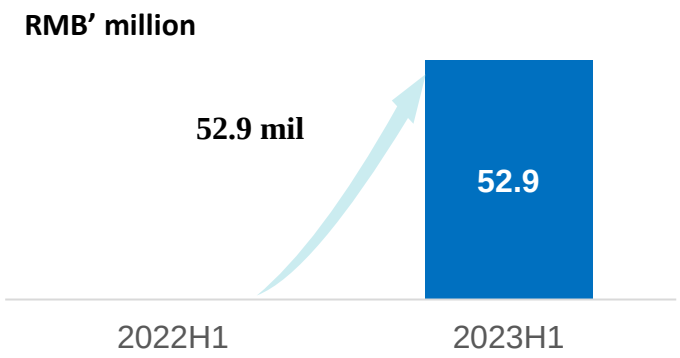
Other income RMB38.6 million for the six months ended June 30, 2023.

Our other income increased by RMB17.2 million to RMB38.6 million for the six months ended June 30, 2023 from RMB21.4 million for the six months ended June 30, 2022, which was mainly attributable to an increase of RMB21.7 million in Bayer milestone income and RMB6.2 million in bank interest income from short-term deposits for the six months ended June 30, 2023, adjusted for a decrease of RMB10.7 million in government grants.

Loss before tax Loss before tax decreased by approximately RMB14.5 million or approximately 13.9% to approximately RMB90.1 million for the six months ended June 30, 2023, compared with the six months ended June 30, 2022.

Selling expenses Our selling expenses was RMB52.9 million for the six months ended June 30, 2023.

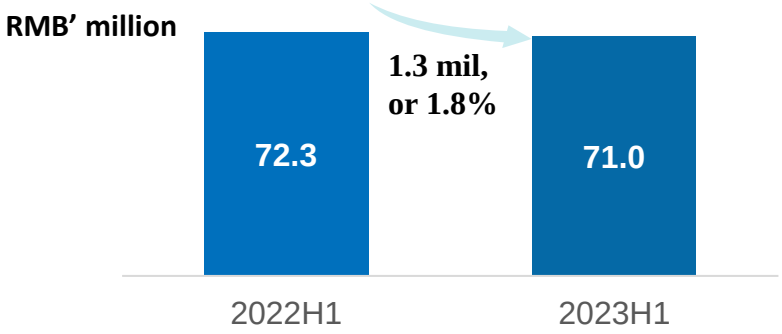
which consisted primarily of RMB15.0 million of employee compensation, RMB29.0 million of promotion expense and RMB8.9 million of meeting expense, consulting expense, logistics expense and other related expenses.



Financial Summary- continued

Research and development expenses decreased by RMB1.3 million to RMB71.0 million for the six months ended June 30, 2023 from RMB72.3 million for the six months ended June 30, 2022.

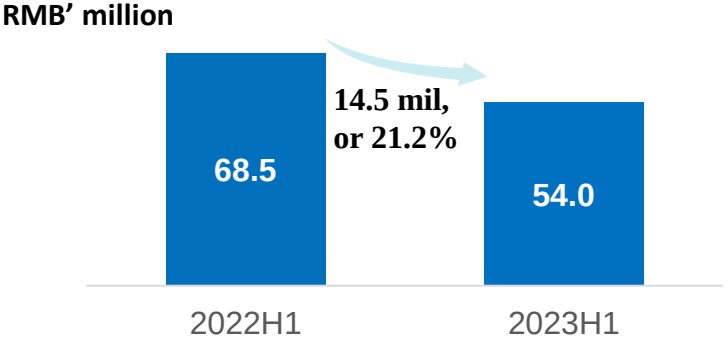
- An increase of RMB3.2 million for dorzagliatin non-clinical studies from RMB0.8 million for the six months ended June 30, 2022 to RMB4.0 million for the six months ended June 30, 2023, which was primarily attributable to the pre-clinical studies of second generation glucokinase activator conducted in the United States in the first half of 2023 and no such studies were conducted in the first half of 2022;
- An increase of RMB2.9 million in chemical, manufacturing, and control expenses from RMB9.0 million for the six months ended June 30, 2022 to RMB11.9 million for the six months ended June 30, 2023. We focused on the scale up and process development for existing production line and process validation for intermediate product in the first half of 2023. In the first half of 2022, we focused on the process validation, drug substance and production for clinical trial which was required by the NMPA;
- A decrease of RMB12.4 million in labor cost from RMB47.3 million for the six months ended June 30, 2022 to RMB34.9 million for the six months ended June 30, 2023, which was primarily attributable to the labor cost reallocation of manufacturing department to cost from first commercial sales and the decrease of share-based payment under the accelerated amortization method;
- An increase of RMB4.4 million in other expenses from RMB11.5 million for the six months ended June 30, 2022 to RMB15.9 million for the six months ended June 30, 2023, which was primarily attributable to increased travelling expense, meeting expense and utility expense due to the impact of COVID-19 in the first half of year 2022 and recovered in the first half of year 2023.



Financial Summary- continued

Administrative expenses decreased by RMB14.5 million to RMB54.0 million for the six months ended June 30, 2023 from RMB68.5 million for the six months ended June 30, 2022

- A decrease of RMB11.2 million in labor cost, which was primarily attributable to the labor cost reallocation of marketing department to selling expense from first commercial sales and the decrease of share-based payment under the accelerated amortization method;
- A decrease of RMB5.3 million in consultant fee, which was mainly due to the reallocation of marketing related consulting to selling expense and less NDA application related consulting was conducted during the six months ended June 30, 2023, since we got our NDA approval in the fourth quarter of year 2022;
- An adjustment for the increase of RMB1.1 million in recruitment expense due to our recruitment strategy.



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