Hua Medicine
华领医药

2020 Annual Results Presentation

March 2021

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Company Overview

Advancing innovative solutions for unmet medical needs from China, starting with Type 2 diabetes

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 = unsatisfactory treatment and control rates
- Diabetes complications USD 760B
- Impaired glucose and insulin sensitivity:
  - **β-cell secretion and mass**
  - **Insulin resistance**

Hua Medicine's dorzagliatin (HMS5552)

- Global first-in-class oral-diabetic drug: dorzagliatin
- Profiled for combination with other approved OADs that offer systematic diabetes care
- Successful completion of Phase III with well tolerated and good safety profile
- Improves glucose and insulin sensitivity
  - **Increase Insulin early phase secretion**
  - **Reduce Insulin resistance**
- Leading diabetes partner selected for commercialization
- Launch first in China, then global markets

5 Major Activities for 2021

1. China NDA submission for dorzagliatin
2. China commercialization preparation with partner, Bayer AG
3. Advancing dorzagliatin focused pipeline to establish dorzagliatin as cornerstone treatment for diabetes
4. Manufacturing optimization
5. Development and advancement of new molecules: mGlur5 for PD-LID and FKI for metabolic diseases

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2020 Annual Highlights

Successful Completion of Phase III Registration Trials in China

5 positive clinical trial study results: 2 Phase III & 3 Phase I

- ✓ Successfully **completed SEED (HMM0301)** Phase III monotherapy trial with sustained efficacy and good safety and tolerability profiles
- ✓ Presented at the American Diabetes Association (ADA) and Chinese Diabetes Society (CDS), demonstrating significant **improvements in β-cell function and 2h-PPG reduction**
- ✓ Successfully **completed DAWN (HMM0302)** Phase III metformin combination study with sustained efficacy, and good safety and tolerability profiles
- ✓ **Completed HMM0110**, indicating the potential use of dorzagliatin with no dose adjustment among T2D patients with diabetic kidney disease
- ✓ **Completed HMM0111**, demonstrating potential for combination with DPP-4 inhibitor, and demonstrated a clear synergistic effect in blood glucose reduction, endogenous GLP-1 release and improvement of β-cell function
- ✓ **Completed HMM0112**, demonstrating potential for combination with SGLT-2 inhibitor, with clear synergistic effect in efficacy of blood glucose reduction and improvement of β-cell function

Other Corporate Milestones

Manufacturing scale up & commercialization partner ready for drug launch

- ✓ Entered into a commercialization agreement and strategic partnership with Bayer Healthcare Company Limited for mainland China
- ✓ Entered into a commercial supply agreement with Zhejiang Raybow Pharmaceutical as an additional supplier to existing manufacturing partners
- ✓ Granted the Drug Manufacturing Permit for dorzagliatin in China by the Shanghai Municipal Drug Administrative Bureau
- ✓ Announced global operation headquarters and research and development center in Shanghai's ZhangJiang Science City officially established

Roche · BAYER · 药明康德 WuXi AppTec · COVANCE · Tigermed 泰格医药 · DESANO 迪赛诺 · Raybow 瑞博制药

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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 – **received in 2020**
- Milestone payments: Up to RMB 4.18 billion
- Bayer: exclusive rights to commercialize product in China, tiered service fee based on net sales

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Dorzagliatin

First-In-Class (FIC) glucokinase activator globally

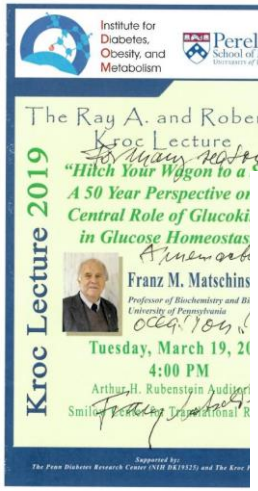
Fix sensor, restore glucose homeostasis, treat diabetes from root cause

Synergy with targeted diabetes therapy in disease control

Opportunity for personalized diabetes care

Key Recognitions of Glucokinase

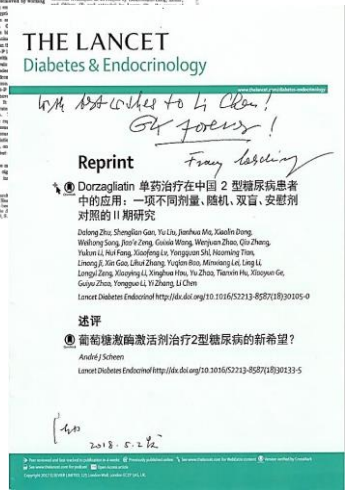
- ✓ Discovered in the 1960s by Dr. Franz Matschinsky, "Godfather of Glucokinase"
- ✓ The 1st GKA Published in Science Magazine in 2003, Roche
- ✓ Dorzagliatin completed POC in 2016, Lancet DE 2018
- ✓ Winner of Rolf Luft Award 2020



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: Dalong 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

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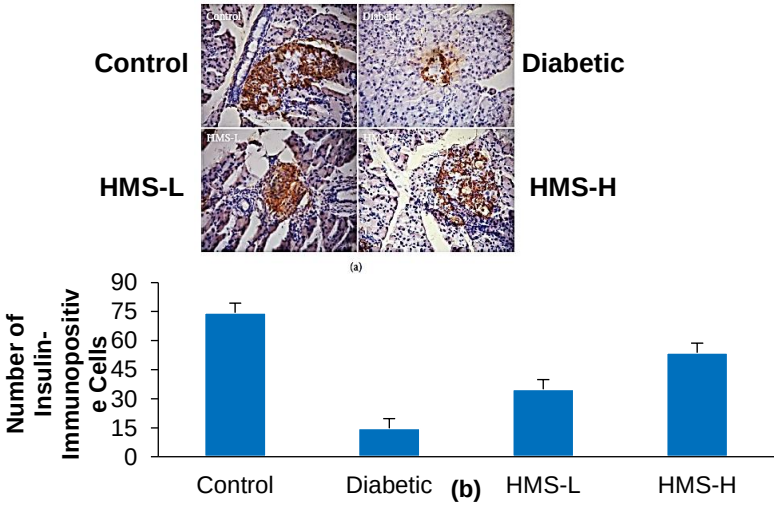
Dorzagliatin Has the Potential to Repair the Glucokinase Glucose Sensor

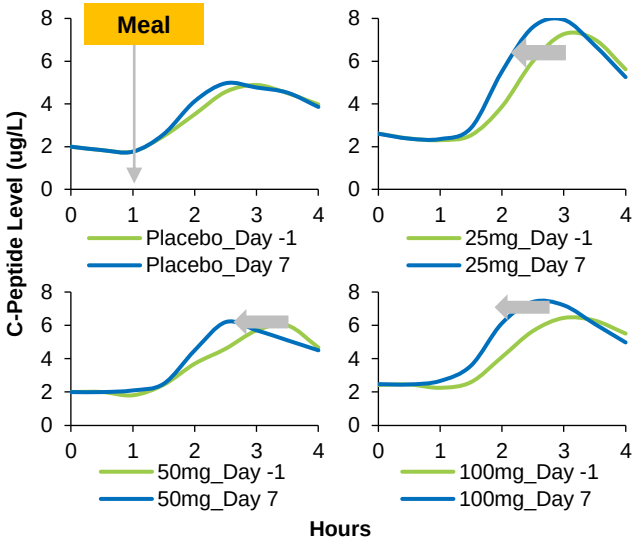
Type 2 Diabetes Rat Pancreas

Pre-clinical



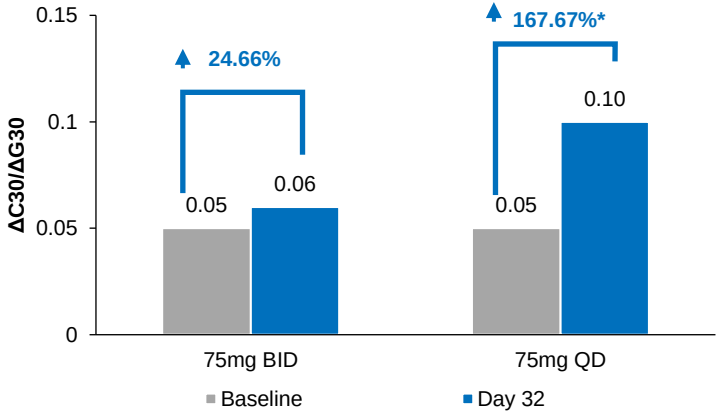
T2D Patient Early-stage insulin release

Phase Ib



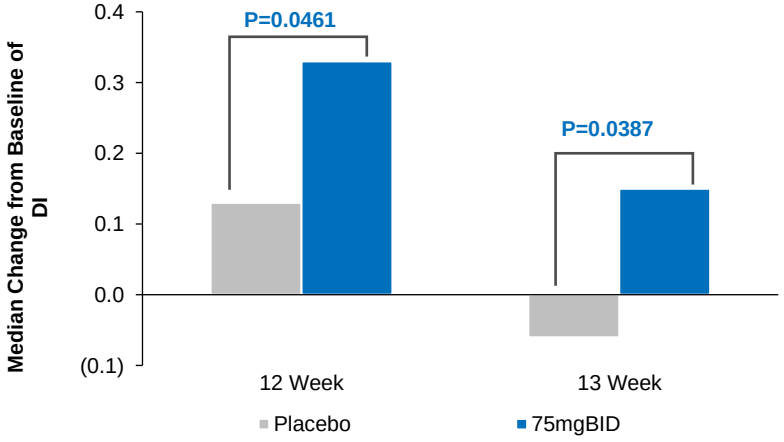
T2D Patient Early Insulinogenic index

Phase Ic



T2D Patients Disposition Index

Phase II



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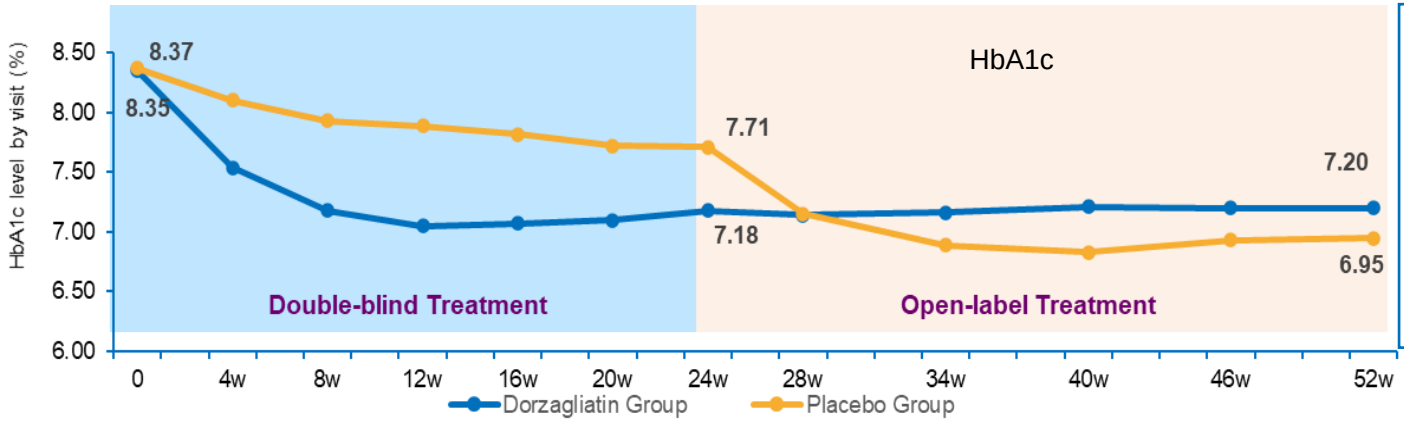
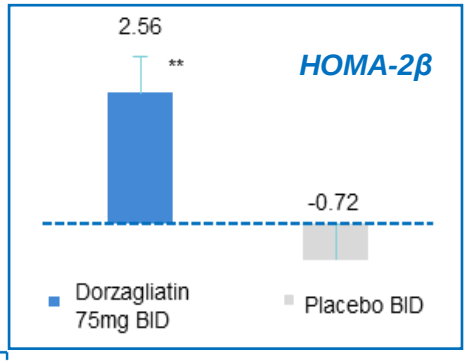
Dorzagliatin Phase III Results: SEED and DAWN Significantly reduce insulin resistance during 52 week

SEED HMM0301

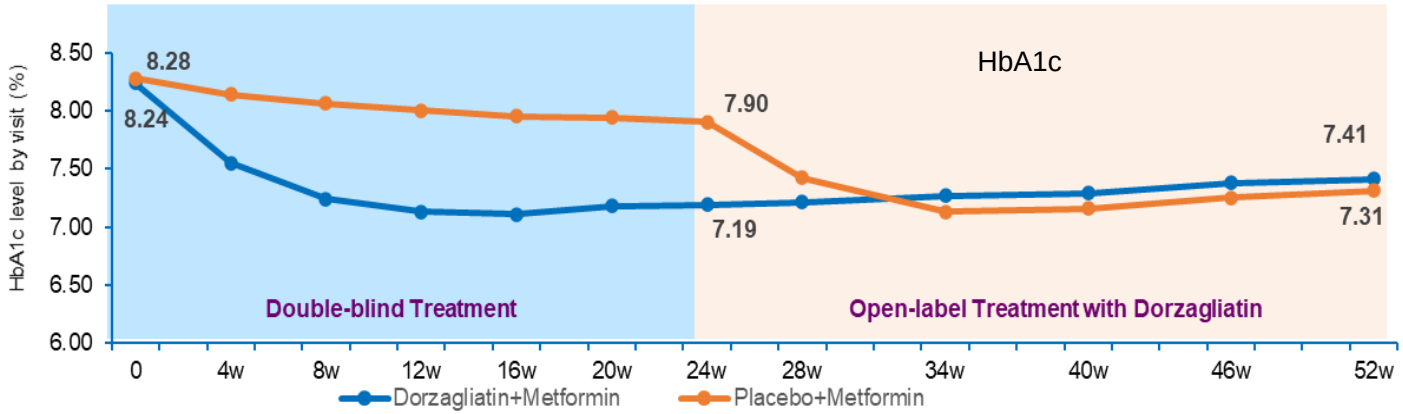


Significantly improve β-cell function at week 24

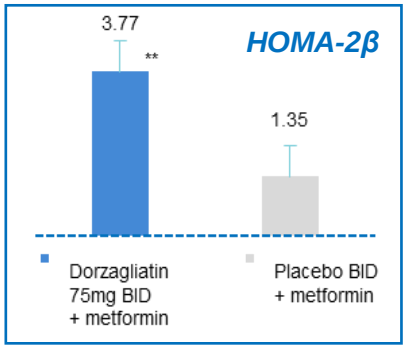


Change from Baseline to Week 24

DAWN HMM0302



Significantly improve β-cell function at week 24



Change from Baseline to Week 24

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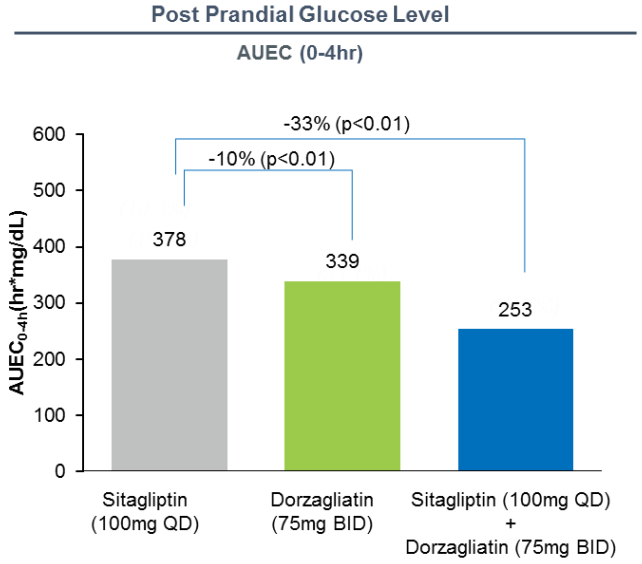
Dorzagliatin Has Demonstrated Successful Combination Potential with other Global Top Oral Anti-Diabetic Drugs

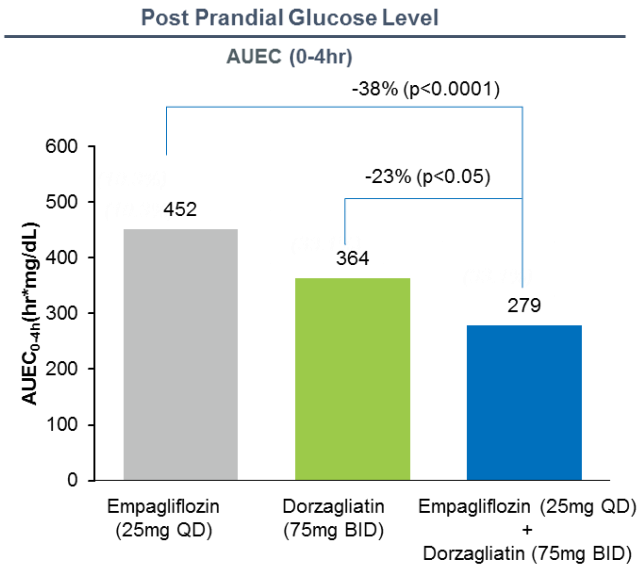
- No drug-drug interaction observed in Phase I trials in USA with sitagliptin (DPP-4 inhibitor) and empagliflozin (SGLT-2 inhibitor)

- **Significant synergies demonstrated in glycemic control and improvement of beta cell function**
  - Data demonstrating dorzagliatin stimulates GLP-1 release in T2D patients, increasing circulating active GLP-1 when used in combination with sitagliptin
  - In both trials, the combined use of sitagliptin or empagliflozin in combination with dorzagliatin increases insulin secretion as measured by C-peptide and reduces glucose over using each of the drugs alone



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.

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Dorzagliatin has potential to be the ONLY oral anti-T2D therapeutic for select DKD patients

Drug use guidelines for T2D patients with diabetic kidney disease		
Dorzagliatin		*Oral*
Metformin		
DPP-4		
SGLT-2		
GLP-1		*Injectibles*
Insulin		

 No dose adjustment required

 Dose adjustment required

 Contraindicated

- Patients with diabetic kidney disease make **up 20-40% of the total** T2D patient population globally
- In China, **patients with moderate, severe, and end-stage chronic kidney disease comprise 21.9%** of the T2D patients

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 in subjects treated with 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**.

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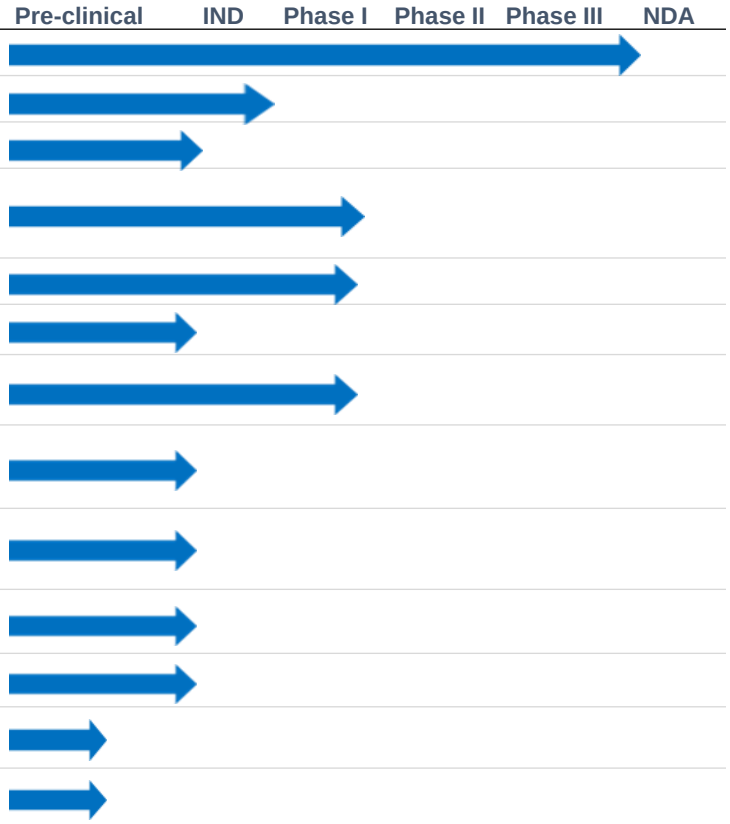
Outlook

Hua Medicine R&D Pipeline

Product Name	Indication	Development phase
Dorzagliatin HMS5552	T2D	NDA Filing (China)
	DKD	Phase I enabling
	T1D	IND-enabling
HMSFDC 6857 Dorzagliatin + Metformin	T2D	Phase I ready
HMSFDC 6868 Dorzagliatin +Sitagliptin	T2D	Phase I ready
	Insulin Sparing	IND-enabling
HMSFDC 5868 Dorzagliatin +Empagliflozin	T2D CVR	Phase I ready
HMSFDC 5688 Dorzagliatin +pioglitazone	NASH	IND-enabling
HMS 5678 Dorzagliatin + GLP-1	Alzheimer Disease	IND-enabling
HMS 6789 Dorzagliatin + Insulin	Late Stage T2D Insulin sparing	IND-enabling
	T1D	IND-enabling
mGLUR5 NAM	PD-LID	Pre-clinical
Fructose Kinase Inhibitor	Metabolic Disease	Pre-clinical



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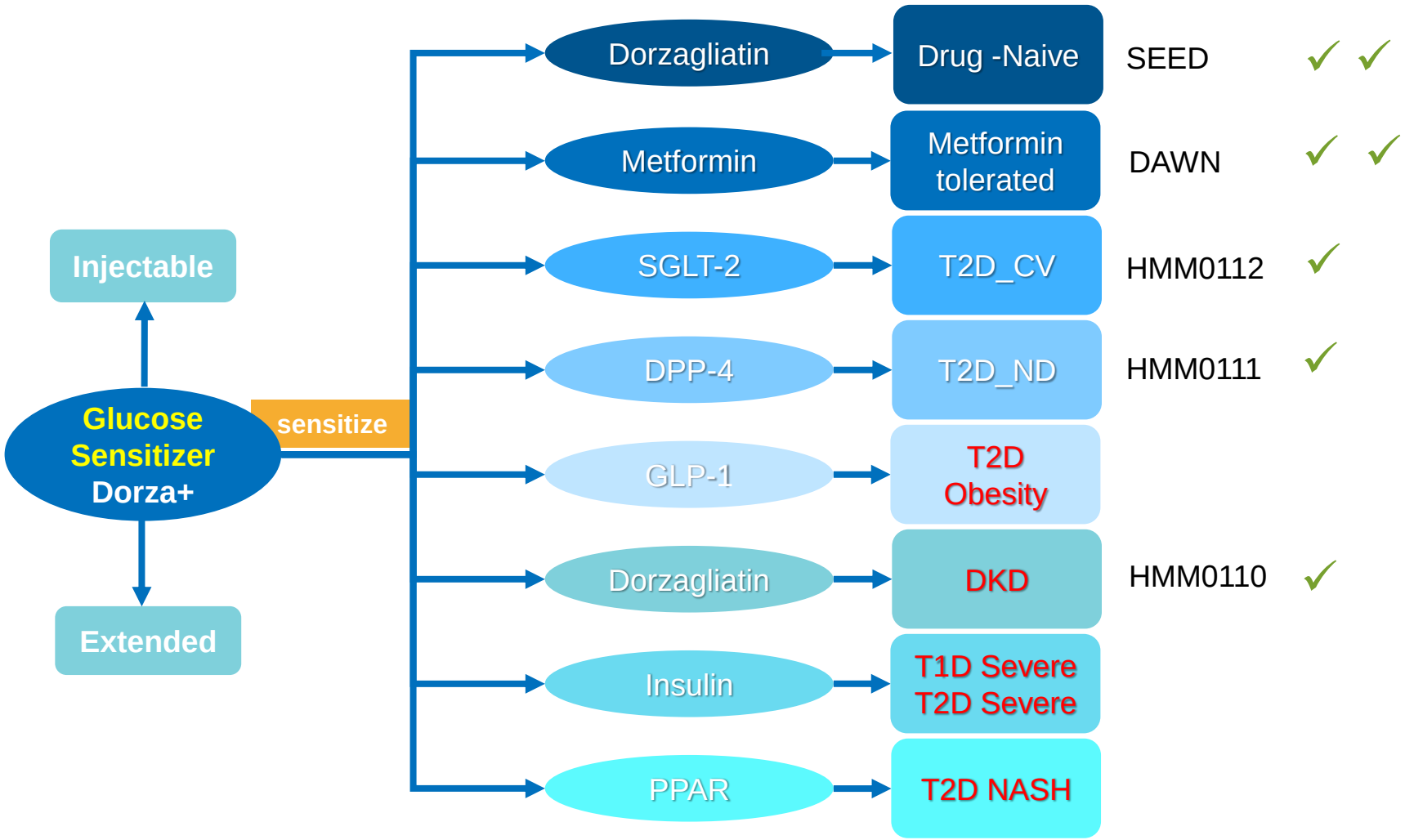
New FIC Product, New Medication, New Opportunity



Fix Sensor, Repair Homeostasis and Treat Root Cause of Diseases

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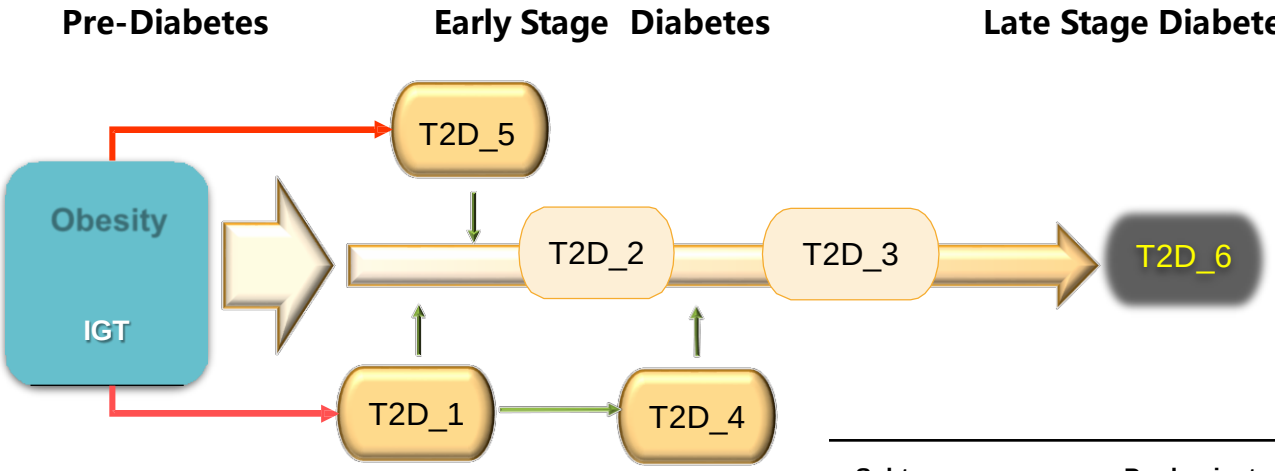
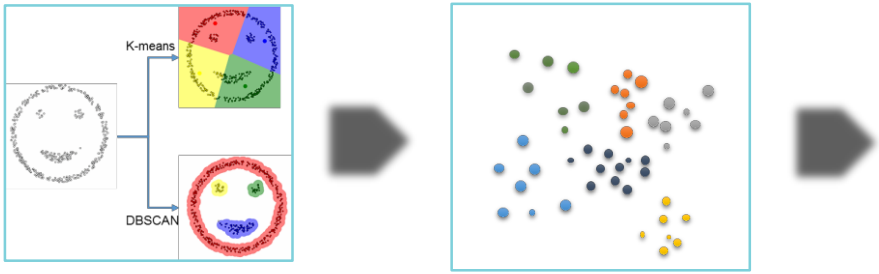
AI for Diabetes Care

- Clinical data from China clinical studies
- Unbiased machine learning
- Disease relevant descriptions
- Algorism for personalized treatment





Subtype	Predominate Influential Factor
T2D_1	Severe Impaired Glucose Tolerance
T2D_2	Impaired β-cell Function
T2D_3	Severe Impaired β-cell Function
T2D_4	Impaired Glucose Tolerance with aging
T2D_5	Severe Insulin Resistance with obesity
T2D_6	Impaired β-cell Function and Severe insulin resistance

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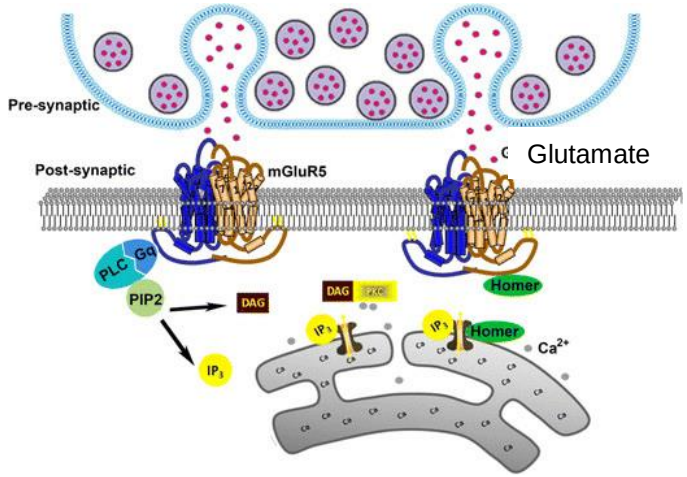
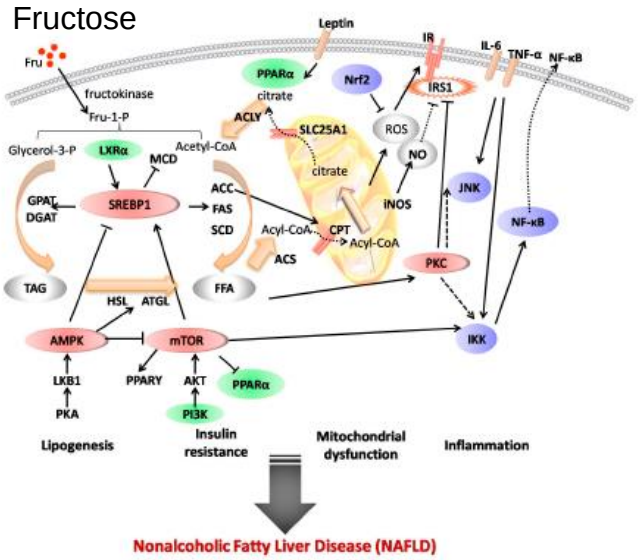
New Opportunity in Homeostasis Control



mGLUR5 NAM

Parkinson's
Levodopa-induced
dyskinesia



Fructose kinase Inhibitor

Metabolic Syndrome

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Financial Review

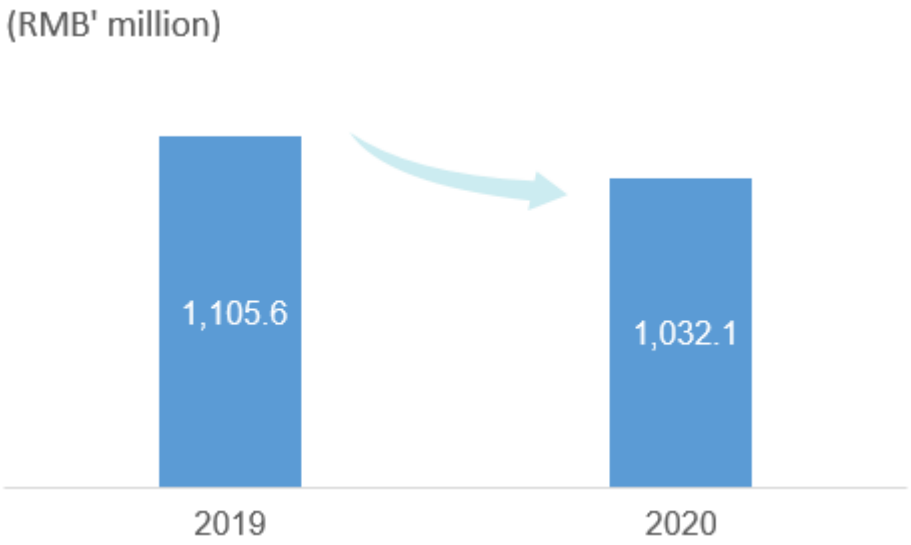
Financial Summary

Cash Balance: RMB1,032.1 million of cash at 12/31/2020 vs. 1,105.6 million at 12/31/2019.

Total cash decrease of RMB73.5 million, consisted of

- Net cash used in operating activities was RMB20.9 million – accounts for RMB 300 million up front payment from Bayer
- Net cash used in investing activities was RMB14.1 million
- Net cash used in financing activities was RMB7.3 million
- Net effect of exchange rate changes was RMB31.2 million

Net cash used in operation activities of RMB20.9 million mainly includes cash payment of RMB 161.4 million for the research and development activities and of RMB159.5 million for the administrative activities, adjusted for the received upfront payment of RMB300.0 million from Bayer for commercialization and strategic partnership.



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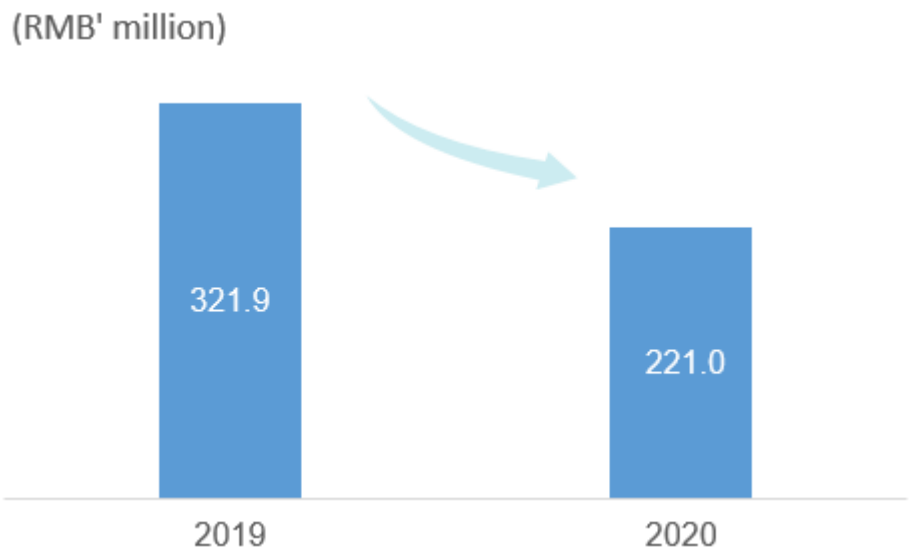
Financial Summary- continued

Loss before tax of RMB393.1 million in the year of 2020 vs. RMB425.3 million in the year of 2019

Research and development expenses of RMB221.0 million in the year of 2020 vs. RMB321.9 million in the year of 2019

- a decrease of RMB78.9 million for dorzagliatin clinical trials, which was primarily attributable to decreased costs associated with the last patient out of the 52-week study period of SEED/HMM0301 in March 2020 and DAWN/HMM0302 in September 2020
- a decrease of RMB23.3 million in chemical, manufacturing, and control (CMC) expenses, which was primarily attributable to scaling-up development, method validation and process validation for spray dried powder (SDP) manufacturing and drug product manufacturing completed in 2019



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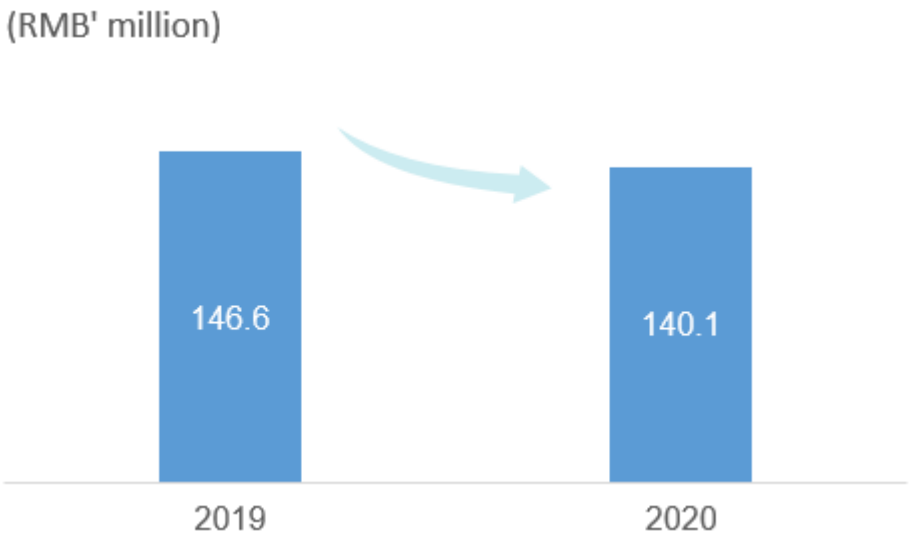
Financial Summary- continued

Administrative expenses of RMB140.1 million in the year of 2020 vs. RMB146.6 million in the year of 2019

- decrease in labour costs which was attributable to the decrease of RMB10.6 million in share-based payment under the accelerated amortization method
- decrease of RMB4.2 million in travelling costs due to the impact of COVID-19 and decrease of RMB2.4 million in recruitment cost based on the recruitment plan
- Adjusted for the rental increase of RMB7.4 million with entering into the tenancy agreement for leasing office building in December, 2019 to establish the Global Operation Headquarters and Research and Development Center in China and Research and Development Center in China and low-value IT consumable expenditure of RMB 1.2million for the office building incurred in the year of 2020.



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Hua Medicine – A Global First-in-Class Biotech

Hua Medicine

Li Chen
CEO & CSO

Bob Nelsen
Chairman

Roche

Arch Ventures

JUNO THERAPEUTICS
DENALI THERAPEUTICS
GRAIL
UNITY BIOTECHNOLOGY
gossamerbio

Arch Ventures | Fidelity INVESTMENTS | venrock

SAIL | Ge Li | J Baldwin

Founding Investors

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 Healthcare China**
- **Met Primary Endpoint** in both pivotal Phase III monotherapy and combination with metformin trials at 24-week period, for China regulatory approval purposes; successfully **completed 52-week monotherapy trial** demonstrating sustained & comparable best-in-therapeutics efficacy and safety profile at 52-weeks
- **First-in-Class (GKA) drug** to significantly and sustainably reduce HbA1c safely
- **First Novel Concept** addressing impaired glucose homeostasis - the underlying cause of T2D
- Demonstrated viability in combination with DPP-4 inhibitor & SGLT-2 inhibitor
- Suitable for T2D patients with chronic kidney disease
- **Massive market opportunity** – global T2D population is 453 mm (120 mm in China alone)
- **RMB 1,032.1mn cash** as of December 31, 2020

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