



Hua Medicine  
华领医药



**2022 Interim Results  
Presentation**

August 2022

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# Company Overview

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# Hua Medicine: A Roadmap to Global First-In-Class

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- **June 2010:** Dr. Li Chen served as CEO
- **June 2011:** Hua Medicine (Shanghai) Ltd. established, initiates R&D operations
- **Feb. 2012:** Initiated glucokinase activator (GKA) program
- **Sep. 2012:** Submitted IND, initiated Phase I clinical study in China in September 2013
- **Sep. 2016:** Successfully completed Phase II clinical trial; validates the scientific concept of dorzagliatin in the treatment of T2D
- **Sep. 2018:** IPO on HKEX
- **Aug. 2020:** Signed commercialization agreement and strategic partnership with Bayer for investigational first-in-class novel diabetes treatment dorzagliatin in China
- **Sep. 2020:** Successfully completed Phase III trials: SEED and DAWN
- **Apr. 2021:** NDA for dorzagliatin for the treatment of T2D was accepted by the China NMPA
- **Feb. 2021:** Shanghai Hua Medicine Biotechnology Ltd. established
- **June 2021:** Presentation at 2021 ADA: dorzagliatin can regulate GLP-1 release in T2D patients
- **Sep. 2021:** Signed a supply chain strategic cooperation agreement with Sinopharm
- **Sep. 2021:** Announced positive results for DREAM study: remission rate reached 65.2% within 1 year after drug withdrawal
- **Feb. 2022:** Announced supply agreement with WuXi STA for commercial manufacturing of dorzagliatin
- **May 2022:** Published two peer-reviewed papers in *Nature Medicine* on the results of the Phase III trials of dorzagliatin
- **June 2022:** 2022 ADA conference 3 presentations on DREAM, SENSITIZE, and IGI of Dorzagliatin

# 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
- Former Adjunct professor at Tongji University, Ph D advisor



**George Lin J.D**  
*EVP, CFO*



**Yi Zhang, Ph.D., MD**  
*SVP, Pharma Development,  
Chief Medical Officer*



**Jin She, Ph.D.**  
*SVP, CMC  
Chief Manufacture Officer,*



**FuxingTang, Ph.D.**  
*President Hua USA, CTO*



**Yilei Fu, BS, MBA**  
*SVP, Quality Assurance  
Chief Quality Officer*



**Di Hong, DBA**  
*VP, Corp Alliance and Operation*

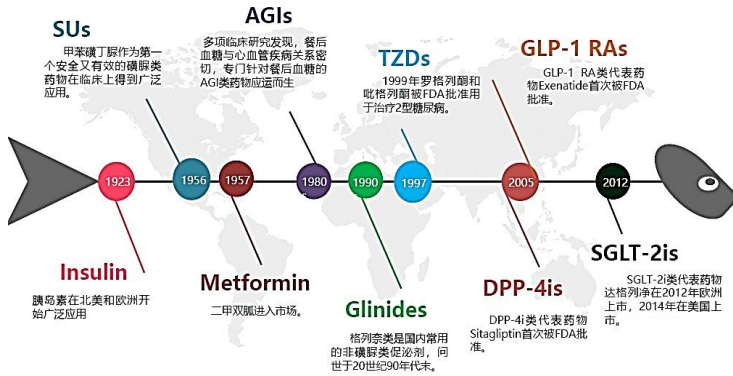


**Qing Dong, BP**  
*VP, Pharmaceutical  
Commercialization*



# Global Unmet Medical Needs in Glycemic Control

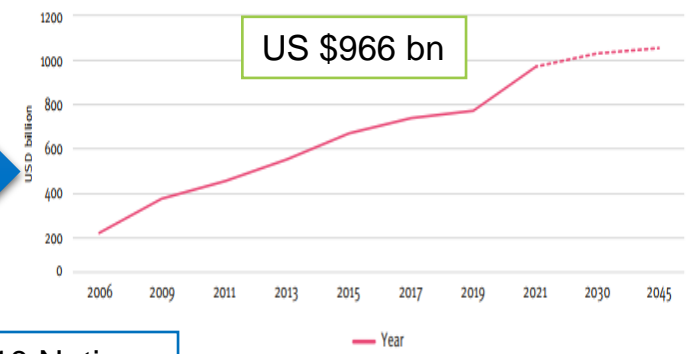
## 9 Classes of Drugs



IDF 2021

**537 Mn Diabetes  
Many  
Complications**

Figure 3.14 Total diabetes-related health expenditure for adults (20-79 years) with diabetes from 2006 to 2045

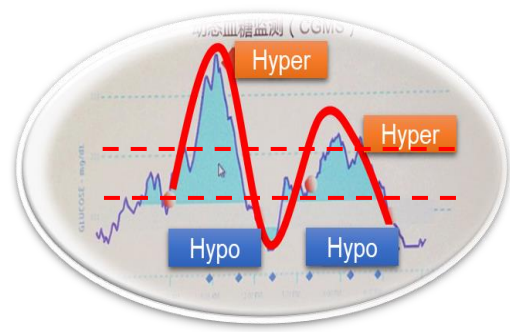


新近: 2型糖尿病的药物治疗(1). 临床药物学杂志, 2015, 13(3): 18-22.  
Bae E J. DPP-4 inhibitors in diabetic complications: role of DPP-4 beyond glucose control[J]. Archives of pharmaceutical research, 2016, 33(8): 1114-1128.  
Knop F K, Branden A, Vilsbøll T. Exenatide: pharmacokinetics, clinical use, and future directions[J]. Expert opinion on pharmacotherapy, 2012, 13(6): 555-571.

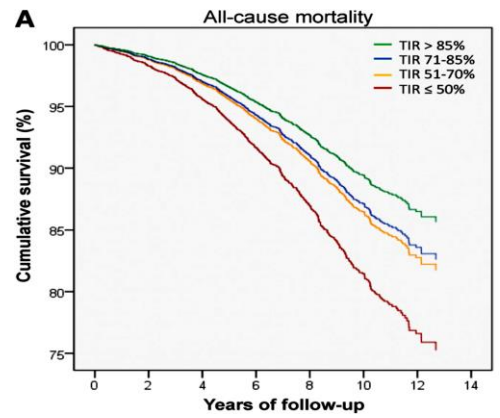
## Top 10 Nations

Rank	Country or territory	Total diabetes-related health expenditure in 2021 (USD billion) in adults (20-79 years)
1	United States of America	379.5
2	China	165.3
3	Brazil	42.9
4	Germany	41.3
5	Japan	35.6
6	United Kingdom	23.4
7	France	22.7
8	Mexico	19.9
9	Spain	15.5
10	Italy	14.7

## Economic Burden



## Lost Glucose Homeostasis



## TIR in Diabetes Survival

Source: Cheng YY, Chen L. Global J Obesity, Diabetes and Metabolic Syndrome 2020, 7: 018-023  
Source: IDF DIABETES ATLAS Tenth edition 2021

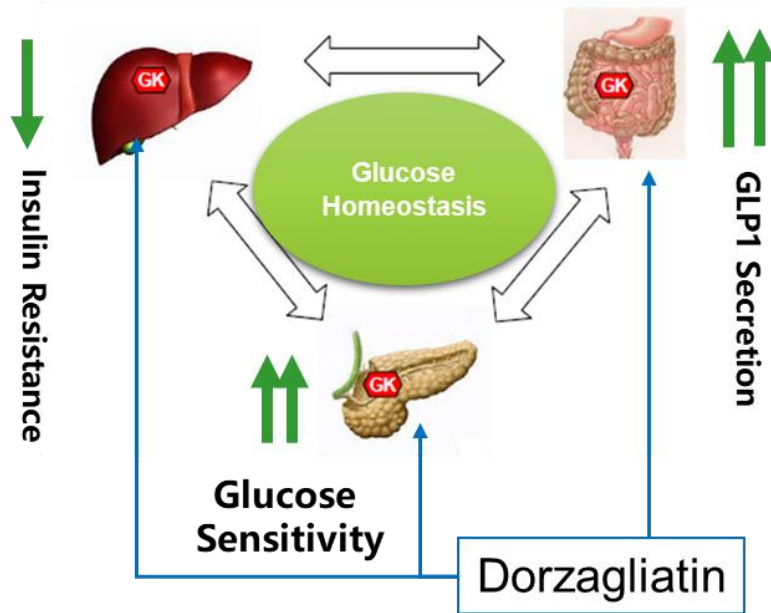
# Dorzagliatin – A Differentiated First-In-Class Antidiabetic Drug Advance Diabetes Care Globally



Glucokinase (GK) as glucose sensor plays central role in glucose homeostasis  
Loss of GK sensor function leads to impaired glucose sensitivity and diabetes

Dorzagliatin improves glucose sensitivity and beta cell function as novel mechanism to treat diabetes

- In clinical trials - Dorzagliatin improves  $\beta$ -cell function in T2D in China, and repairs GLP-1 secretion in obese T2D patients in US
- Phase 3 SEED, DAWN studies demonstrated the potential for best homeostasis control for drug naïve and metformin-tolerant T2D patients in China
- Diabetes remission achieved in Dorzagliatin treated drug naïve T2D patients in the DREAM study



# SEED and DAWN Results on Nature Medicine

- President Dalong Zhu, Ex-President Wenyang Yang of Chinese Diabetes Society led SEED and DAWN studies and as 1<sup>st</sup> authors in back-to-back Nature Medicine (2021 IF: 87.24) on 12<sup>th</sup> May 2022
- Dr John Buse, former ADA president: A New Class of Drug in Diabetes Toolbox (NMED)
- The news of SEED and DAWN publication in NM were reported or forwarded by multiple media. In particular, it was reported 6 times in 3 days by relevant platforms of the mainstream media People's Daily (人民日报).

南京鼓楼医院 **朱大龙** 教授  
中日友好医院 **杨文英** 教授  
领衔研究

## 多格列艾汀 Dorzagliatin

### 2型糖尿病治疗研究SEED & DAWN 同时荣登 Nature Medicine 杂志!

• 影响因子: **87.24**

### 首创全新机制 葡萄糖激酶激活剂 (GKA) III期临床

- 迅速起效, 稳定控制餐后血糖
- 长期治疗显著改善β细胞功能
- 24周治疗HbA1c降低均>1%
- 52周低血糖发生率低

谨献给葡萄糖激酶研究的先驱  
**Franz M. Matschinsky** 教授

**ARTICLES**  
nature medicine

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

Dalong Zhu<sup>1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,141,142,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,204,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,280,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,309,310,311,312,313,314,315,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,603,604,605,606,607,608,609,610,611,612,613,614,615,616,617,618,619,620,621,622,623,624,625,626,627,628,629,630,631,632,633,634,635,636,637,638,639,640,641,642,643,644,645,646,647,648,649,650,651,652,653,654,655,656,657,658,659,660,661,662,663,664,665,666,667,668,669,670,671,672,673,674,675,676,677,678,679,680,681,682,683,684,685,686,687,688,689,690,691,692,693,694,695,696,697,698,699,700,701,702,703,704,705,706,707,708,709,710,711,712,713,714,715,716,717,718,719,720,721,722,723,724,725,726,727,728,729,730,731,732,733,734,735,736,737,738,739,740,741,742,743,744,745,746,747,748,749,750,751,752,753,754,755,756,757,758,759,760,761,762,763,764,765,766,767,768,769,770,771,772,773,774,775,776,777,778,779,780,781,782,783,784,785,786,787,788,789,790,791,792,793,794,795,796,797,798,799,800,801,802,803,804,805,806,807,808,809,810,811,812,813,814,815,816,817,818,819,820,821,822,823,824,825,826,827,828,829,830,831,832,833,834,835,836,837,838,839,840,841,842,843,844,845,846,847,848,849,850,851,852,853,854,855,856,857,858,859,860,861,862,863,864,865,866,867,868,869,870,871,872,873,874,875,876,877,878,879,880,881,882,883,884,885,886,887,888,889,890,891,892,893,894,895,896,897,898,899,900,901,902,903,904,905,906,907,908,909,910,911,912,913,914,915,916,917,918,919,920,921,922,923,924,925,926,927,928,929,930,931,932,933,934,935,936,937,938,939,940,941,942,943,944,945,946,947,948,949,950,951,952,953,954,955,956,957,958,959,960,961,962,963,964,965,966,967,968,969,970,971,972,973,974,975,976,977,978,979,980,981,982,983,984,985,986,987,988,989,990,991,992,993,994,995,996,997,998,999,1000</sup>

**ARTICLES**  
nature medicine

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

Wenyang Yang<sup>1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,141,142,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,204,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,280,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,309,310,311,312,313,314,315,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,603,604,605,606,607,608,609,610,611,612,613,614,615,616,617,618,619,620,621,622,623,624,625,626,627,628,629,630,631,632,633,634,635,636,637,638,639,640,641,642,643,644,645,646,647,648,649,650,651,652,653,654,655,656,657,658,659,660,661,662,663,664,665,666,667,668,669,670,671,672,673,674,675,676,677,678,679,680,681,682,683,684,685,686,687,688,689,690,691,692,693,694,695,696,697,698,699,700,701,702,703,704,705,706,707,708,709,710,711,712,713,714,715,716,717,718,719,720,721,722,723,724,725,726,727,728,729,730,731,732,733,734,735,736,737,738,739,740,741,742,743,744,745,746,747,748,749,750,751,752,753,754,755,756,757,758,759,760,761,762,763,764,765,766,767,768,769,770,771,772,773,774,775,776,777,778,779,780,781,782,783,784,785,786,787,788,789,790,791,792,793,794,795,796,797,798,799,800,801,802,803,804,805,806,807,808,809,810,811,812,813,814,815,816,817,818,819,820,821,822,823,824,825,826,827,828,829,830,831,832,833,834,835,836,837,838,839,840,841,842,843,844,845,846,847,848,849,850,851,852,853,854,855,856,857,858,859,860,861,862,863,864,865,866,867,868,869,870,871,872,873,874,875,876,877,878,879,880,881,882,883,884,885,886,887,888,889,890,891,892,893,894,895,896,897,898,899,900,901,902,903,904,905,906,907,908,909,910,911,912,913,914,915,916,917,918,919,920,921,922,923,924,925,926,927,928,929,930,931,932,933,934,935,936,937,938,939,940,941,942,943,944,945,946,947,948,949,950,951,952,953,954,955,956,957,958,959,960,961,962,963,964,965,966,967,968,969,970,971,972,973,974,975,976,977,978,979,980,981,982,983,984,985,986,987,988,989,990,991,992,993,994,995,996,997,998,999,1000</sup>

**news & views**

### 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

For nearly three decades, scientists have searched for an orally active insulin-sensitizing agent of the glucokinase (GKA) for the treatment of diabetes. Because of the experimental difficulties associated with this class of drugs, the first report of a potential GKA was published in 1992, and was followed by more than 30 years and considerable investment.

Grid of 12 screenshots showing media coverage of the SEED and DAWN studies across various platforms including Weibo, People's Daily, and other news outlets.

序号	人民日报平台	标题
1		荣登顶刊! 中国原研全球首创降糖药新成果来了
2	人民日报健康客户端	人民端学术频道首页推荐位 历时10年! 我国原研全球首创糖尿病新药登上顶刊
3		中国原创糖尿病新药研究成果登上《自然-医学》
4		人民端首页推荐位第一条 多格列艾汀三期结果发布: 为2型糖尿病治疗提供新靶点
5	今日头条 人民康养	朱大龙教授学术论文登上国际顶级医学期刊《自然-医学》
6	微博人民康养	喜讯! 南京鼓楼医院朱大龙教授学术论文登上国际顶级医学期刊《自然-医学》



# Connect with Medical and Academic Community

- Dorzagliatin *Nature Medicine* Symposium was held on 13<sup>th</sup> May. In particular, Prof. Kaixian Chen, Prof. Zhiyi He and Prof. Xiaoming Zhu as the industry leader recognized Dorzagliatin as a break through in GKA drug development and a major achievement in China drug discovery.
- Leading KOLs in Dorzagliatin, Prof Dalong Zhu, Wenying Yang and Xiaoying Li presented discovery stories
- SEED and DAWN Publication Sharing meeting with 80 Co-Authors on 28<sup>th</sup> May
- DREAM Presentation shared with investigators at 5 clinical sites on 5<sup>th</sup> June.

**Nature Medicine 《自然-医学》**  
杂志中国重要临床研究暨多格列艾汀中国III期临床研究成果分享会

多位专家肖像及姓名：陈凯先、何志毅、朱小明、朱达龙、杨文莹、李 Xiaoying 等。

**多格列艾汀SEED&DAWN研究**  
**Nature Medicine** 论文分享会  
主办单位：华领医药技术(上海)有限公司

线上直播：腾讯视频 166-261-491  
中国·上海 2022年5月28日

**DoRzagliatin Effect in Diabetes**

Abstract: This study evaluated the efficacy and safety of DoRzagliatin in patients with type 2 diabetes mellitus (T2DM) who were inadequately controlled on oral glucose-lowering therapy (OGLT). The study was a randomized, double-blind, placebo-controlled, parallel-group trial. The primary endpoint was the change in HbA1c from baseline to week 24. Secondary endpoints included changes in fasting plasma glucose (FPG), postprandial glucose (PPG), and weight. The study was conducted at multiple sites in China.

Figure 1 Study Design  
Figure 2 Baseline Characteristics  
Figure 3 Change of HbA1c from baseline to week 24

Poster: 115-LB, American Diabetes Association's 82<sup>nd</sup> Scientific Sessions, June 3-7, 2022 in New Orleans, Louisiana, USA. Presenter contact information: Jianhua Ma, majinhuo2022@126.com

南京鼓楼医院  
河科大一附院内分泌代谢中心  
【健康荆州】我国全球首创糖尿病新药即将上市，荆医专家参与试验

**多格列艾汀 DREAM 研究**

首个葡萄糖激酶激活剂促进糖尿病缓解研究  
亮相第82届ADA科学会议

点燃糖尿病患者血糖管理新希望，期待精彩结果学术交流！

暨报展示时间：6月6日  
暨报编号：115-LB

研究单位：  
南京市第一医院  
长江大学荆州医院  
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济南市中心医院  
山西医科大学第一医院

- Dorzagliatin has been included into a new Expert Opinions on <Evaluation and Protection of beta cell Function in T2D Patients> published on 20<sup>th</sup> June. The latest SEED and DAWN results and publications were cited in the Opinions.
- Dorzagliatin rescues insulin secretion in rat  $\beta$ -cell, and improves HOMA2- $\beta$  in type 2 diabetes patients either drug naïve or metformin tolerated.

中华糖尿病杂志 2022年6月第14卷第6期 Chin J Diabetes Mellitus, June 2022, Vol. 14, No. 6

· 533 ·

· 规范与指南 ·

## 2型糖尿病胰岛 $\beta$ 细胞功能评估与保护 临床专家共识

中华医学会糖尿病学分会胰岛 $\beta$ 细胞学组 江苏省医学会内分泌学分会

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【摘要】 胰岛 $\beta$ 细胞功能缺陷是2型糖尿病的基本病理生理学特征之一, 正确评估胰岛 $\beta$ 细胞功能对于糖尿病的诊断和治疗具有重要价值, 保护胰岛 $\beta$ 细胞功能对于延缓2型糖尿病进展具有重要的临床意义。因此, 中华医学会糖尿病学分会胰岛 $\beta$ 细胞学组、江苏省医学会内分泌学分会组织专家撰写了《2型糖尿病胰岛 $\beta$ 细胞功能评估与保护临床专家共识》。本共识提出临床上可以通过基于血糖的方法简单评估, 或结合血糖、内源性胰岛素(C肽检测)的方法评估胰岛 $\beta$ 细胞功能; 强调通过减轻体重、及早干预并持久平稳控制血糖等代谢指标可有效保护胰岛 $\beta$ 细胞功能, 部分药物还可能具有降糖之外的改善胰岛 $\beta$ 细胞功能的作用。

【关键词】 胰岛 $\beta$ 细胞; 功能评估; 减轻体重; 胰岛素强化治疗; 专家共识



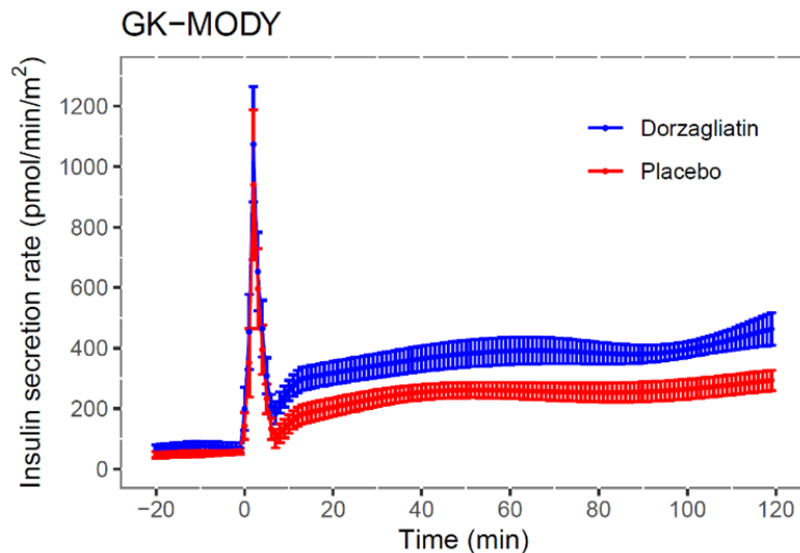
4. 葡萄糖激酶激活剂 (glucokinase activator, GKA): GKA多格列艾汀可通过葡萄糖浓度依赖性促进胰岛素分泌、抑制胰高糖素释放、促进GLP-1分泌和肝糖原合成, 维持人体血糖稳态。除了降糖作用外, 动物实验还显示多格列艾汀可以显著提升胰岛素阳性细胞数量, 修复胰岛 $\beta$ 细胞功能<sup>[75]</sup>。小样本的探索性研究显示, T2DM患者接受多格列艾汀治疗 28 d后, HOMA- $\beta$ 较基线提高36.31%~40.59%, C肽 30 min分泌功能动态参数提升24.66%~167.67%<sup>[76]</sup>。随机对照试验显示, 多格列艾汀可显著改善患者的葡萄糖处置指数和稳态模型评估胰岛素抵抗指数 (homeostasis model assessment insulin resistance, HOMA-IR)<sup>[77]</sup>。2项注册3期试验显示, 对于初治T2DM患者或二甲双胍足量稳定治疗仍血糖控制不佳的T2DM患者, 多格列艾汀可显著改善新的稳态模型评估胰岛 $\beta$ 细胞功能指数 (HOMA2- $\beta$ )<sup>[78-79]</sup>。

- [75] Wang P, Liu H, Chen L, et al. Effects of a novel glucokinase activator, HMS552, on glucose metabolism in a rat model of type 2 diabetes mellitus[J]. J Diabetes Res, 2017, 2017: 5812607. DOI: 10.1155/2017/5812607.
- [76] Zhu XX, Zhu DL, Li XY, et al. Dorzagliatin (HMS552), a novel dual-acting glucokinase activator, improves glycaemic control and pancreatic  $\beta$ -cell function in patients with type 2 diabetes: a 28-day treatment study using biomarker-guided patient selection[J]. Diabetes Obes Metab, 2018, 20(9): 2113-2120. DOI: 10.1111/dom.13338.
- [77] Zhu D, Gan S, Liu Y, et al. Dorzagliatin monotherapy in Chinese patients with type 2 diabetes: a dose-ranging, randomised, double-blind, placebo-controlled, phase 2 study[J]. Lancet Diabetes Endocrinol, 2018, 6(8):627-636. DOI: 10.1016/S2213-8587(18)30105-0.
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- [79] Yang W, Zhu D, Gan S, et al. Dorzagliatin add-on therapy to metformin in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled phase 3 trial[J]. Nat Med, 2022, 28(5): 974-981. DOI: 10.1038/s41591-022-01803-5.

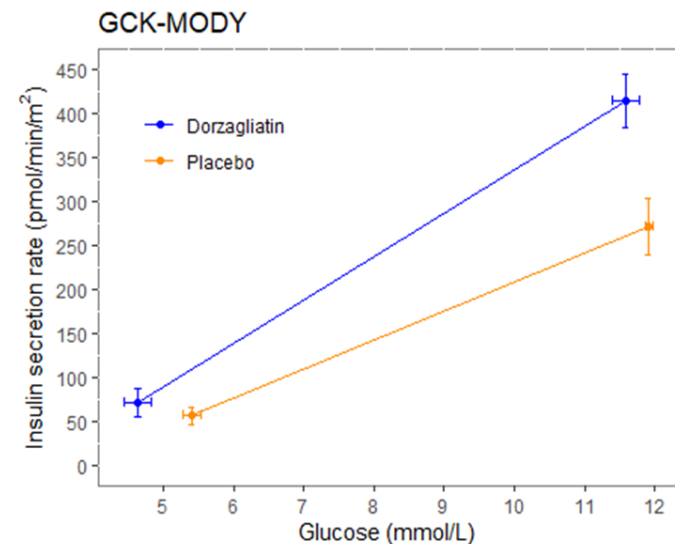
# Improve Glucose Sensitivity in MODY-2 Patients

- Heterozygous GCK mutation leads MODY-2 disease condition:
  - elevated blood glucose
  - reduced 2<sup>nd</sup> Phase insulin secretion
- A single dose of Dorzagliatin improves 2<sup>nd</sup> phase insulin secretion and improves the beta cell glucose sensitivity
- Proof of mechanism of action (MOA) of Dorzagliatin in hyperglycemic clamp study

## Significant Improves 2<sup>nd</sup> P Insulin Secretion



## Significant Improves Glucose Sensitivity

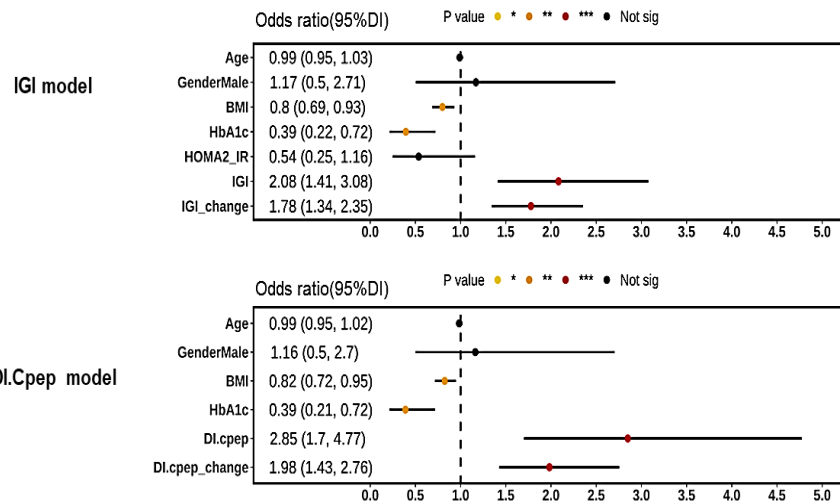


# Improvement of GSIS by Dorzagliatin Drives Glycemic Control

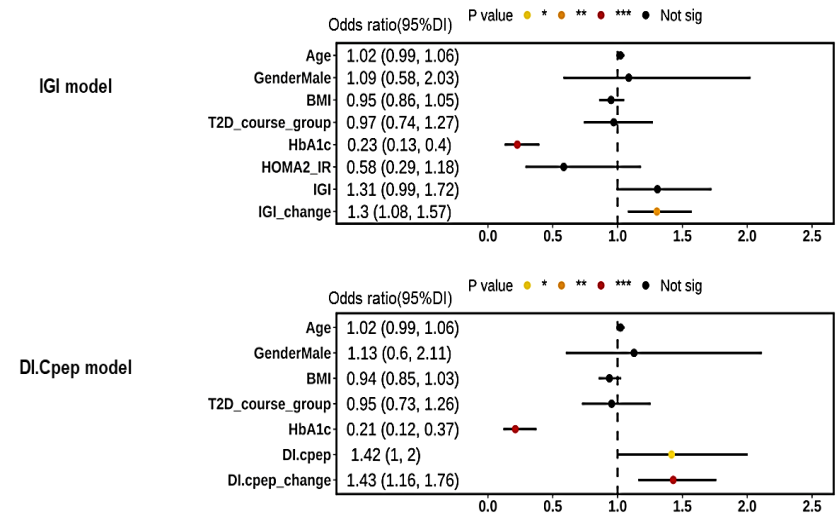


- Patients in SEED and DAWN achieved effective glycemic control in 43-45%
- Glycemic control (HbA1c < 7%) in SEED and DAWN is dependent on the early phase insulin secretion (IGI & DI) baseline status and improvement from baseline by Dorzagliatin treatment
- Improvement of disposition index (DI) and IGI are validated in large Ph III registration trials

## SEED: Drug Naïve T2D

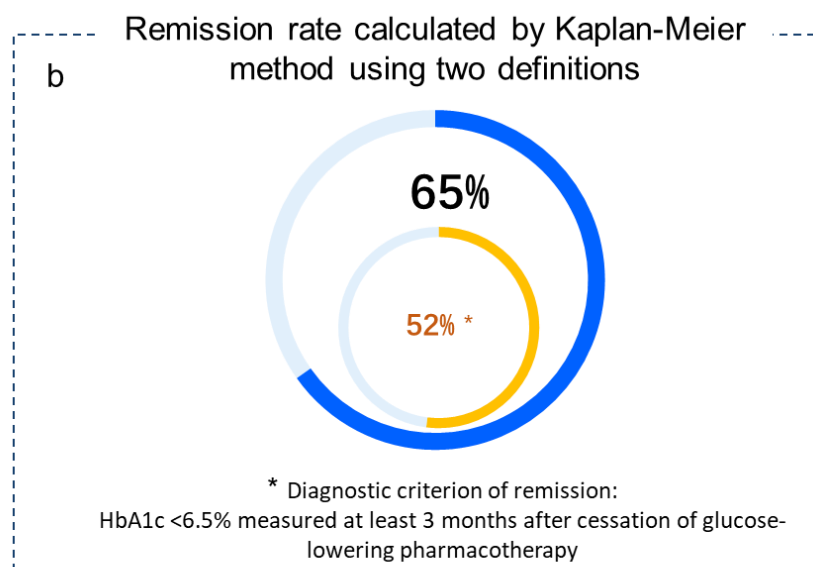
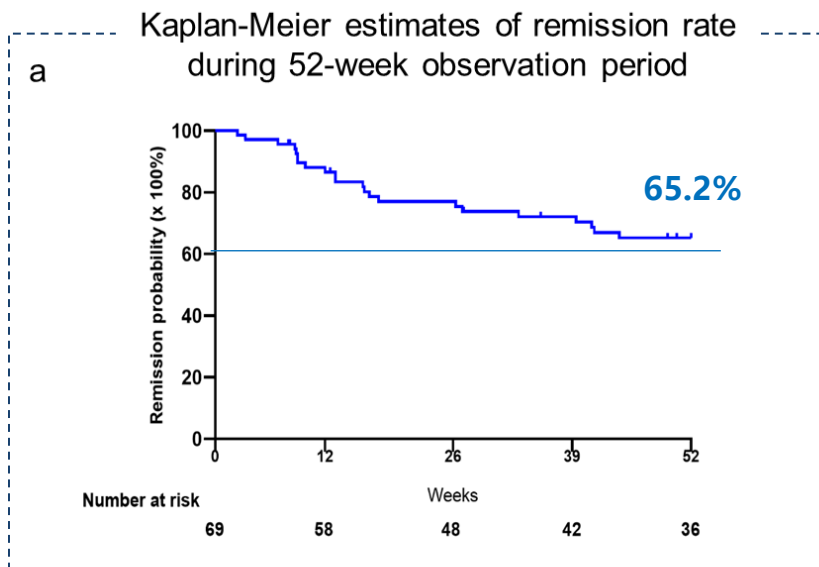
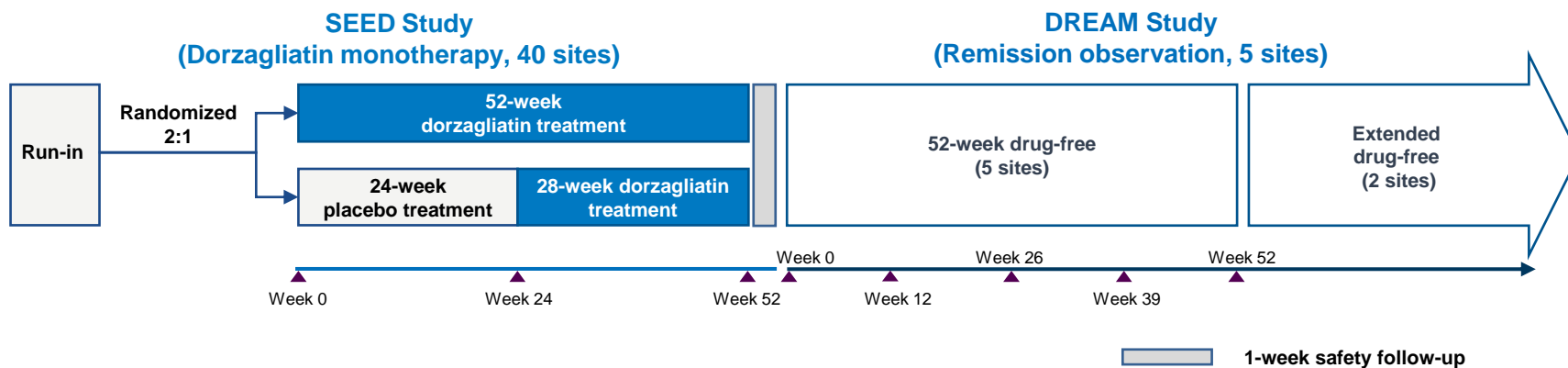


## DAWN: Metformin Failed T2D



Source: LG Feng, L Chen, WY Yang, 2022 ADA 117-LB; *Diabetes* 2022;71(Supplement\_1):117-LB

# Dorzagliatin Treatment Leads to Diabetes Remission



Source: JH Ma, et al 2022 ADA 115-LB; Diabetes 2022;71(Supplement\_1):115-LB

Source; Matthew C Riddle, et al. Diabetes Care. 2021 Aug 30;44(10):2438-2444.

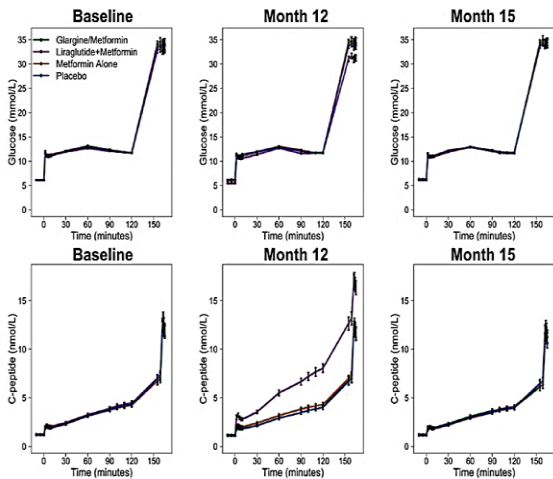
# Loss of GSIS function in $\beta$ -cells

## The root cause of T2D

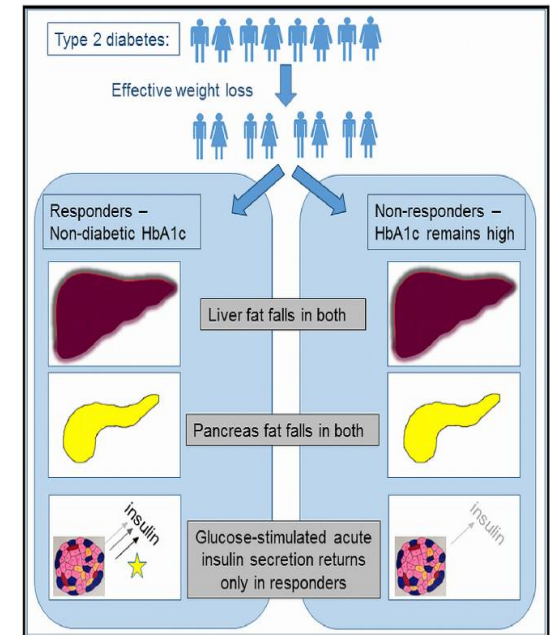
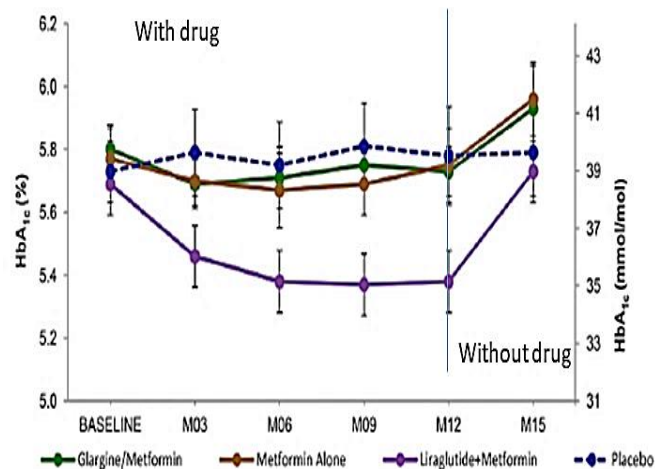


- RISE Study:** Drug naive T2D and IGT subjects were treated for 12 month with **Metformin (Red)**, **GLP-1 + Metformin (Purple)** and **Glargine + Metformin (Green)** did not show sustained improvement of beta cell function in 15 Month, 3 months after drug withdraw
- DiRECT Study:** Weight loss driven diabetes remission is dependent on restoring glucose stimulated acute-insulin secretion. That is, through external factors (weight loss) affecting the root of the disease (glucose-stimulated early-phase insulin secretion) to promote remission (Hb1Ac <6.5%) for 2 months (8 weeks)

Lack of insulin secretion enhancement by leading T2D drugs



Blood glucose well controlled by drugs (A1c < 6.0) but not when drug withdrawn

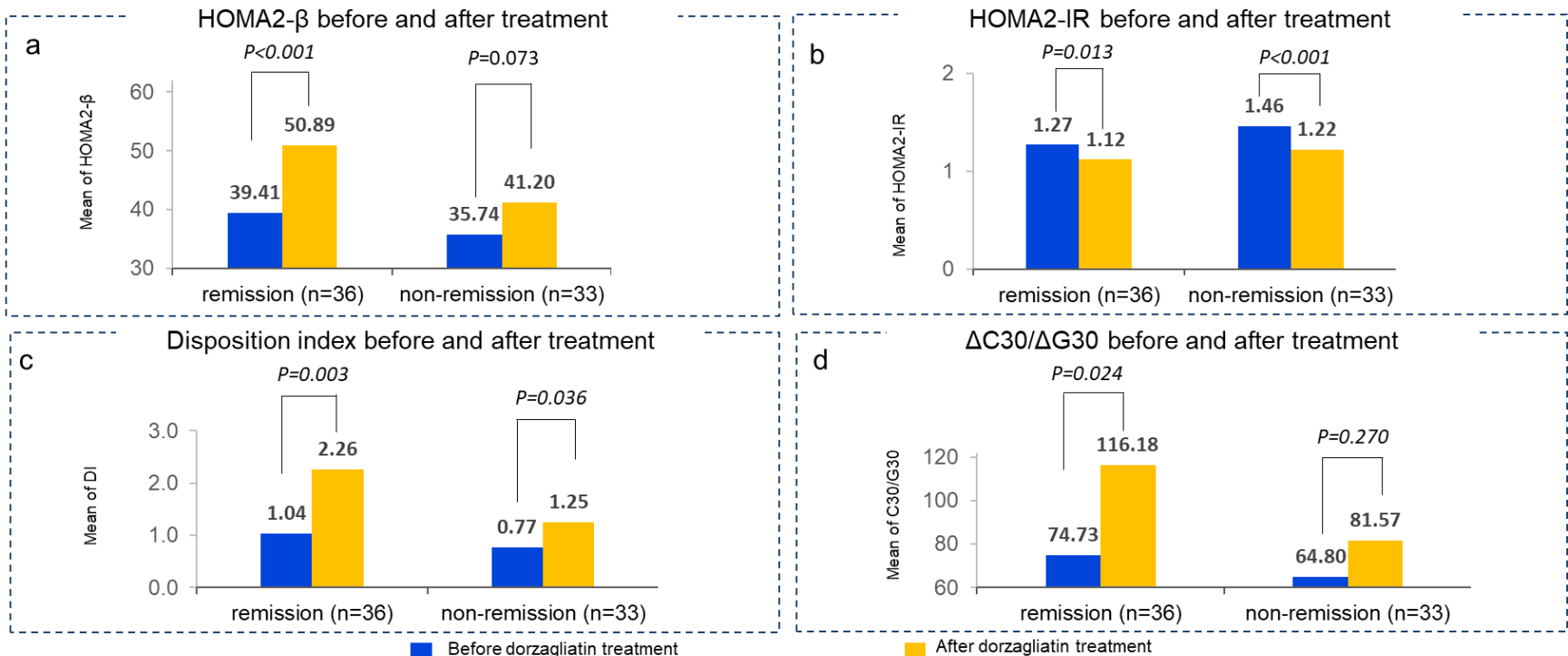


source: RISE Consortium. *Diabetes Care*. 2019 Sep;42(9):1742-1751. DiRECT *Cell Metabolism* 2018;28:547-556

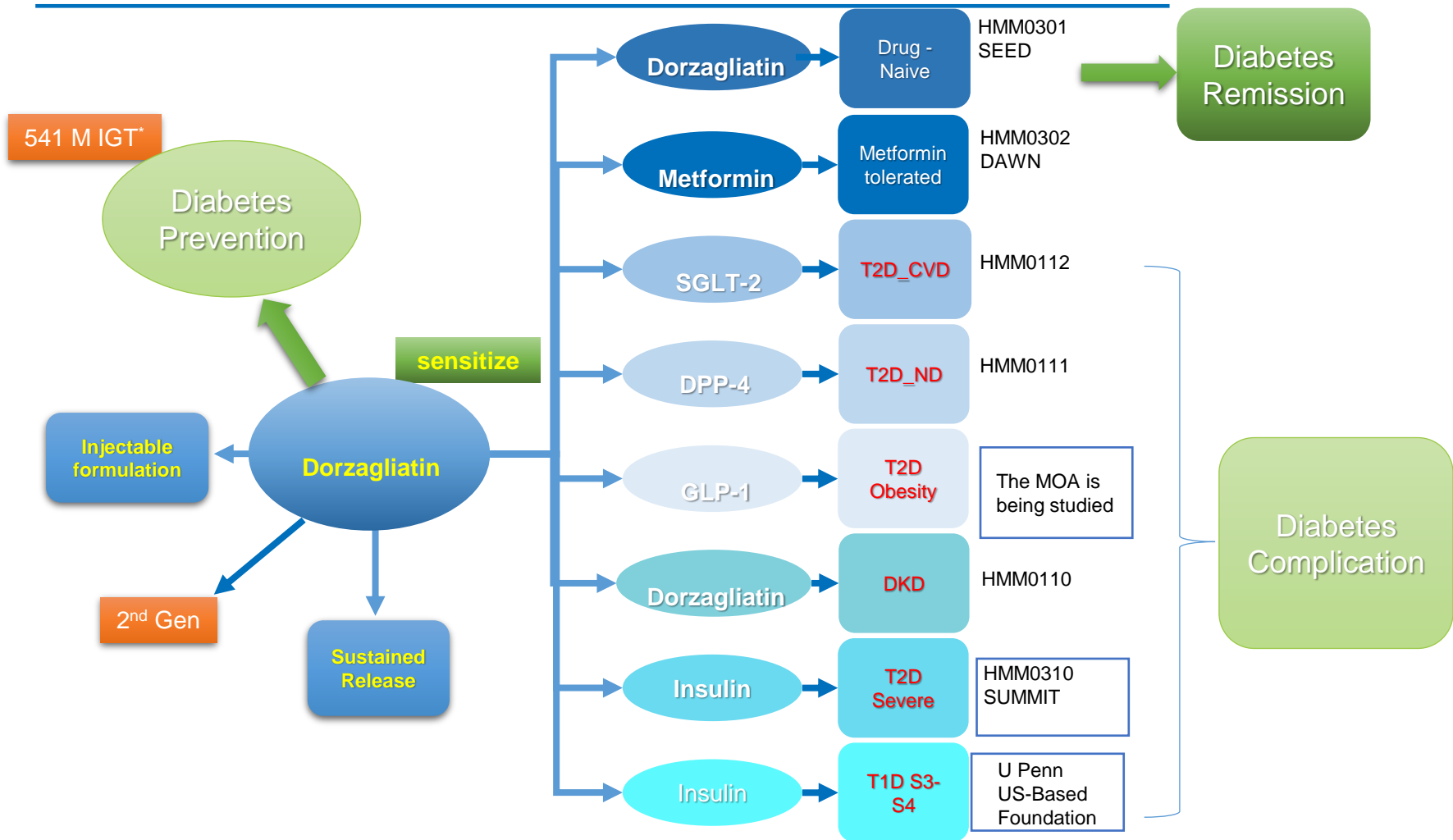
# Improved beta cell Function Drives Diabetes Remission



- HOMA2- $\beta$ , HOMA2-IR, disposition index (DI) and IGI ( $\Delta C30/\Delta G30$ ) have been improved in all participants after Dorzagliatin treatment during SEED study, which leads to 44% patients achieved glycemic control
- Improvement of HOMA2- $\beta$ , disposition index (DI) and IGI ( $\Delta C30/\Delta G30$ ) is statistically significant and in intensity in the remission group when compared between before and after treatment.



# Restore glucose homeostasis and advance diabetes care 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





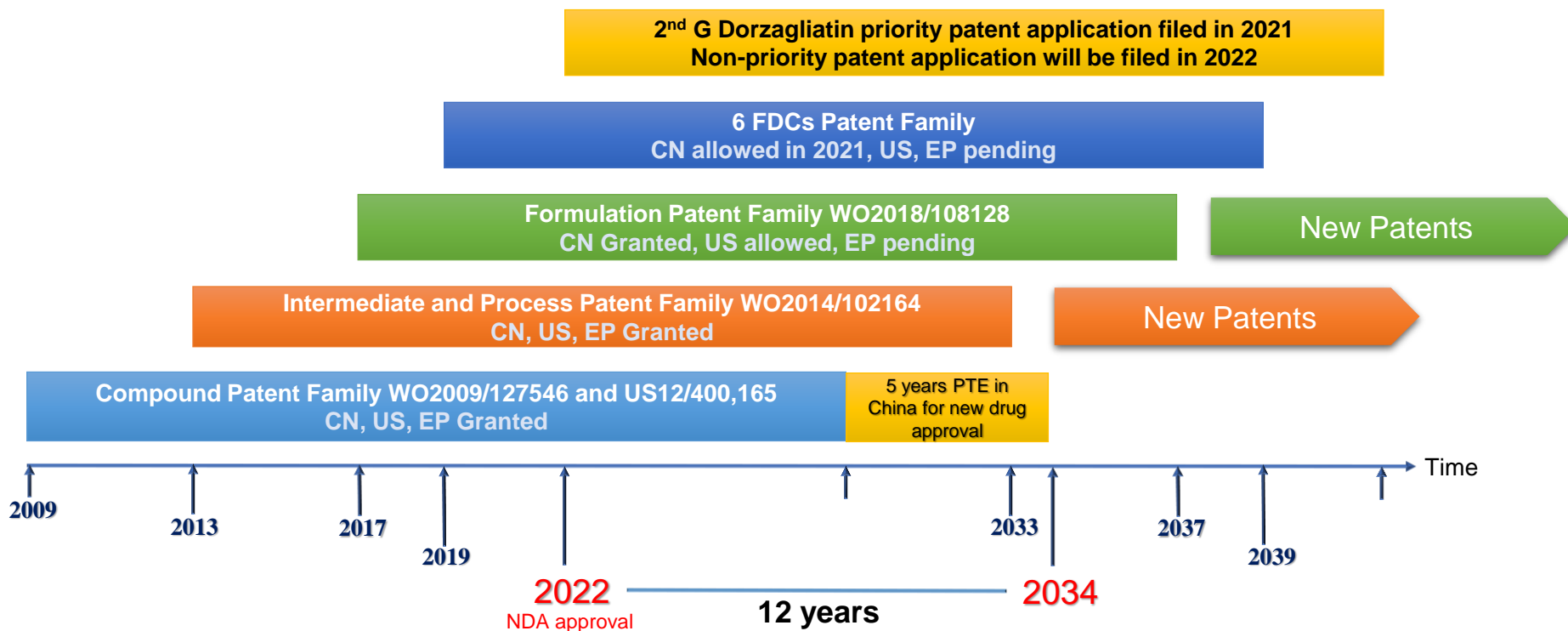
# Outlook

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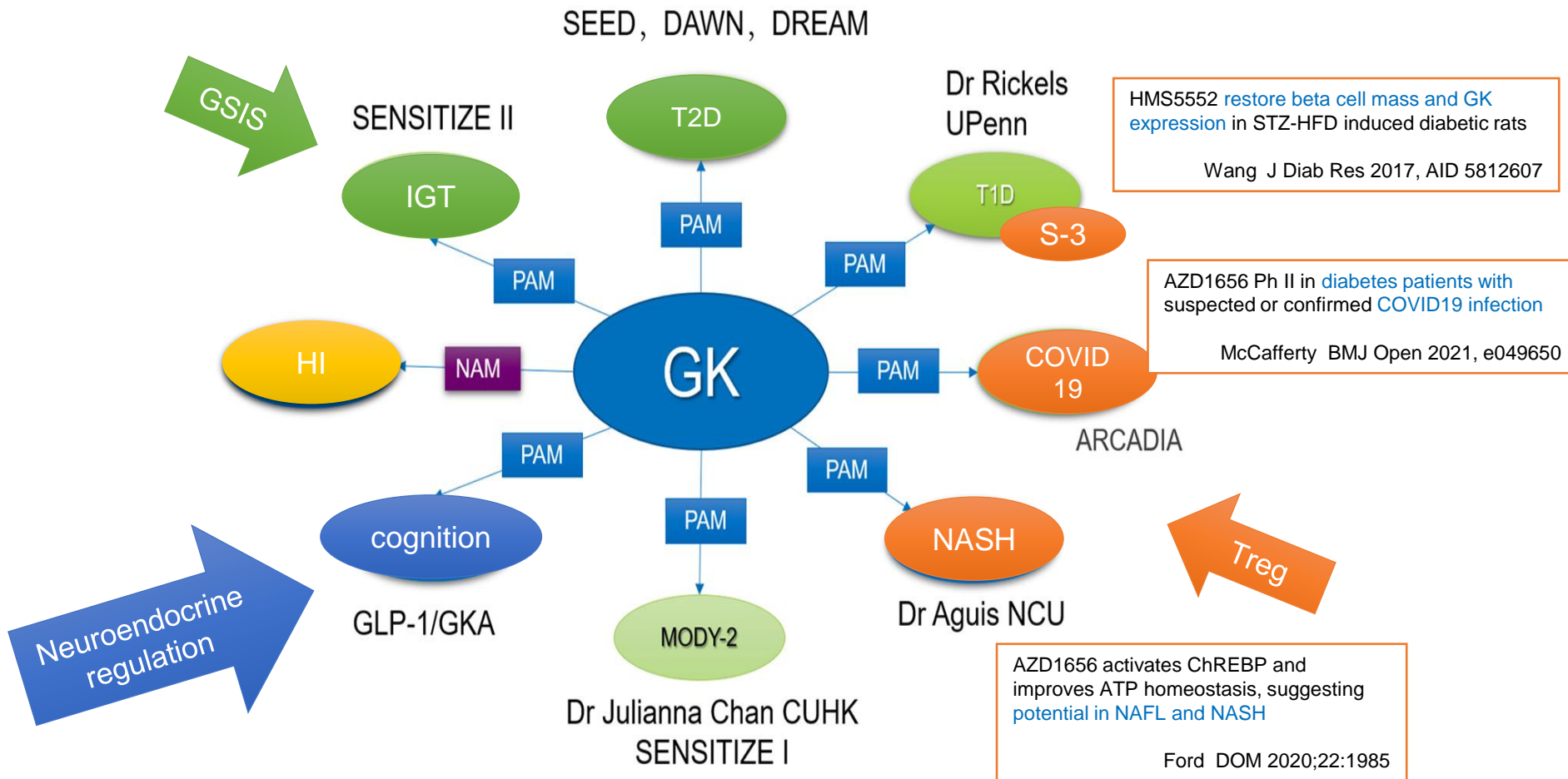
# Dorzagliatin Patent Portfolio



The Chinese patent for dorzagliatin is expected to be extended to 2034, and various global patents including the 2<sup>nd</sup> generation GKA are in urgent application and prosecution



# Glucokinase with a broader indication in homeostatic control of endocrine, immunity and neurology



# Dorzagliatin business development strategy

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Seek opportunities to continue to expand the development opportunities of dorzagliatin in the European, American and Japanese markets, Southeast Asian market and the "Belt and Road" market to realize the value of innovation.

- Partner with Bayer China and achieve commercial excellence in Diabetes Care
  - An innovative model to shape the Chinese diabetes market and management
  - Raising the standard of care and management of diabetes and related diseases
- Partner with local leader in China for drug development clinical opportunities for diabetes prevention, mitigation and elimination of complications
  - Opportunity in diabetes prevention in China and SE Asia (IGT population)
- Partner with local leader in US and EU for drug development and market entry with FDC (once a day tablet) and 2nd generation of dorzagliatin
  - Opportunity in T1D and T2D care in US
  - Opportunity in DKD care in US and EU
  - Opportunity in T2D partners in the Middle East and North Africa

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



## Hua Medicine



**Li Chen**  
CEO & CSO

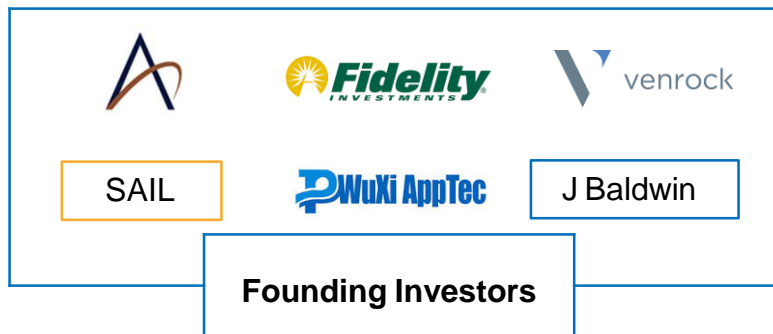


**Bob Nelsen**  
Chairman



## 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, NDA under active review in China**
- **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
- **First oral antidiabetes drug to demonstrate potential for diabetes remission** – in DREAM Study, 65% diabetes remission rate at week 52 without any antidiabetes medication
- Broad indications diabetes care
  - Diabetes remission
  - Demonstrated viability in combination with DPP-4 inhibitor & SGLT-2 inhibitor
  - Suitable for DKD patients





# Financial Section

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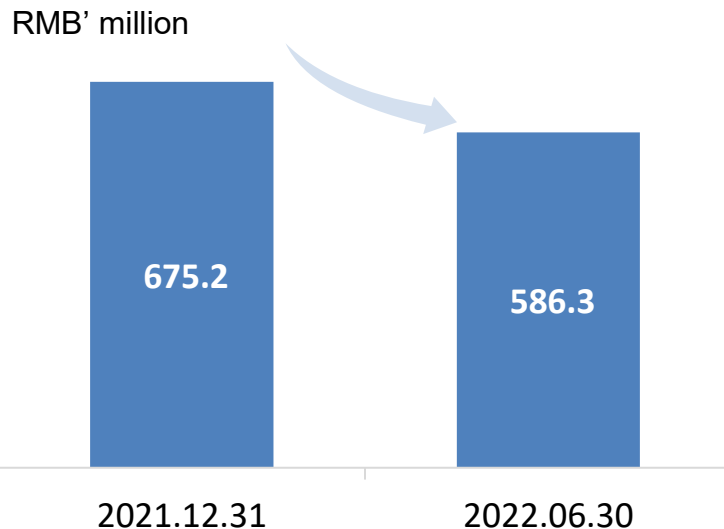
# Financial Summary

**Cash Balance:** RMB586.3 million of cash at 06/30/2022 vs. 675.2 million at 12/31/2021.

Total cash decrease of RMB88.9 million, consisted of:

- Net cash used in operating activities was RMB116.6 million
- Net cash from investing activities was RMB17.0 million
- Net cash used in financing activities was RMB4.3 million
- Net effect of exchange rate changes was RMB15.0 million

Net cash used in operation activities of RMB116.6 million, mainly includes cash payment of RMB70.6 million for the research and development activities and of RMB91.6 million for the administrative activities, adjusted for cash received of RMB45.6 million for government grants and VAT refund.



**Loss before tax** of RMB104.6 million in the first half of 2022 vs. RMB165.3 million in the first half of 2021.

**Research and development expenses** of RMB72.3 million in the first half of 2022 vs. RMB98.0 million in the first half of 2021.

- A decrease of RMB15.6 million for dorzagliatin clinical trials, which was primarily attributable to the data analysis and TMF report preparation of SEED/HMM0301 and DAWN/HMM0302 were conducted in the first half of 2021. In the first half of 2022, we primarily focused on our NDA approval and conducted several additional clinical research to support the review of NMPA;
- A decrease of RMB2.4 million for dorzagliatin non-clinical studies, which was primarily attributable to the ISS data and analysis expense for NDA filing, FDC efficacy study of dorzagliatin with insulin/acarbose and efficacy study of dorzagliatin in animal model of T2D complicating cognitive disorder conducted in the first half of 2021 and no such studies happened in the first half of 2022;
- A decrease of RMB7.0 million for labor costs, which was primarily attributable to decreased annual bonus and the decrease of share-based payment under the accelerated amortization method;
- A decrease of RMB3.0 million for other expenses, which was primarily attributable to the less travelling cost, meeting cost and utility cost due to the impact of COVID-19 in the first half of 2022;
- Adjusted for an increase of RMB1.6 million in chemical, manufacturing, and control expenses, which was primarily attributable to the process validation, drug substance and production for clinical trail for the review of our NDA approval conducted in the first half of 2022.



**Administrative expenses** of RMB68.5 million in the first half of 2022 vs. RMB63.5 million in the first half of 2021.

- An increase of RMB6.9 million in consultant fee, which was mainly due to our NDA application related consulting, pricing strategy consulting and economic evaluation consulting of dorzagliatin conducted during the six months ended June 30, 2022 and no such consulting activities conducted during the six months ended June 30, 2021;
- Adjusted for a decrease of RMB1.2 million in recruitment expense due to our recruitment strategy;
- Adjusted for a decrease of RMB0.4 million in meeting fee and RMB0.5 million in travelling expense due to less meeting and travelling activities compared to the six months ended June 30, 2021, which was impacted by COVID-19 in the first half of 2022.



Hua Medicine  
华领医药