



Hua Medicine

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China Healthcare Summit

November 14, 2018

2010 – 2014



Li Chen

*Chief Scientific Officer and
Founding Director of Roche
R&D Shanghai*



ARCH Venture Partners



Drs. Ge Li & John J. Baldwin
(WuXi AppTec) (Merck)

A
Differentiated
Global Biotech
Story Based
in
Shanghai
China

2018

Global Rights to Dorzagliatin (HMS5552)

- The 4th Gen Roche GKA drug candidate
- Successful **Proof-of-concept** Phase II clinical trial in China (published - **Lancet** in May 2018)
- Demonstrated **Disease Modifying Effect**
- **First-in-class GKA** with 2 Phase III China trials ongoing
- Immediately targeting for **First-line Therapy** as well as combo therapy with metformin
- **Massive market opportunity** – global T2D population 453m (120 mm in China alone)
- **Personalized medicine** approach proven

Successful Hong Kong IPO – Sep 2018

- Raised US\$114m with US\$1.1b market cap
- HK\$8.28 per share / ticker 2552

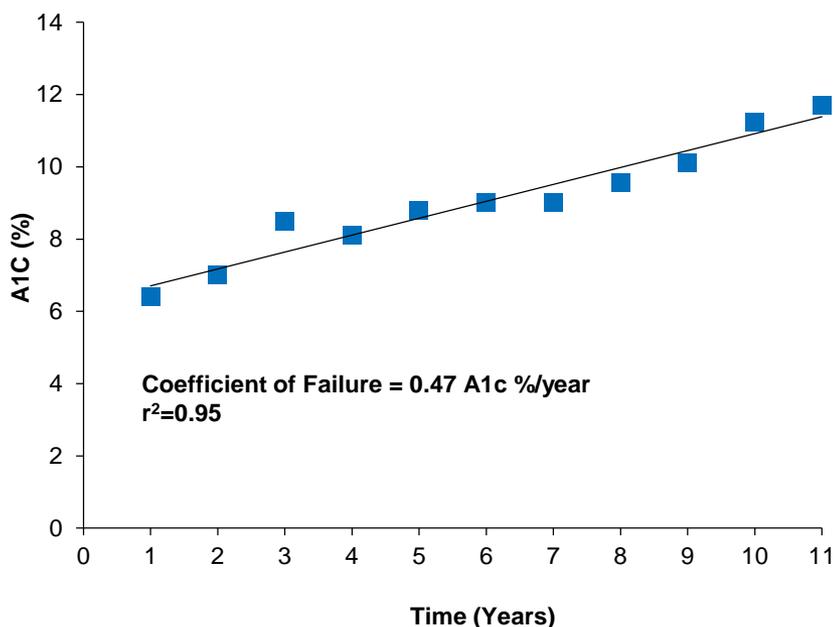
T2D is a Progressive Disease with Degeneration of β Cell Function and Increasing Insulin Resistance



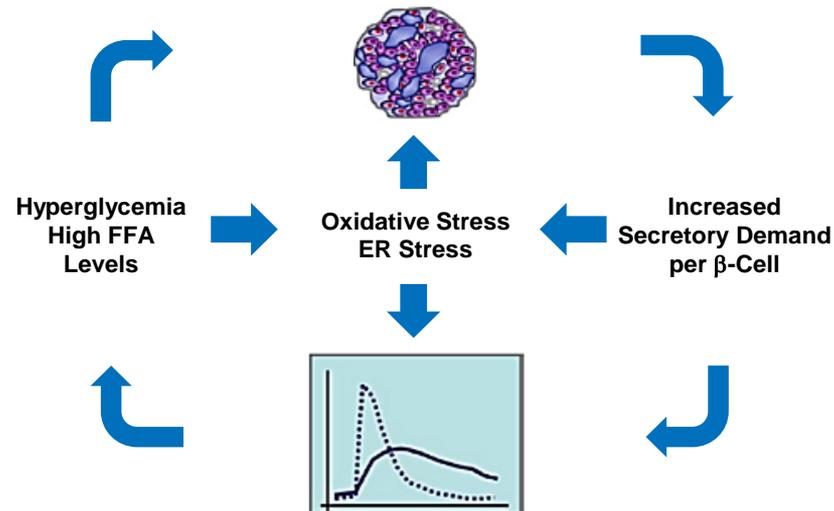
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- Type 2 diabetes is a progressive disease with deterioration of β cell function with monotherapy
- Loss of glucose sensitivity in Type 2 diabetes patients is the first step in the progressive destruction of β cells
- Impaired β cell function results in hyperglycemia stress which causes progressive damage of β cells

Patients with Monotherapy: HbA1c Increased by 1% Every 2 Years, β -Cell Function Decreased Accordingly¹



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



Glucokinase GK is a Glucose Sensor in Glucose Homeostasis



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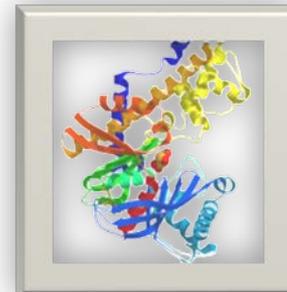
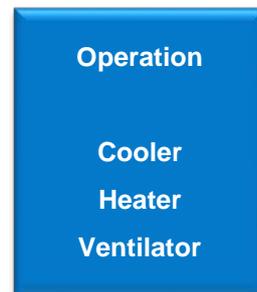
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Thermostat in a Building

- Messenger: air temperature
- Set Point: 22° Celsius
- Threshold: 21-23° Celsius
- Controller: Thermo Sensor (thermostat)
- Effector: Electronic signal
- Operator: Heater, Cooler, Ventilator

Glucose Homeostasis in Human Body

- Messenger: glucose level
- Set Point: 5 mmol/liter¹
- Threshold: 4-6 mmol/liter¹
- Controller: Glucokinase in the pancreas and small intestine-Glucose Sensor
- Effector: insulin, glucagon, GLP-1 (glucagon-like peptide 1)
- Operator: hexokinase 1-3², SGLT-2, GK_L (Liver GK)



When the sensor malfunctions or is impaired, automatic control is lost

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.

Sustained Efficacy in HbA1c Reduction

Proof of Concept in Phase II Study



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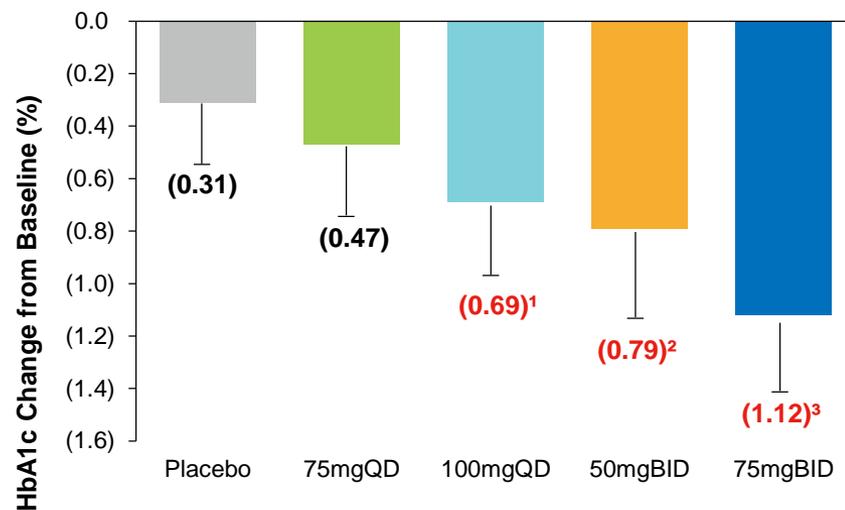
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Phase II

Dorzagliatin: Proof-of-Concept (POC) Achieved with Sustained Efficacy

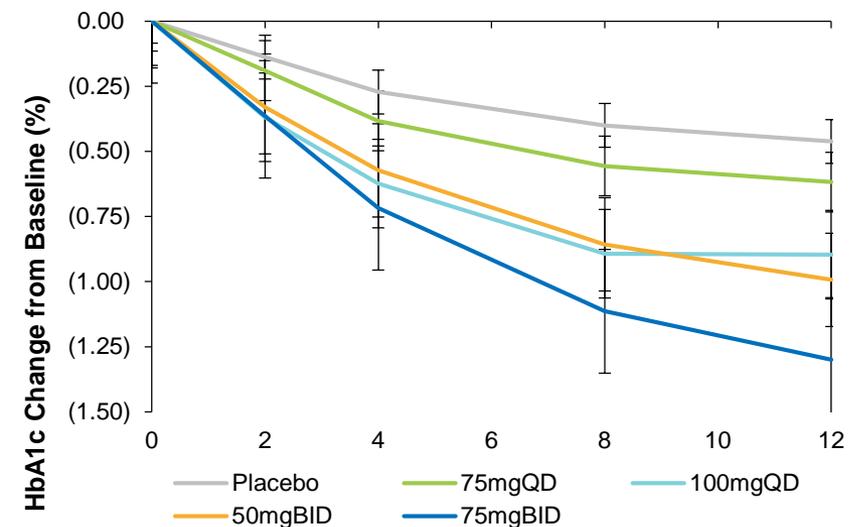
- Double blinded, placebo controlled and randomized Phase II trial with 258 patients in China over 22 clinical centers
- Published in Lancet in May 2018

Dorzagliatin reduced HbA1c levels dose dependently...



- The chart above showcases HbA1c change from baseline after the 12-week treatment period (PPS, LOCF⁴)⁵, with the results showing that Dorzagliatin reduced HbA1c levels dose dependently with 75 mg QD, 100 mg QD, 50 mg BID and 75 mg BID, after the treatment period
- In the 75mg BID group, both fasting plasma glucose level (FPG) and post-prandial glucose level (PPG) were well controlled without increasing hypoglycemia or dyslipidemia risk

...with the 75 mg BID group showing HbA1c reduction effect starting from week four



- The chart above showcases HbA1c change from baseline over time (PPS)⁶
- Results showed that HbA1c reduction was significant starting from week four, and continued in weeks eight and 12

¹ P<0.05 compared to placebo group. ² P<0.01 compared to placebo group. ³ P<0.001 compared to placebo group. ⁴ LOCF represents for "last observation carried forward".

⁵ The averages calculated applied least-square mean averages. ⁶ The averages calculated applied mean square averages.

Compelling Sets of Composite Endpoint Observed

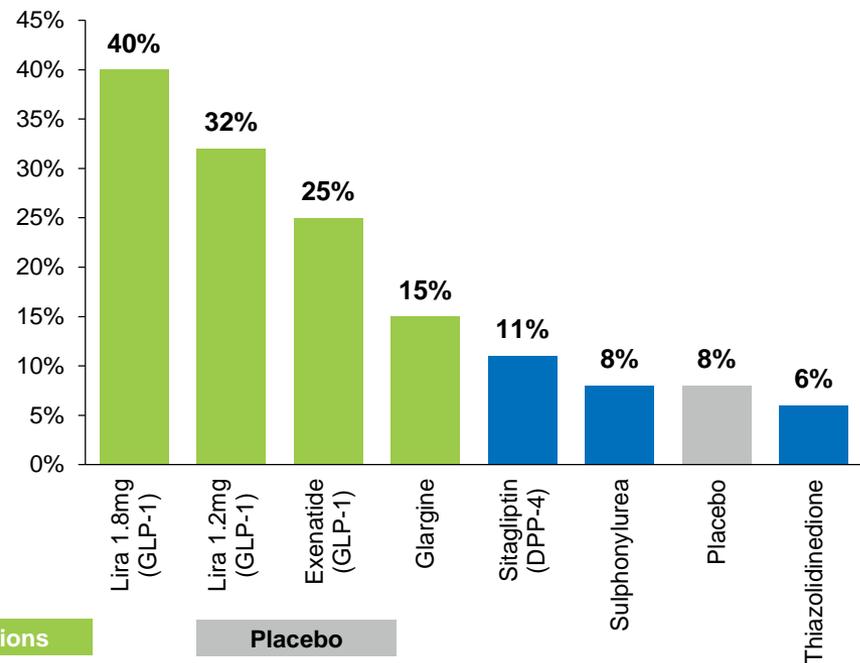
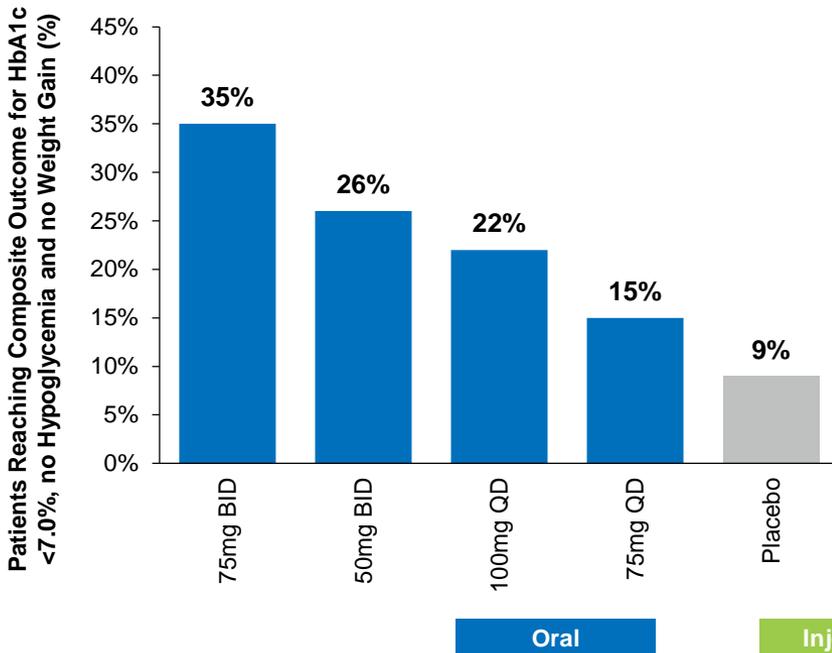


Phase II

- The composite response rate of Dorzagliatin in a 12-week treatment reached 35.4% in the 75 mg twice daily group and demonstrated its favorable profile in glucose reduction, as well as low risk of hypoglycemia and weight gain
- The clinical trial results have been published on Lancet

Favorable composite response rate of Dorzagliatin in a 12-week treatment period...

...compared with other Type 2 diabetes treatment composite endpoints over 26-week treatment periods



- In the trial, the 75 mg BID group reached a composite response rate of 35.4% over a 12-week treatment period, which compares favorably with other treatment methods tested over a 26-week period

Source: "Achieving a clinically relevant composite outcome of an HbA1c of <7% without weight gain or hypoglycemia in Type 2 diabetes: a meta-analysis of the liraglutide clinical trial programme" by B. Zinman et al Diabetes, Obesity and Metabolism 14:77-82, 2012

Note: Dorzagliatin data was from Phase II trial conducted over 12 weeks, while the study comparison was conducted on 26 week clinical trials.

Dorzagliatin Improved β -cell Function and Decreased Insulin Resistance



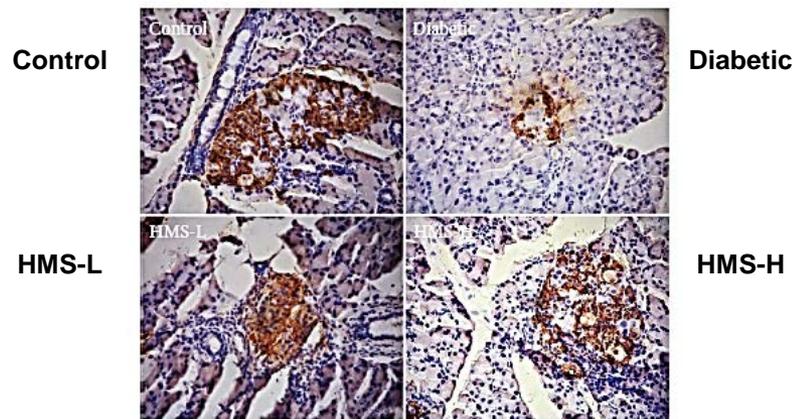
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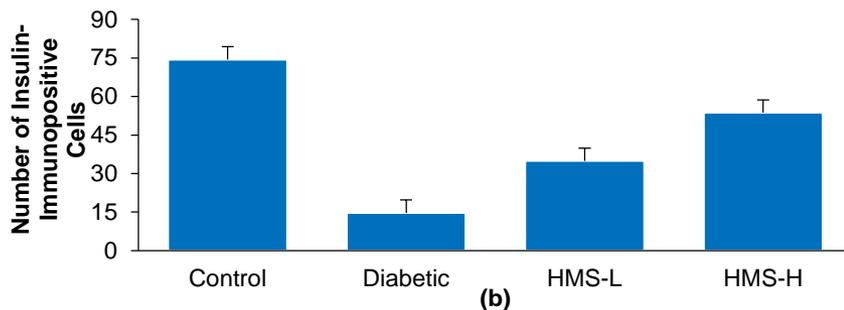
Phase I

- 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

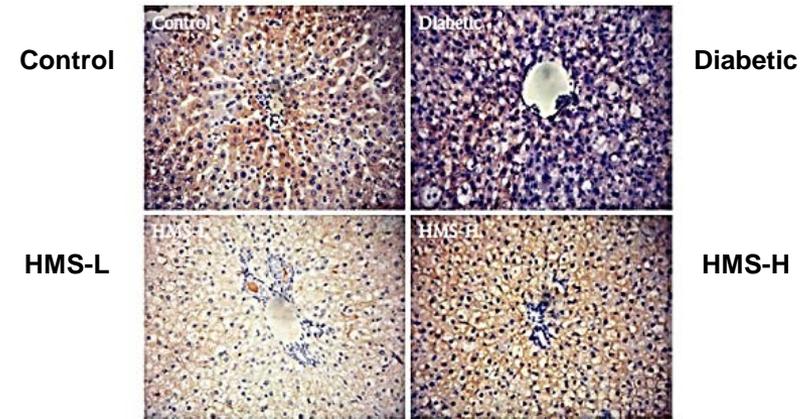
Type 2 Diabetes Rat Pancreas



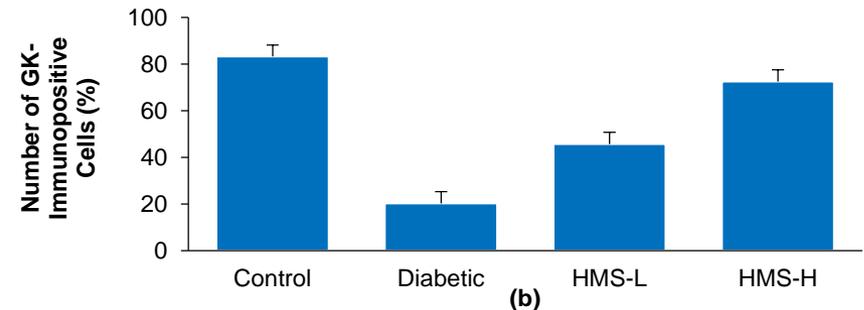
(a)



Type 2 Diabetes Rat Liver



(a)



Dorzagliatin Improved β -cell function and Reduced Insulin Resistance



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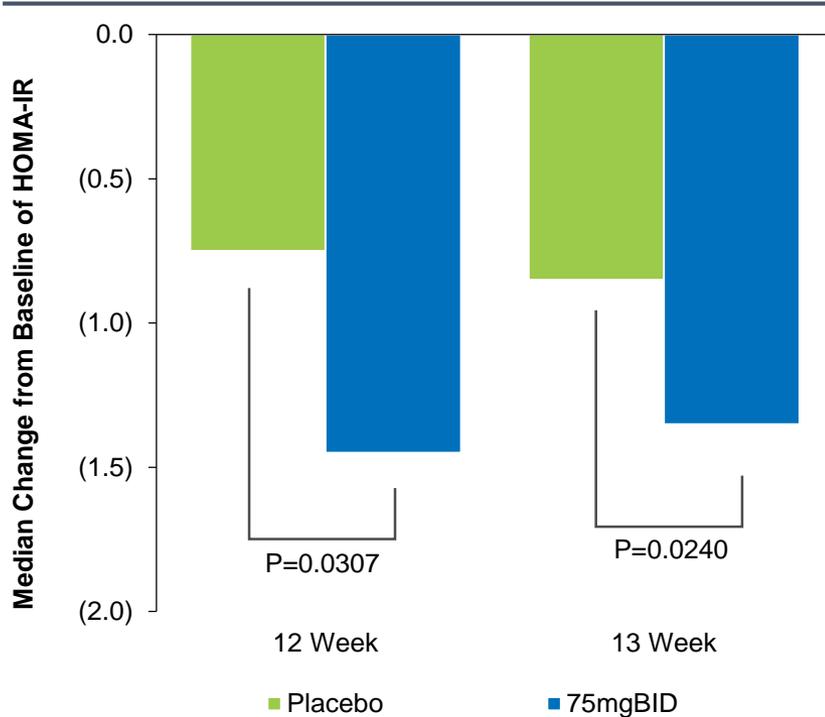
Phase II

Chinese drug naive Type 2 diabetes patients 3 month treatment

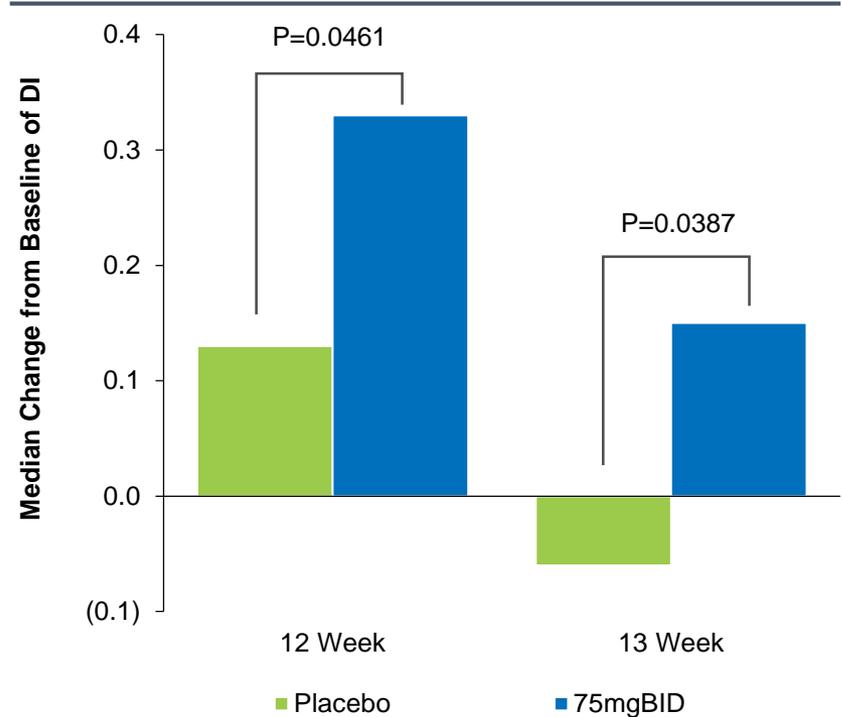


Improves pancreatic β -cell function
Reduces insulin resistance

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

Phase III Trial Designed and Powered for Success



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Study Design for:

Phase III GKA Mono-therapy Trial for Drug Naive T2D Patients (~450 Patients)

Phase III GKA Metformin Add-on Therapy Trial for Metformin Users (~750 Patients)



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

Potential as Cornerstone Therapy for Tailored Personalized Diabetes Care

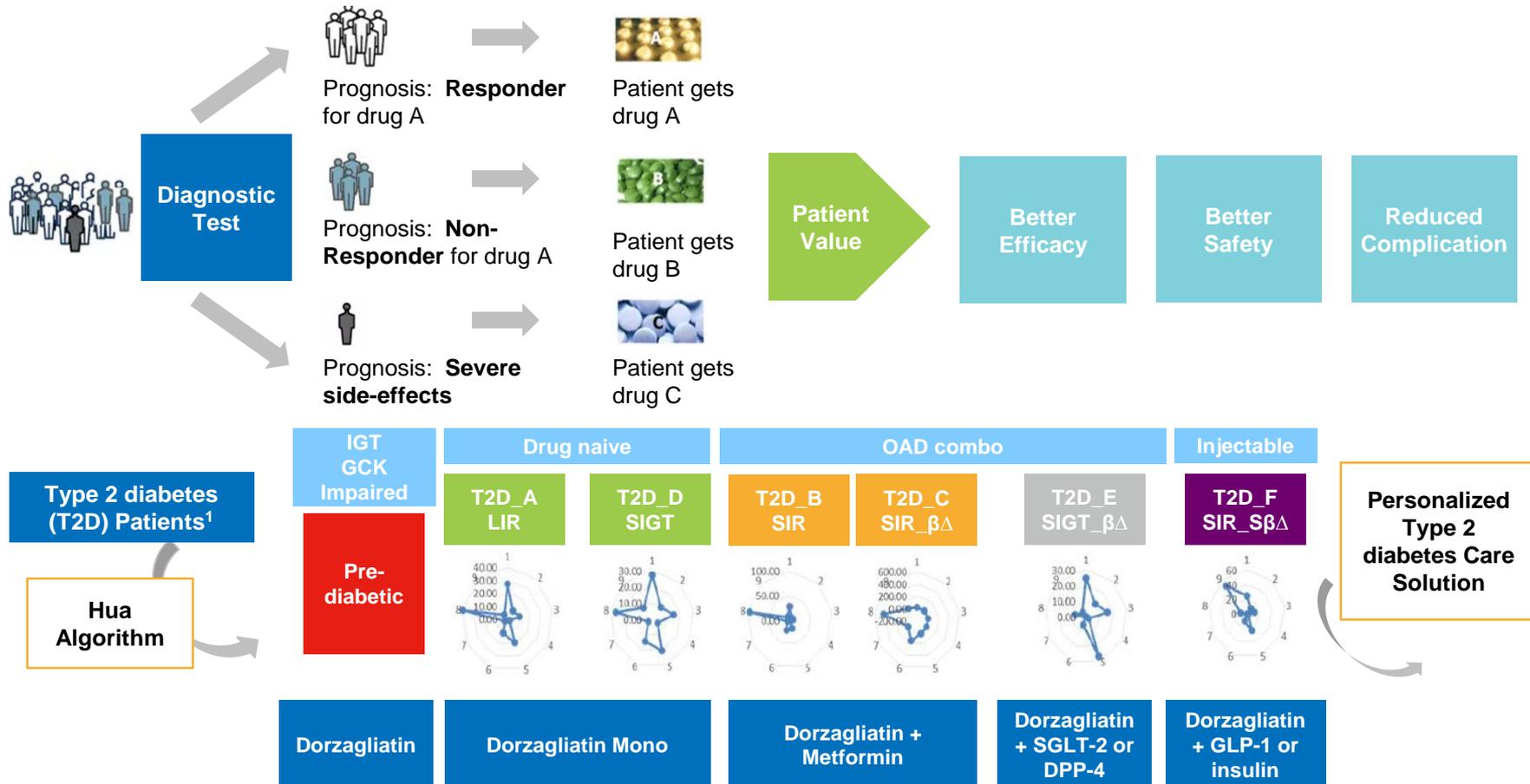


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Dorzagliatin has the potential to serve as the next generation cornerstone treatment of Type 2 diabetes
– Personalized diabetes care in progress with novel algorithm development

Personalized Type 2 diabetes Medicine: A Comprehensive Solution for Diabetes Patients

- A proprietary algorithm is developed at Hua Medicine based on clinically validated biomarkers



¹ The Type 2 diabetes (T2D) patients are classified into 6 different subtypes: low insulin resistance (LIR), severe insulin resistance (SIR), SIR with diminished β-cell function (SIR_βΔ), severe impaired glucose intolerance (SIGT), SIGT with diminished β-cell function (SIGT_βΔ), and IR with severely diminished β-cell function (SIR_SβΔ)

Massive China Diabetes Market



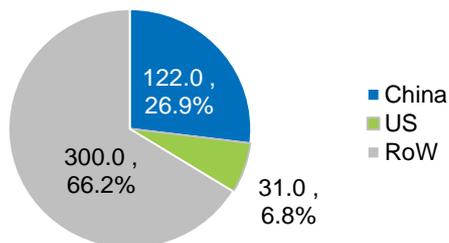
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China has the largest diabetes population globally, with half undiagnosed

China Has the Largest Diabetes Population with c.120 million T2D

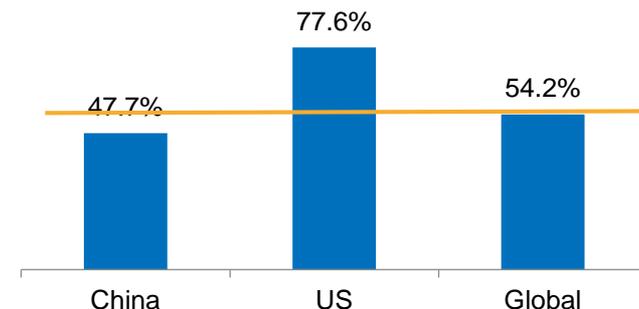
...with Diagnosis Rate Lower than Global Average

Geographic Distribution of Global T2D Patients, 2017



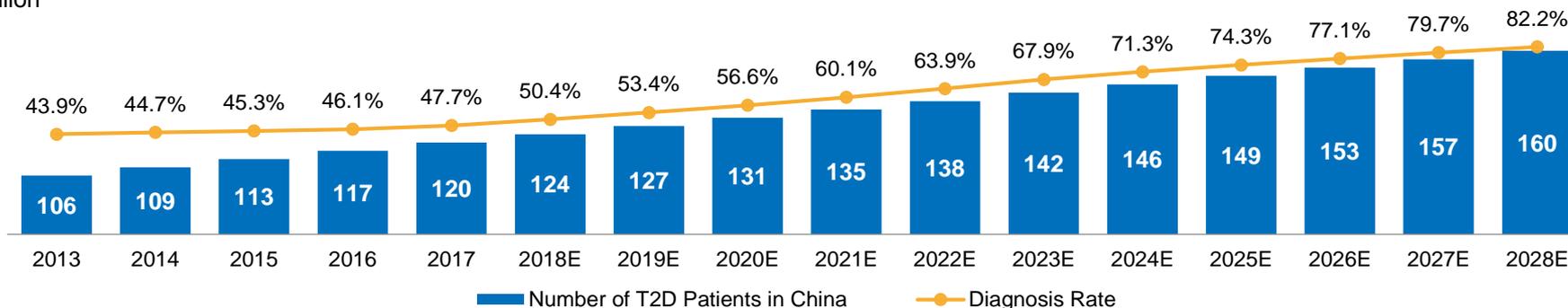
China Diabetics:

- ✓ Increase in aging population
- ✓ Unhealthy diet
- ✓ Lack of physical activity



Number of Type 2 Diabetes Patients and Diagnosis Rate, Expected to Grow Significantly

Million



With improvements in social healthcare insurance system, increased healthcare expenditures and healthcare awareness, and rising penetration of medical examination, diagnosis rate in China is expected to rise from 47.7% in 2017 to 82.2% in 2028

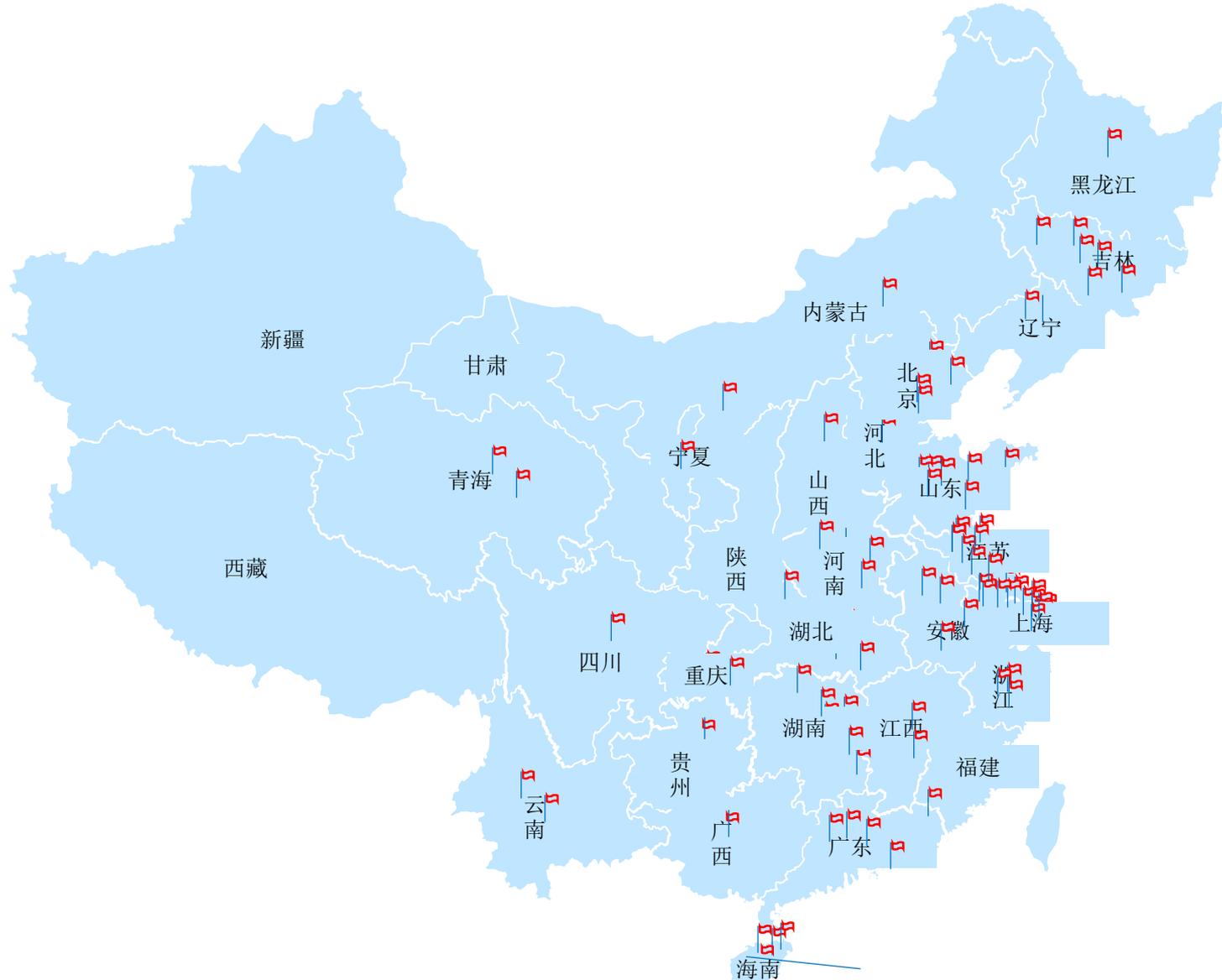
Source: Frost & Sullivan

The best marketing is our clinical trials



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



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Founder & Angel Investors



25

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
- President of SAPA 2001
- Over 90 publications and patents in basic research and medical sciences



Ge Li, Ph.D., *Angel Investor*

- Chairman and CEO of WuXi AppTec
- Named as one of "The 25 Most Influential People in Biopharma in 2015" by FierceBiotech



John J. Baldwin, Ph.D., *Angel Investor & Portfolio Advisory Board Member*

- Director of WuXi PharmaTech, GlycoMimetics (GLYC) and IVIEW Therapeutics Inc.

Years of Experience

Management Team



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Li Chen, Ph.D.
Founder, CEO and CSO



23

George Lin
EVP, CFO



Daniel Du, Ph.D., MD
SVP, RCM



18

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



Fred Li, Ph.D.
SVP, CMC



Jin She, Ph.D.
VP, Chemistry CMC



Yilei Fu, BS, MBA
VP, Quality Assurance



Wenjie Xu, BS, MBA
VP, Commercial Strategy and Marketing



World-renowned Senior Advisor, Portfolio Advisory Board and Influential Key Opinion Leaders



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Senior Advisor and Portfolio Advisory Board



Franz Matschinsky, M.D.

- University of Pennsylvania, Perelman School of Medicine
- Formulated the glucokinase glucose sensor concept
- *"Glucokinase is a glucose sensor, diabetes gene and drug target"*



Bennett Shapiro, M.D.

- Ex-executive VP Merck
- Well known Pharmacologists
- Professor and Chairman, Department of Biochemistry, University of Washington



Christopher Walsh, Ph.D.

- Ex-professor, Harvard Medical School
- Advisor to Stanford ChEM-H institute
- Advisor to Global Pharma



James MacDonald, Ph.D.

- CEO, Synergy Partners
- SVP, Drug Safety at Schering-Plough



John J. Baldwin, Ph.D.

- Hall of Fame Medicinal Chemist
- Published 125+ scientific articles
- Holds over 200 issued US patents



Catherine Strader, Ph.D.

- Held executive positions at Schering-Plough and Merck
- 30 years of pharmaceutical R&D experience



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
- President-elect, 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
- President, 8th Youth Committee, Chinese Diabetes Society
- Published articles in numerous prestigious journals such as the Lancet Diabetes and Endocrinology, Cell Metabolism

A Blue Chip Board



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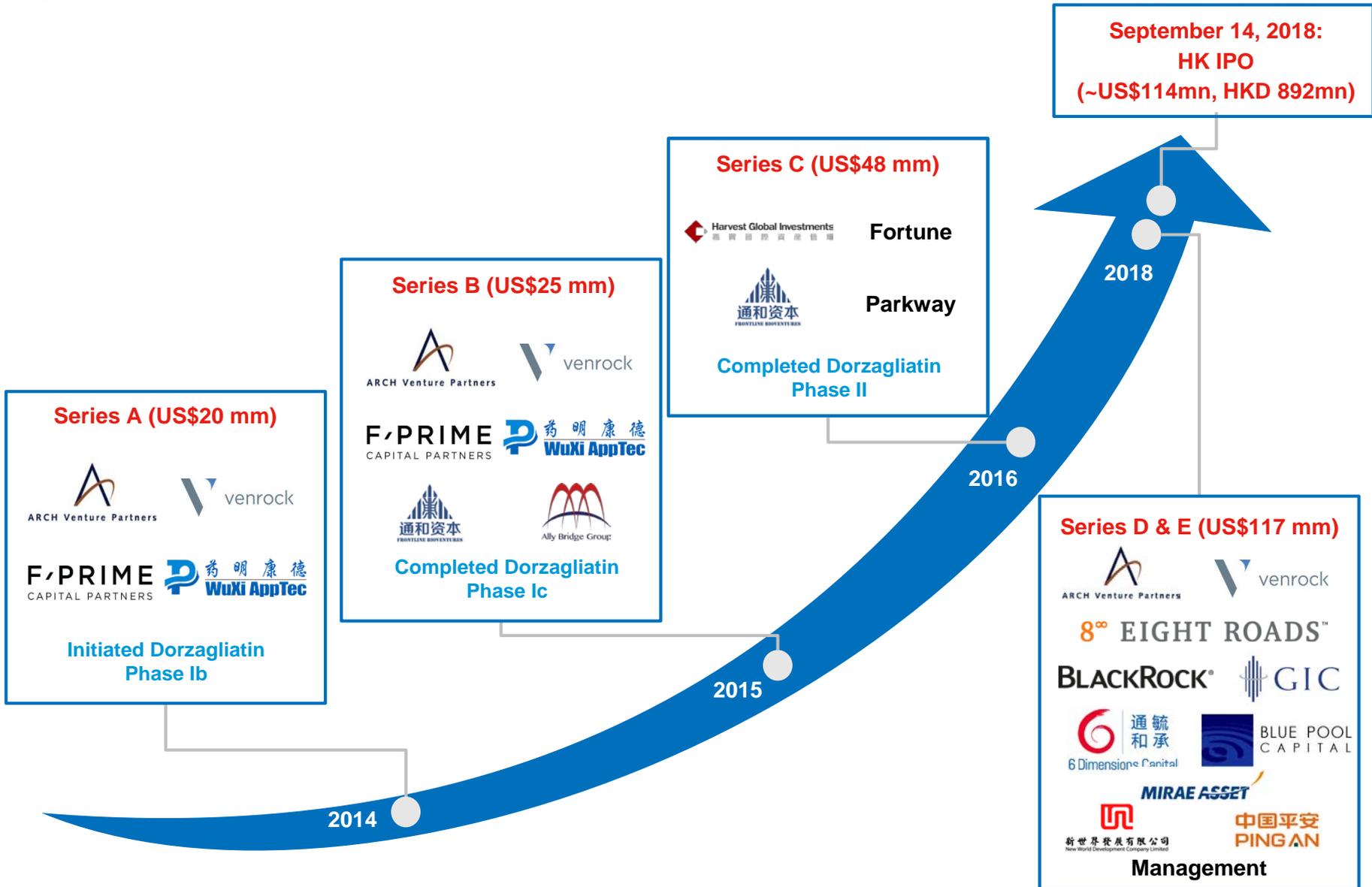
Alec Tsui



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