Phase III Monotherapy Trial - Dorzagliatin 24-Weeks Topline Results

November 12, 2019

Current State of the Type 2 Diabetes Landscape

Over **450 million** people with type 2 diabetes, globally; **120 million+ in China alone**

Over **US$80 billion** plus of pharmaceutical sales globally every year

Not one approved drug **currently treats the underlying cause** of type 2 diabetes – loss of glucose sensitivity and impairment of glucose homeostasis

Restoring the function of impaired glucokinase is the only scientifically validated means to restore glucose sensitivity in homeostasis

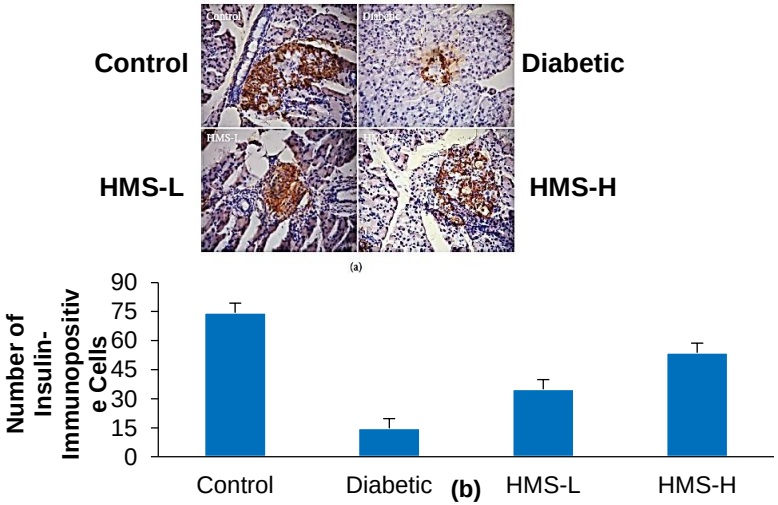
However, although most all large multinational pharmaceutical companies with a metabolic disease franchise have tried to create a viable and safe glucokinase activator (GKA) to treat type 2 diabetes, **none has successfully passed through their primary efficacy endpoint with desirable safety profile at 24-weeks in their Phase 3 trial until now**

Key differentiation of dorzagliatin from previous GKA is **targeting the modulation of the glucose sensor role of GK** rather than a rate limiting glucose processing enzyme like the other hexokinases

Dorzagliatin Repairs the Glucokinase Glucose Sensor Function in T2D – *Improved β-cell function*

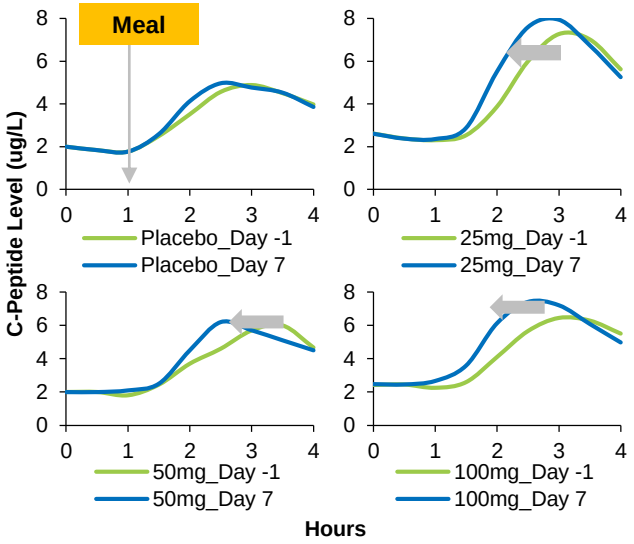
Type 2 Diabetes Rat Pancreas

Pre-clinical



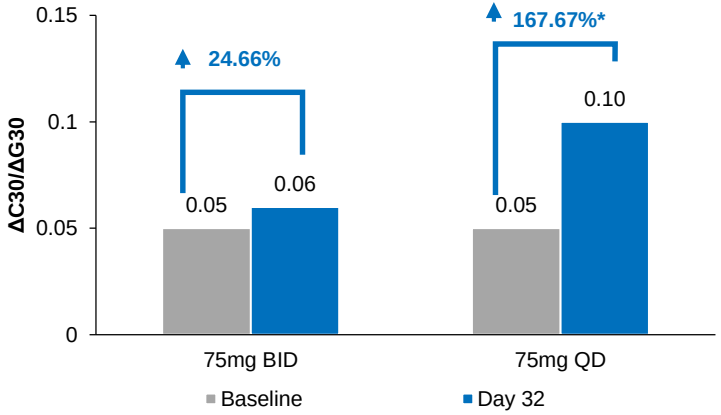
Early-stage insulin release

Phase Ib



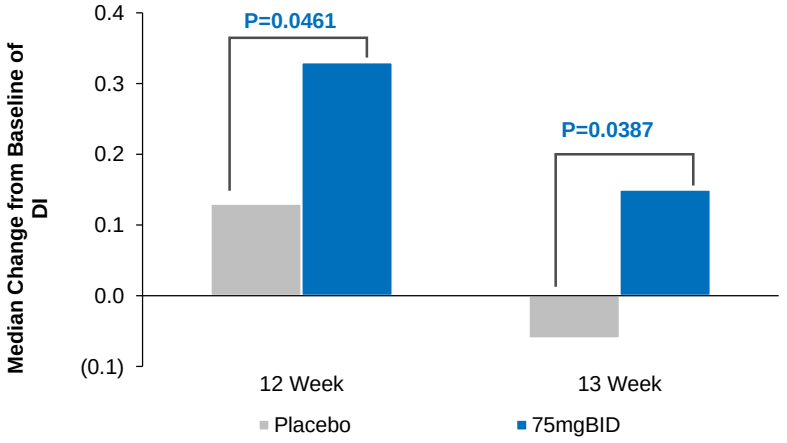
Early Insulinogenic index

Phase Ic



Disposition Index

Phase II



Implications of HMM0301 Phase 3 Topline Results to the Global Type 2 Diabetes Landscape

HMM0301 Phase III 24-week topline results in Chinese drug-naïve patients with Type 2 Diabetes

First drug candidate focused on the underlying cause of type 2 diabetes, glucose sensing, to meet its primary efficacy endpoint over 24 week Phase III trial

- 1.07% HbA1c reduction from baseline in dorzagliatin treated group compared to 0.5% HbA1c reduction in placebo (p-value < 0.0001)
- 45.4% of patients treated with dorzagliatin achieved target HbA1c level of 7.0% or less at 24-weeks compared to 21.5%% of patients treated with placebo (p-value < 0.0001)
- Patients treated with dorzagliatin achieved homeostasis control rate of 45.0% compared with 21.5% in placebo group (p-value < 0.0001)

Dorzagliatin was well tolerated and had a good safety profile

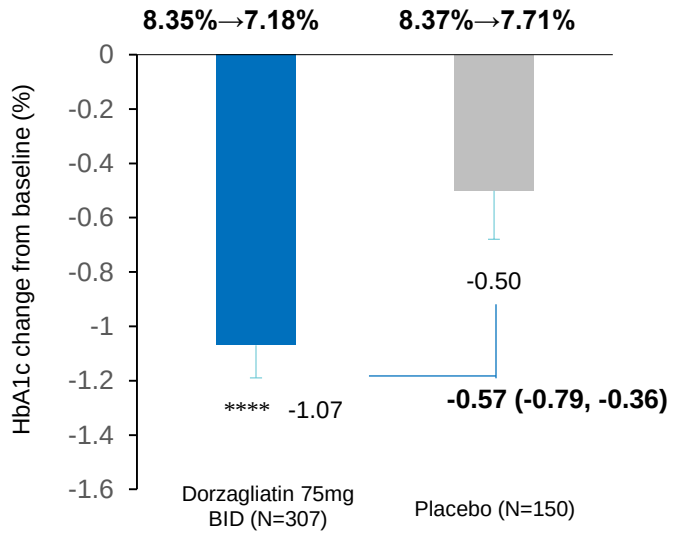
- No death, no drug-related serious adverse event over 24 week
- Less than 1% incidence of hypoglycemia over 24 week and no severe hypoglycemia

The 28 week open label safety outcome trial of HMM0301 is ongoing

HMM0301 Dorzagliatin Monotherapy Efficacy Endpoints

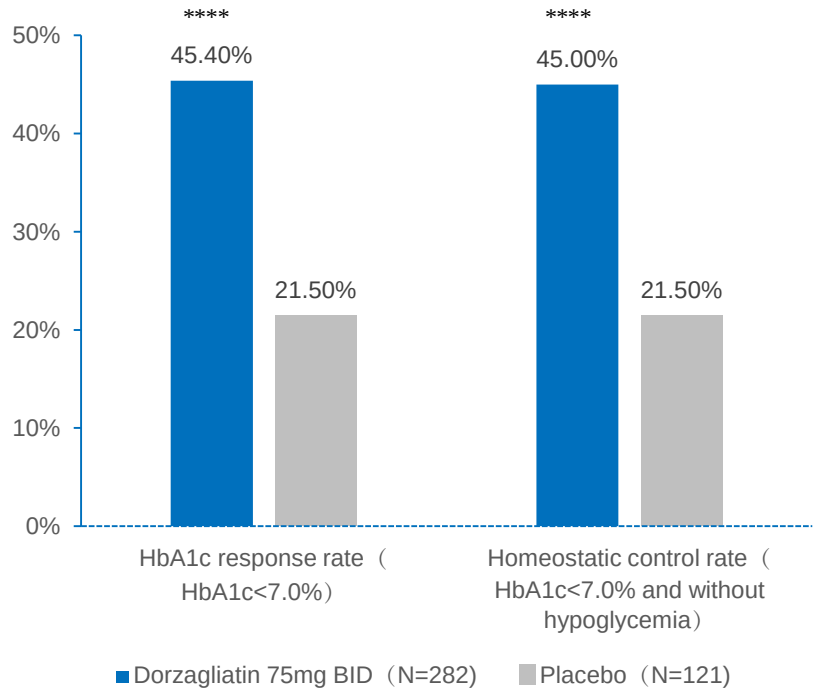
HbA1c change from baseline to week 24 (FAS)
at therapeutically minimum effective dose

Greater lowering of mean HbA1c (%) was achieved with dorzagliatin 75mg BID (-1.07%, 95% CI -1.19 to -0.95, n=307) than with placebo (-0.50%, -0.68 to -0.32, n=150). Estimated mean treatment difference for dorzagliatin versus placebo was -0.57% (95%CI -0.79 to -0.36, p<0.0001). Analysis results based on FAS and PPS led to the same conclusions.



The analysis results from mixed model for repeated measurements (MMRM).
Data are least squares means (95%CI). The bars show lower limits of 95% CIs. ****p<0.0001 vs placebo.

HbA1c response rate and homeostatic control rate at week 24 (PPS)

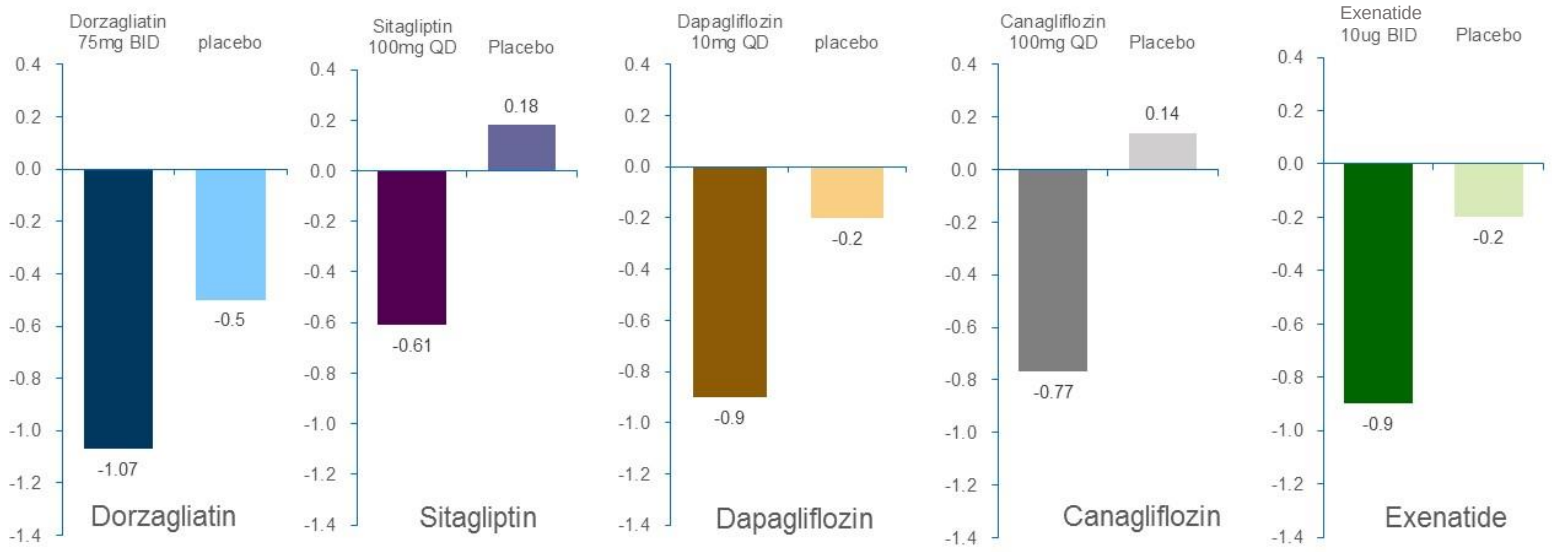


Homeostatic control rate: HbA1c <7% and without hypoglycemia.
The response rates between dorzagliatin and placebo were compared by using logistic regression model. ****p<0.0001 vs placebo. Analysis results based on FAS and PPS led to the same conclusions.

Comparison with Main Efficacy Results of other Anti-Diabetic Drugs

Phase III Monotherapy Treatment Studies of the First-In-Class T2D therapies

Dorzagliatin demonstrates excellent primary efficacy endpoint among the new classes of diabetes medicine



Drug	Dorzagliatin	Sitagliptin	Dapagliflozin	Canagliflozin	Exenatide
Randomized number	463	741	485	587	233
Duration	24w	24w	24w	26w	24w
Run-in period	4w	2w	2w	2w	2w
Antidiabetic drug history	Drug-naive	On/not on an OHA	Drug-naive	Drug-naïve or AHA monotherapy	Treat with diet and exercise
HbA1c change from baseline (%)	-1.07 vs -0.5	-0.61 vs 0.18	-0.9 vs -0.2	-0.77 vs 014	-0.9 vs -0.2

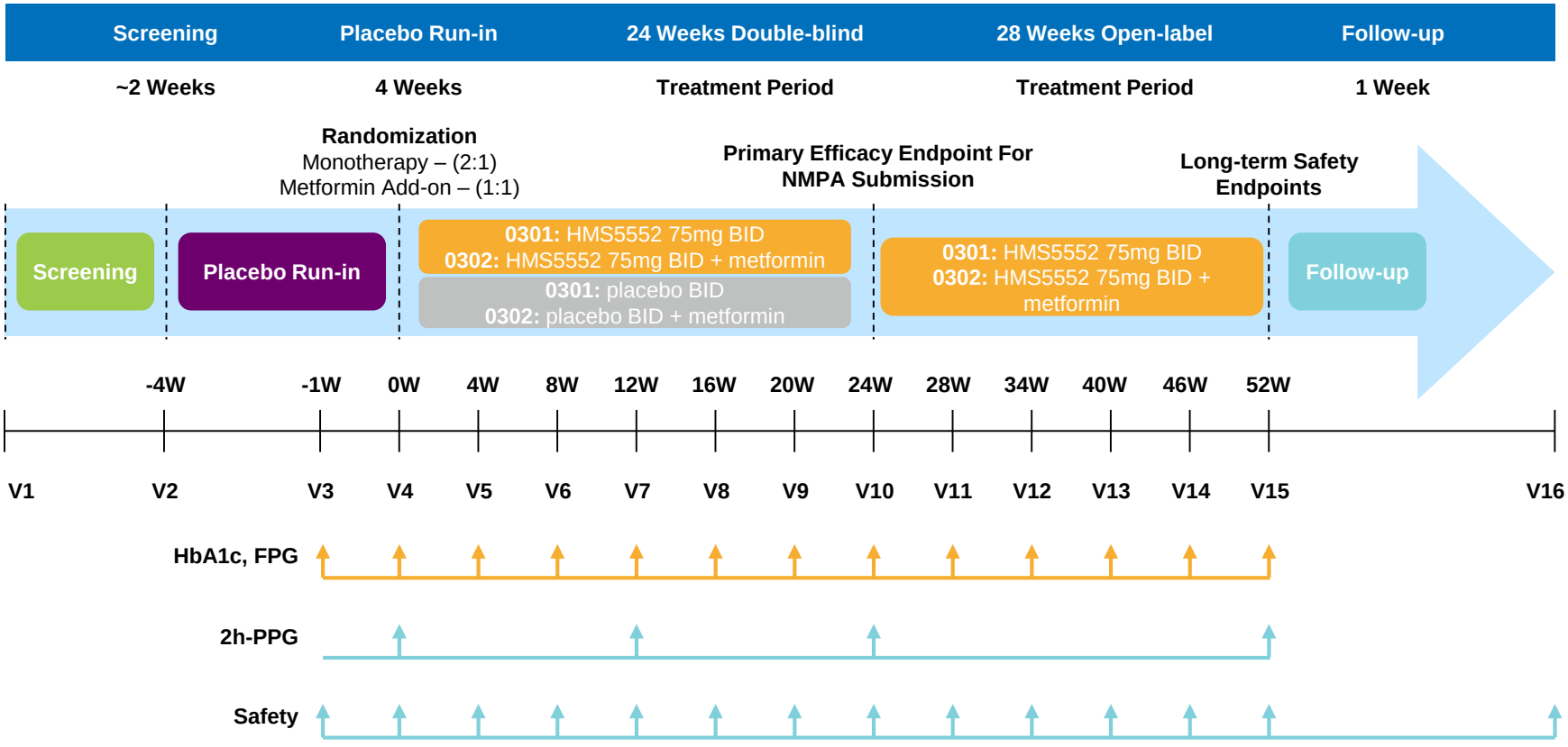
Sources:

- *Pablo Aschner,et al, Effect of the Dipeptidyl Peptidase-4 Inhibitor Sitagliptin as Monotherapy on Glycemic Control in Patients With Type 2 Diabetes. Diabetes Care 29:2632–2637, 2006*
- *ThomasJ. Moretto, et al. Efficacy and Tolerability of Exenatide Monotherapy Over 24 Weeks in Antidiabetic Drug-Naive Patients with Type 2 Diabetes: A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study. Clinical Therapeutics/Volume 30, Number 8, 2008*
- *Ferrannini, E., et al., Dapagliflozin monotherapy in type 2 diabetic patients with inadequate glycemic control by diet and exercise: a randomized, double-blind, placebo-controlled, phase 3 trial. Diabetes Care, 2010. 33(10): p. 2217-24.(Label)*
- *K. Stenlöf., et al., Efficacy and safety of canagliflozin monotherapy in subjects with type 2 diabetes mellitus inadequately controlled with diet and exercise. Diabetes, Obesity and Metabolism Volume 15, Issue 4*

HMM0301 / HMM0302 Study Design

Study Design for:

- HMM0301: Dorzagliatin Mono-therapy Trial for Drug NaïveT2D Patients (463 Patients)
- HMM0302: Dorzagliatin Metformin Add-on Therapy Trial for Metformin Users (766 Patients)



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

Hua Medicine R&D Pipeline

Trial #	Drugs	Disease indication	Study type	Pre-clinical	Phase I	Phase II	Phase III	NDA
HMM0301	Dorzagliatin	Drug naïve T2D	Registration trial					
HMM0302	Dorzagliatin & metformin	Metformin tolerated T2D	Registration trial					
HMM0311	Dorzagliatin vs. DPP-4	T2D	Head to head					
HMM0312	Dorzagliatin vs. acarbose	T2D	Head to head					
HMM0109	Dorzagliatin	Hepatic impaired T2D	Label expansion					
HMM0110	Dorzagliatin	Renal impaired T2D	Label expansion					
HMM0111	Dorzagliatin + DPP-4	Obese T2D	PK/PD & DDI					
HMM0112	Dorzagliatin + SGLT-2	Metabolic syndrome	PK/PD & DDI					
HMM0113	Dorzagliatin + atorvastatin	Label expansion	PK/PD & DDI					
HMM0114	Dorzagliatin + valsartan	Label expansion	PK/PD & DDI					
HMM0115	Dorzagliatin + sulfonylurea	SU-tolerated T2D	PK/PD & DDI					
HMM0116	Dorzagliatin + acarbose	Acarbose tolerated T2D	PK/PD & DDI					
HMM0117	Dorzagliatin + liraglutide	GLP-1 tolerated T2D	PK/PD & DDI					
HMM0119	Dorzagliatin + pioglitazone	NASH T2D	PK/PD & DDI					
HMM1201	Dorzagliatin + insulin	Basal insulin tolerated T2D	Insulin sparing					
HMM1202	Dorzagliatin + insulin	Drug naïve severe T2D	Pre-clinical					
	mGLUR5	PD-LID	Pre-clinical					

Currently Ongoing

Planned

What to expect in the next 12 months

	Trial #	Trial description	Milestone
✓	HMM0301	Dorzagliatin monotherapy	Phase III 24-week top-line data
1	HMM0111	Dorzagliatin & sitagliptin combination	Phase I trial data
2	HMM0112	Dorzagliatin & empagliflozin combination	Phase I trial data
3	HMM0302	Dorzagliatin combination with metformin	Phase III 24-week top-line data
4	HMM0301	Dorzagliatin monotherapy	Phase III 52-week data
5	HMM0311	Dorzagliatin comparison against sitagliptin	Phase III trial initiation
6	HMM0302	Dorzagliatin combination with metformin	Phase III 52-week data

Hua Medicine – A Global First-in-Class Biotech

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Drs. Ge Li & John J. Baldwin

(WuXi AppTec) (Merck)

China-Based First-In-Class

- **Met Primary Endpoint** in pivotal Phase III monotherapy trial, for China regulatory approval purposes
- **First-in-Class (GKA) drug** to significantly and sustainably reduce HbA1c safely
- **First Novel Concept** targeting restoration of glucose homeostasis – the underlying cause of T2D
- Both 52-week Phase III trials (over 1200 patients) in China expected to be completed by year end 2020
- **Global rights** to dorzagliatin
- **Massive market opportunity** – global T2D population is 453 mm (120 mm in China alone)
- **RMB 1,246.4 million** as of June 30, 2018