TRANSTECH PHARMA

156-OR

TTP054, a Novel, Orally-Available Glucagon-Like Peptide-1 (GLP-1) Agonist, Lowers HbA_{1c} in Subjects with Type 2 Diabetes Mellitus (T2DM)

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Presenter Disclosure Information

The American Diabetes Association requires the following disclosure to the participants:

Stephanie Gustavson, PhD, MSCI

Employee of TransTech Pharma, LLC

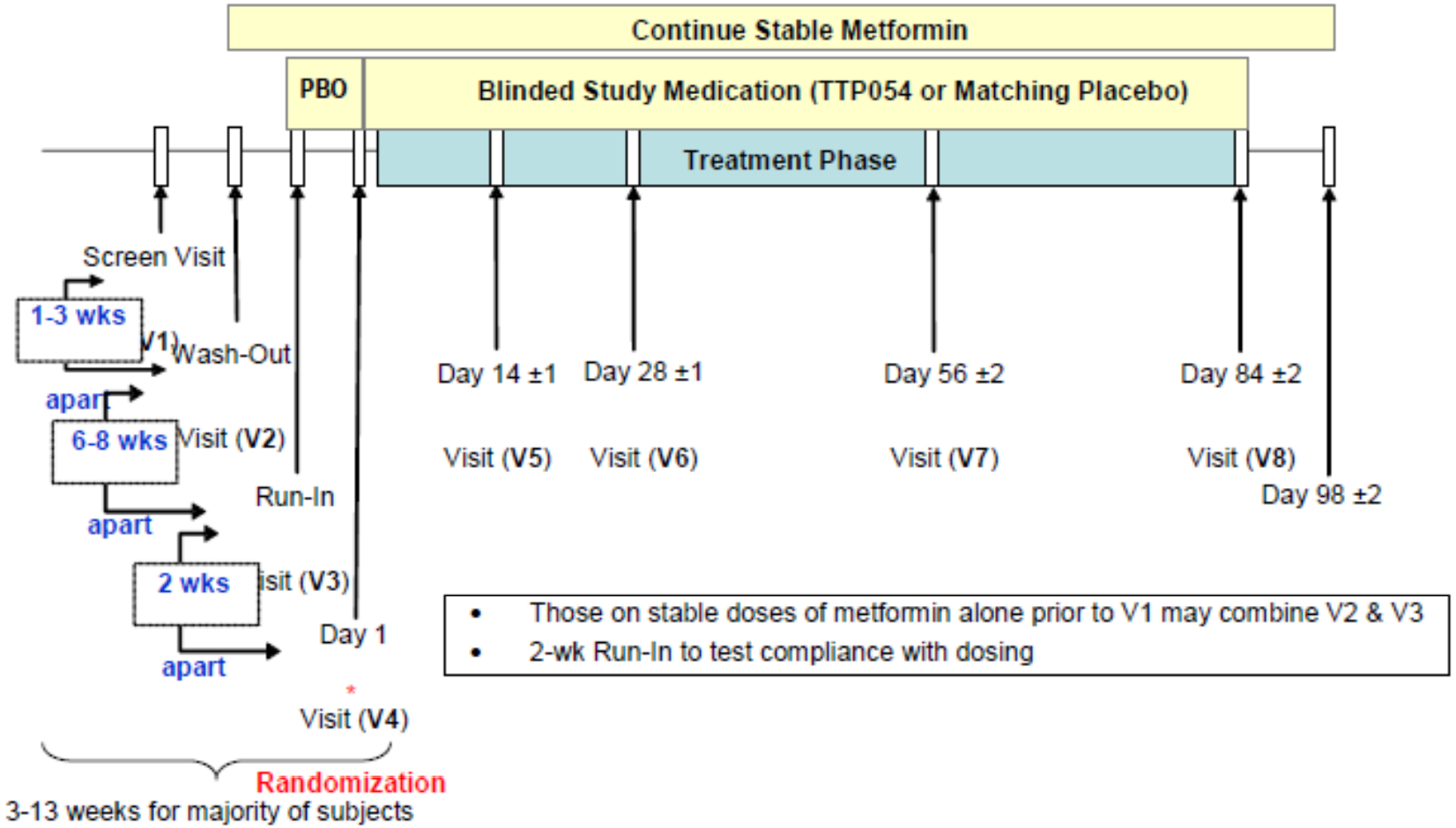
1st in Class: Oral, Small Molecule, Non-Peptide GLP-1R Agonists

	TTP054 (First Generation)	TTP273 (Second Generation)
Overview	***Achieved POC for Program*** ❖ *HbA_{1c} reduction with no GI side effect signal*	***Achieved POM*** ❖ *Glucose reduction with no GI side effect signal* ❖ *More potent than TTP054* ❖ *Appears more efficacious (based on short-term glucose lowering) than TTP054*
Clinical Status	Phase 2: 3 months in patients with T2DM ❖ **TTP054-201 (#156 Oral)**	Phase 1: 14 days in patients with T2DM ❖ **TTP273-102 (#155 Oral)**

TTP054-201 Primary Study Objective

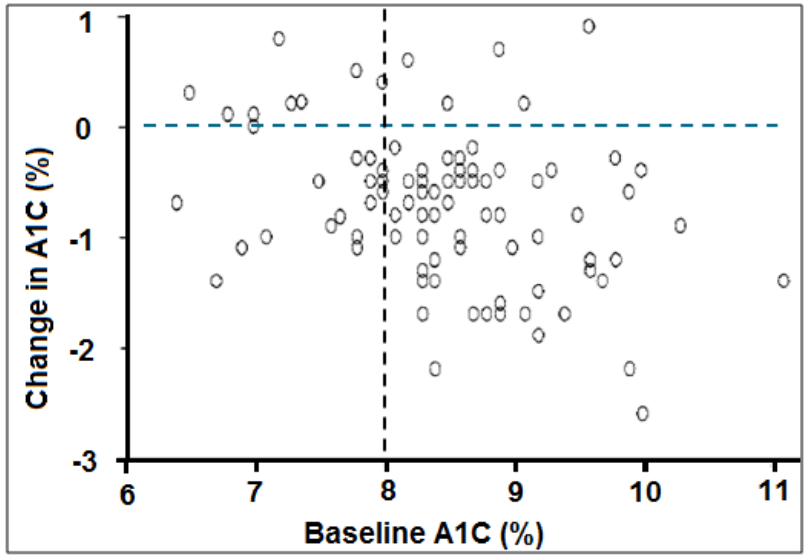
- To evaluate the efficacy and safety of TTP054 administered once daily for 12 weeks in adults with type 2 diabetes mellitus (T2DM) on stable doses of metformin

Study Design



Statistical Analysis:

- Enrichment strategies *(FDA guidance; December 2012)*
  - Enrolled broad population to understand safety (Baseline HbA_{1c} 6.5-11%)
  - Utilize enrichment strategy to evaluate magnitude of drug effects
    - Primary efficacy analysis (ITT principle):
      Protocol Target Population (Baseline HbA_{1c} 8-11%)
    - Standard methodology: ANCOVA, MMRM, MI, LOCF, and OC



- Meta-analysis of 5 OAD Classes
  - SUs, meglitinides, metformin, TZDs, AGI
- When baseline HbA_{1c} < 8%, HbA_{1c} reduction of 0.1-0.2% in active vs. control

Bloomgarden et al, 2006. Diabetes Care 29:2137-9

Subject Disposition

All Subjects Dosed

Number of Subjects	Placebo	200 mg	400 mg	800 mg
Subjects Randomized & Dosed	**50**	**27**	**51**	**56**
Withdrawn for any reason	**17 (33%)**	**5 (19%)**	**10(20%)**	**9 (16%)**
Lack of efficacy	8**	0	2*	3
Lost to follow-up	6	1	5	1
Adverse events	1	1	0	3
Moved away/family emergency	0	0	2	0
Medication/visit compliance/other	2	3	1	2

* *Subject 1075 had baseline HbA_{1c}=11.2%; Subject 1052 had screening HbA_{1c}=10.8; day 14 HbA_{1c}=11.2*

** *4 subjects withdrew prior to day 28; no post baseline HbA_{1c} data*

Treatment-Emergent AEs of Special Interest

All Subjects Dosed

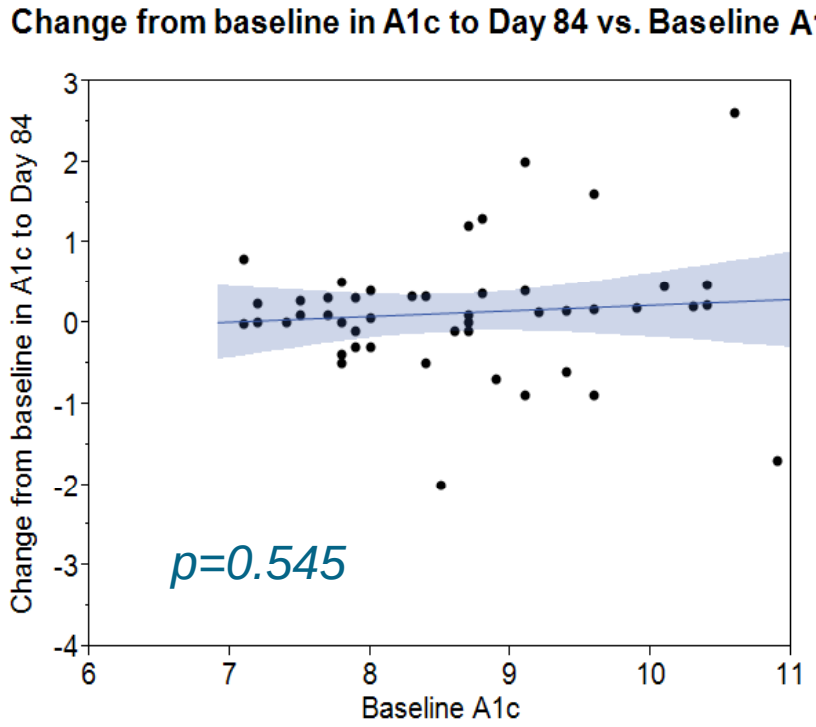
System Organ Class *AE Preferred Term*	Placebo (n=50)	200 mg (n=27)	400 mg (n=51)	800 mg (n=56)
Number of Subjects with any AE	**20 (40%)**	**10 (37%)**	**14 (27%)**	**25 (45%)**
Total Number of Events	**56**	**27**	**28**	**67**
Gastrointestinal Disorders	**5 (10%)**	**1 (4%)**	**2 (4%)**	**9 (16%)**
Gastrointestinal Disorders (Related)	**4 (8%)**	**1 (4%)**	**1 (2%)**	**5 (9%)**
Diarrhoea	0	0	1	2
Dyspepsia	1	0	0	0
Flatulence	1	0	0	0
Nausea	3	1	0	2
Vomiting	2	0	0	1

- SAEs considered treatment-related: 2 LFT elevations, both in 800 mg cohort
  - Both had other potential contributing factors, and both resolved
  - Neither had concerning symptoms or increases in bilirubin
- No major LFT concern
  - No increase in median LFT values over time in any dose group
  - No LFT signal in any other clinical study or in any toxicology study

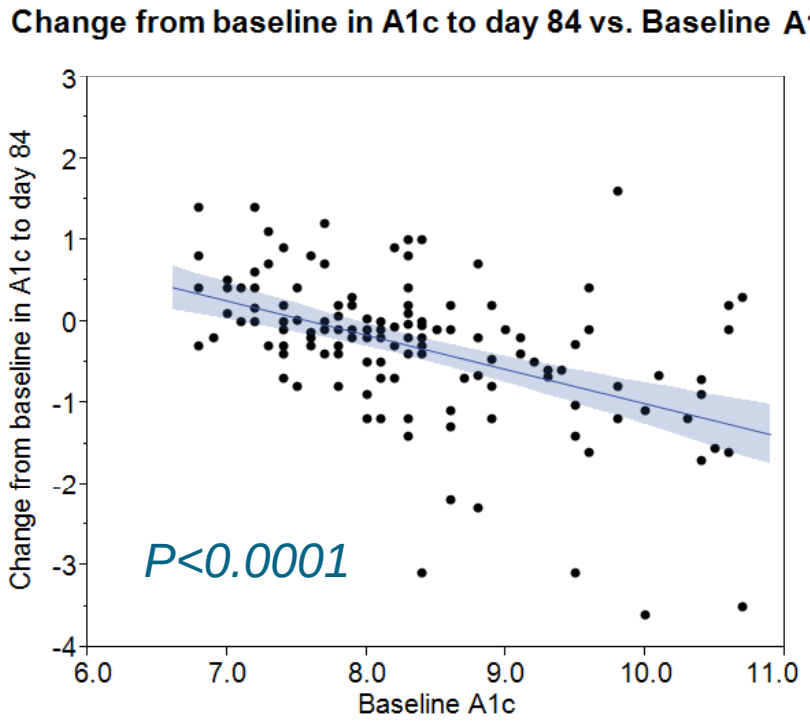
HbA_{1c} at Baseline Influences Response to TTP054

Baseline HbA_{1c} 11% or less

PLACEBO



TTP054



Demography: Protocol Target Population

Baseline HbA_{1c} 8-11%

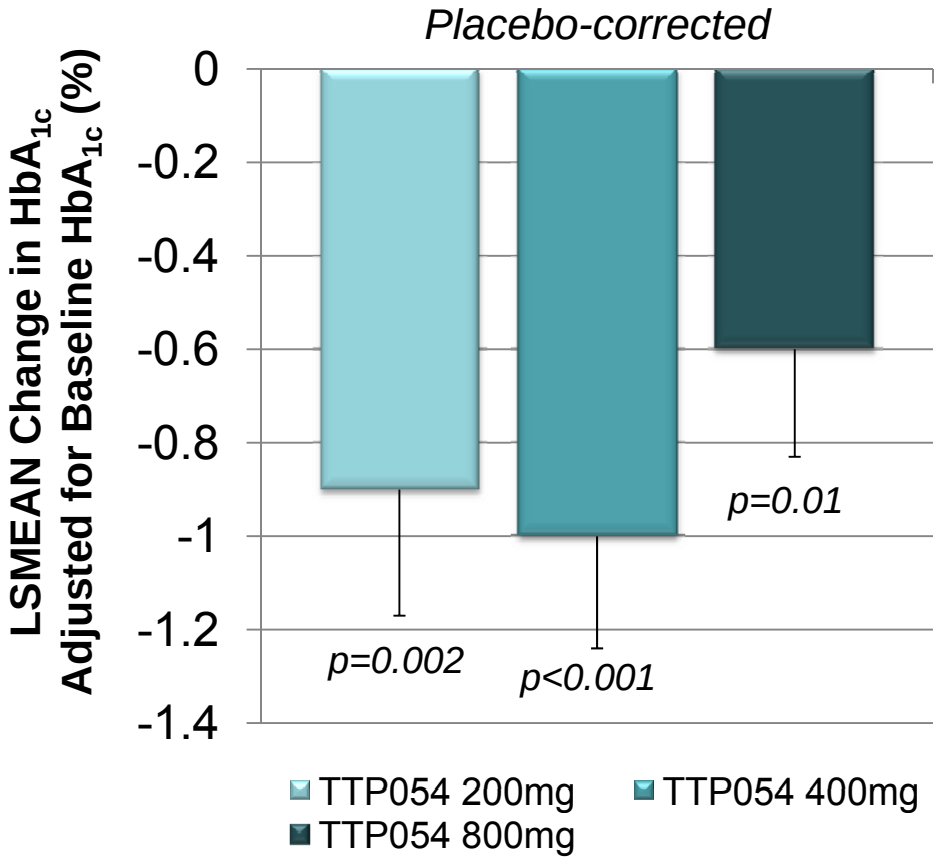
Characteristic	Statistic	Placebo (n=31)	200 mg (n=19)	400 mg (n=28)	800 mg (n=35)
Sex	Male (number)	21	15	17	17
	Female (number)	10	4	11	18
Race	White/Black/Other (number)	27/2/2	16/3/0	25/3/0	24/9/2
Age	Mean (Range)	52 (30-67)	55 (42-70)	54 (26-69)	57 (32-69)
Weight	Mean (Range)	84 (53-125)	83 (59-143)	82 (45-117)	87 (48-132)
Baseline HbA_{1c} (%)	Mean (SD)	9.2 (0.8)	9.1 (0.9)	9.0 (0.9)	8.8 (0.8)
Metformin	Monotherapy (number)	25	13	25	25
	Plus OAD (number)	6	6	3	10
Completers	Completer (Dropout)	20 (11)	15 (4)	21 (7)	28 (7)

TTP054-201

Primary Analysis: LSMean (Baseline-Adjusted) Change in HbA_{1c}

Protocol Target Population (LOCF; ITT)

Subjects with Baseline HbA_{1c} 8-11%



- All groups show statistically significant placebo-corrected, reductions in HbA_{1c}
- No statistically significant difference between doses

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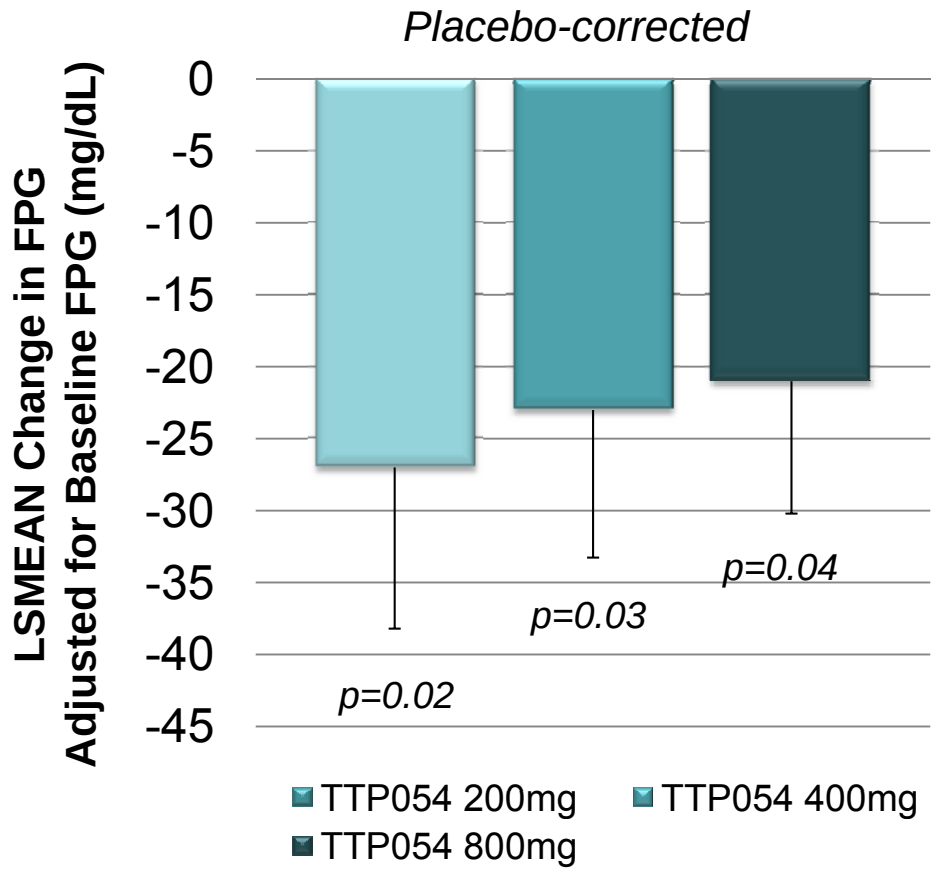
LSMean (Baseline-Adjusted) Change in *FPG*

Protocol Target Population (LOCF; ITT)

Subjects with Baseline HbA_{1c} 8-11%



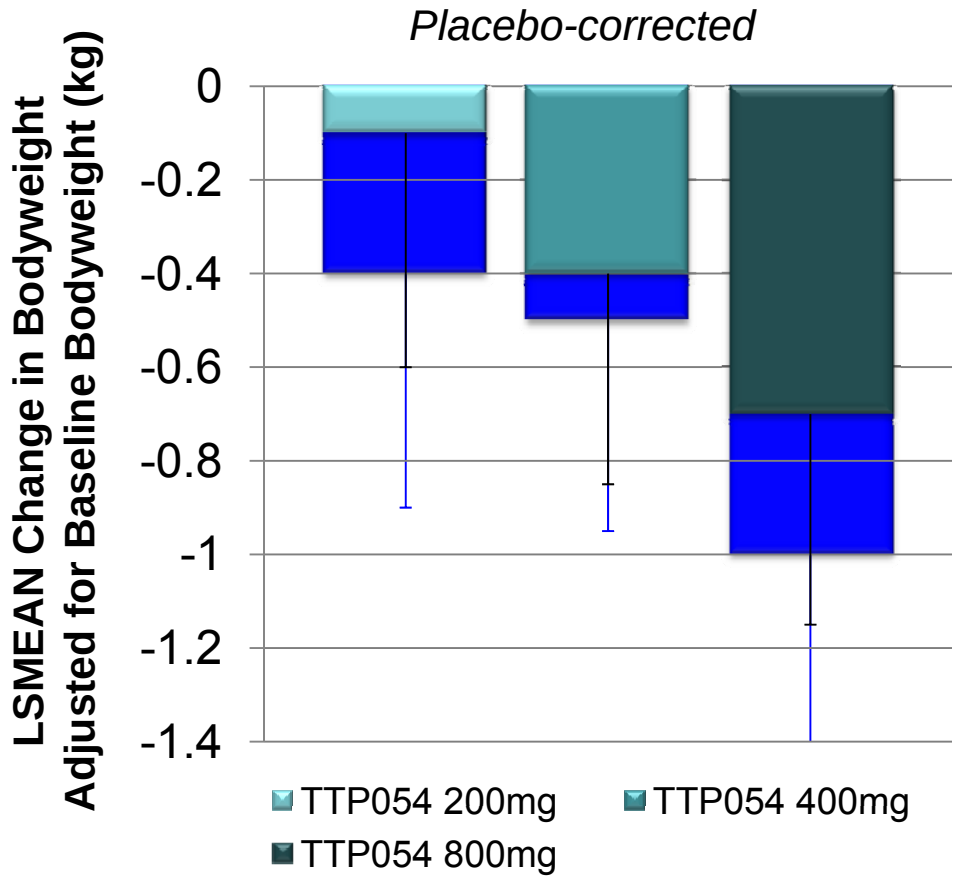
- All groups show statistically significant placebo-corrected, reductions in FPG
- No statistically significant difference between doses

TTP054-201

LSMean (Baseline-Adjusted) Change in *Bodyweight*

Protocol Target Population (LOCF; ITT)

Subjects with Baseline HbA_{1c} 8-11%



- Dose-responsive trend (non-significant) for reduction in body weight (endpoint not adequately powered)
- When OAD-washout patients were excluded (blue bars):
  - More pronounced weight loss observed
  - Significant for 800 mg group ($p<0.05$)

TTP054-201 Summary

- Oral GLP-1R agonist TTP054 demonstrated Proof of Concept
  - Significant HbA_{1c} lowering at all doses tested
    - Same conclusions whether target population used vs. full protocol population
  - Trend for BW reduction (significant for metformin-monotherapy patients)
  - Negligible GI side effects

- Magnitude of HbA_{1c} reduction was similar to that predicted from a previously disclosed 4-week study *[Diabetes, 2013 ADA abstract (115-OR)]*
  - 1% placebo-adjusted decrease in HbA_{1c} was predicted from the results of the 400 mg dose

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