GLP-1R is a well validated target for the treatment of Type 2 Diabetes Mellitus (T2DM). Injectable GLP-1R peptide agonists are effective in lowering blood glucose and reducing weight. They are generally safe and well tolerated except for major side effects related to nausea and vomiting. Data shown herein characterizes orally bioavailable, specific, non-peptide GLP-1R agonists TTP054 and TTP273 through in silico modeling, cellular binding and activation studies, mouse pharmacology models and Phase 1b clinical study results.

TTP273 is currently being evaluated for efficacy and safety in a Phase 2 study in T2DM subjects on stable metformin (logra).
In silico modeling suggests vTv GLP-1R Agonists Bind to an Allosteric Site
In silico modeling suggests vTv GLP-1R Agonists Bind to an Allosteric Site

KRE - Key Recognition Element for Affinity
ACL- Accessory Conformational Locker
KEA - Key Element for Affinity and Activation
Differences in KEA between TTP054 and TTP273 and a key sequence difference between human and mouse receptor drive increased binding and activation of TTP273 in human and mouse.
TTP273: a GLP-1R Agonist with Functionally Selectivity...

...and Typical GLP1 Pharmacology

Enhances insulin secretion

Decreases glucose

Decreases food intake
Improved Tolerability in Type 2 Diabetic subjects

Lowering of Mean Daily Glucose and Fasting Plasma Glucose

Clinical efficacy and safety are reported from a 14 day, multiple ascending dose placebo controlled Phase 1b study of 112 type 2 diabetic subjects on stable doses of metformin. CFB MDG was calculated based on the change in AUC0-24 following a MTT prior to dosing and following 14 days of dosing and CFB FPG was reported following an overnight fast prior to dosing and following 14 days of dosing.

Low incidence of Nausea and Vomiting

<table>
<thead>
<tr>
<th>AEs of Interest</th>
<th>Nausea</th>
<th>Vomiting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo Pooled</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>TTP273 Low Dose*</td>
<td>2 (3.9%)</td>
<td>1 (2.0%)</td>
</tr>
<tr>
<td>TTP273 High Dose*</td>
<td>2 (6.3%)</td>
<td>0</td>
</tr>
<tr>
<td>TTP273 Pooled*</td>
<td>4 (4.8%)</td>
<td>1 (1.2%)</td>
</tr>
</tbody>
</table>

*Groups defined by daily dose: PBO: pooled from all cohorts, Low dose (<150mg: 25-100 QD, 75 QPM, 25 BID), or High dose (≥150mg: 150-450 QD, 75-150 BID)