Taselisib (GDC-0032) is an orally bioavailable, potent, and selective inhibitor of mTOR. PK is comparable with historical data, suggesting no DDI with taselisib. 

OBJECTIVES

Primary Objectives

- Evaluate the safety and tolerability of taselisib in combination with letrozole in postmenopausal female patients with locally advanced or metastatic hormone receptor-positive breast cancer

Secondary and Exploratory Objectives

- Evaluate the antitumor activity of taselisib in combination with letrozole
- Assess the PK of taselisib and letrozole

RESULTS

Table 1. Patient Baseline Characteristics.

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Taselisib 6 mg QD + Letrozole</th>
<th>Taselisib 9 mg QD + Letrozole</th>
<th>All Patients (N=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range)</td>
<td>64 (45-85)</td>
<td>60 (40-71)</td>
<td>62 (40-85)</td>
</tr>
<tr>
<td>ECOG PS</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Prior systemic therapies, median (range)</td>
<td>3 (3-6)</td>
<td>3 (2-6)</td>
<td>3 (2-6)</td>
</tr>
</tbody>
</table>

Safety

- No DDI was observed between taselisib and letrozole in breast cancer xenograft models

Key Inclusion and Exclusion Criteria

- Postmenopausal female with advanced or metastatic hormone receptor-positive breast cancer
- Progression or recurrence on ≥1 prior endocrine therapy in the metastatic setting

Pharmacokinetics

- Plasma samples were collected at predose, 1, 2, 3, 4, 8, and 24 hr post-dose on Day 15 to characterize the PK of taselisib and letrozole.

Figure 2. Steady State Plasma Concentrations of Taselisib in Combination with Letrozole.

Clinical Activity/Efficacy

- Clinical Activity: in 12/19 (63%) patients, Partial Metabolic Response was observed.

Figure 3. Preliminary Data From FDG-PET Evaluating Patients Shows a Partial Metabolic Response as Best Response in 12/19 (63%) Patients.

Figure 4. Anti-Tumor Activity: Best Change in Target Lesions Based on RECIST Measurable Disease.

Figure 5. Time on Study and Dose Received by Patients.

Figure 6. Clinical Activity: pCR in ER+ PIK3CA-Mutant Breast Cancer.

Additional patients are being enrolled to test this letrozole/taselisib combination with the new tablet formulation.

Figure 7. Clinical Activity: pCR in PIK3CA-Mutant Breast Cancer.

CONCLUSIONS

- TAS-1001 (taselisib) is an oral, orally bioavailable, selective and potent mTOR inhibitor
- Clinical Activity: in 12/19 (63%) patients, Partial Metabolic Response was observed.
- Phase Ib Study of the PI3K Inhibitor Taselisib (GDC-0032) in Combination with Letrozole in Patients with Hormone-Receptor-Positive Advanced Breast Cancer.