Activity of TGR-1202, a Novel Once-Daily PI3Kδ Inhibitor, in Patients with Relapsed or Refractory Hematologic Malignancies
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Background

- PI3Kδ is highly expressed in cells of hematopoietic origin and is often upregulated in lymphoid malignancies
- TGR-1202 is a novel, next-generation PI3Kδ inhibitor, with a unique structure which contributes to:
  - Extended half-life and accumulation that enables once-daily dosing
  - Differentiated safety profile from other PI3Kδ inhibitors in development, notably absent of hepatotoxicity

Results

- **Efficacy:** Best Percent Change from Baseline in Nodal Size
  - CCL patients Enrolled at 100 mg QD, Currently at 800 mg QD
  - 78% (9/12) of CCL patients treated at 800 mg or higher achieved ≥80% nodal reduction (median nodal reductions of 93% at 800 mg)
  - Remaining two patients achieved >40% nodal reduction at first response assessment and remain on study awaiting next scan
  - Nodal reductions showed to improve with time on TGR-1202

- **Toxicity:** Overall Efficacy
  - 40 evaluable patients
  - Overall response rate of 33% (13 CR, 26 PR, 1 PD, 11 NR)
  - Efficacy results are impacted by patient’s prior therapy regimen

- **Other Utilized Patients**: 800 mg Fed at Cmax (Food Effect in Patients with Non-Hodgkin Lymphoma (NHL), Celiac Disease Symptoms (CD), Hodgkin’s Lymphoma (HL), and select other B-cell lymphoproliferative disorders

Conclusion

- TGR-1202 is a once-daily PI3Kδ inhibitor with single agent activity observed in patients with a variety of relapsed/refractory hematologic malignancies
- Marked activity has been observed in patients with relapsed refractory CLL, with a 78% nodal response rate at doses ≥800 mg (median time on study of 6 months)
- TGR-1202 has been well tolerated, with no drug related transaminase elevations and no events of colitis reported, with 38% (10/26) of evaluable patients treated at ≥800 mg on study over 6 months and same on daily TGR-1202 for over a year, demonstrating an adverse event profile which supports combination therapy
- No MTD has been achieved and dose escalation is ongoing with micronized formulation and fed state dosing which is projected to provide a 3-4X increase in exposure over dosing to date, with better GI tolerability demonstrated
- Additional studies are ongoing evaluating TGR-1202 in combination with approved and novel agents, with Phase III studies in development

Study Design

- **3+3 Dose Escalation Schema:**
  - TGR-1202 as a single agent
  - Dose levels: 800 mg, 100 mg, 200 mg, 800 mg, 1200 mg
  - Cohorts are initiated at the starting dose level
  - Dose escalation will continue in 250 mg increments

- **Study Group:**
  - Patients with relapsed or refractory hematologic malignancies

- **Study Setting:**
  - Phase 1 study of TGR-1202 in patients with relapsed/refractory hematologic malignancies
  - TGR-1202 dosed orally twice-daily (QD) in continuous 28 Day Cycles
  - Dose-escalating cohorts (DC) assessed in cycle 1 prior to escalation
  - Retro-escalated dose escalation allowed for patients in previous cohorts following establishment of safety at higher doses