BACKGROUND

• RET alterations are targetable oncogenic drivers in multiple tumor types, including ~40% of advanced medullary thyroid cancer (MTC) and ~20% of papillary thyroid cancer (PTC).
• No selective RET inhibitors are approved.

BLU-667: Designed to Treat RET-Altered Cancers

BLU-667 potently and selectively inhibits RET alterations, including those that confer resistance to VEGF.

High kinase selectivity for RET*.

METHODS

• ARROW: BLU-667 Dose-Response/Expansion Study

ARROW: Dose-Response/Expansion Study

Part 1: Dose-Escalation Study (Complete: Na=23)

Part 2: Expansion Study (Ongoing)

1. RET-altered or advanced solid tumors
2. 30-400 mg PO daily (QD) or BID
3. Phase 2 dose determined (400 mg QD)

RESULTS: ADVANCED RET-MUTATED MTC

Patient Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RET-mutated MTC (400 mg QD Starting Dose)</th>
<th>Prior Cabo or Vand (Na=43)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), median (range)</td>
<td>54 (18-85)</td>
<td>57 (21-85)</td>
</tr>
<tr>
<td>ECOG PS, n (%)</td>
<td>0 1 2</td>
<td>0 1 2</td>
</tr>
<tr>
<td>Metastatic disease, n (%)</td>
<td>56 (66)</td>
<td>43 (77)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>55 (64)</td>
<td>34 (53)</td>
</tr>
<tr>
<td>Prior systemic regimens, median (range)</td>
<td>2 (1-5)</td>
<td>2 (1-5)</td>
</tr>
</tbody>
</table>

RESULTS: ADVANCED RET FUSION+ PTC

Patient Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RET fusion + PTC (All Na=19)</th>
<th>Prior Cabo or Vand (Na=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), median (range)</td>
<td>55 (19-72)</td>
<td>50 (24-71)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>10 (53)</td>
<td>10 (91)</td>
</tr>
<tr>
<td>Prior systemic regimens, median (range)</td>
<td>2 (2-4)</td>
<td>3 (2-4)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>9 (58)</td>
<td>2 (18)</td>
</tr>
</tbody>
</table>

Antitumor Activity

Tumor Response 

Best response: CR, PR, SD, PD

Treatment and Response Duration 

Treatment ongoing: PD, SD, PD

Conclusions

• BLU-667 demonstrates broad and durable antitumor activity in patients with advanced, RET-altered MTC and PTC.
• 63% ORR and 94% DCR in RET-mutated MTC previously treated with cabozantinib or vandetanib; 85% ORR in PTC.
• Reponses observed regardless of treatment history or RET mutation type (including gatekeeper mutation V804M).
• Well-tolerated at 400 mg QD: all responding patients with MTC remain on treatment.

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• Well-tolerated at 400 mg QD: all responding patients with MTC remain on treatment.
• Breakthrough therapy designation granted for RET-mutated MTC requiring systemic treatment and for which there are no acceptable alternative treatments.
• Additional cohorts continue to assess benefit of BLU-667 in multiple other RET- and RET fusion+ solid tumors.

Activity and Tolerability of BLU-667, a Highly Potent and Selective RET INHIBITOR, in Patients with Advanced RET-Altered Thyroid Cancers

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