US Respiratory Development Compounds

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☐ Proactive investigator communication

☐ Proactive initiative support
## Respiratory Pipeline Overview

<table>
<thead>
<tr>
<th>Planned filing</th>
<th>Project/Product</th>
<th>Mechanism of action</th>
<th>Potential indication/disease area</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019</td>
<td>Omalizumab</td>
<td>Anti-IgE Ab</td>
<td>Nasal polyposis</td>
<td>3</td>
</tr>
<tr>
<td>2019</td>
<td>QAW039</td>
<td>DP2 antagonist</td>
<td>Asthma</td>
<td>3</td>
</tr>
<tr>
<td>≥ 2021</td>
<td>CJM112</td>
<td>Anti-IL17 Ab</td>
<td>Asthma</td>
<td>2</td>
</tr>
<tr>
<td>≥ 2021</td>
<td>CSJ117</td>
<td>Anti-TSLP antibody fragment</td>
<td>Asthma</td>
<td>1</td>
</tr>
<tr>
<td>≥ 2021</td>
<td>QBW251</td>
<td>CFTR potentiator</td>
<td>COPD</td>
<td>2</td>
</tr>
</tbody>
</table>

**Investigational. Efficacy and safety have not been established**

DP2, D prostanoid type 2 receptor; CFTR, cystic fibrosis transmembrane conductance regulator

Omalizumab
(Anti-IgE antibody)
Xolair: Anti-IgE in nasal polyposis

<table>
<thead>
<tr>
<th>Phase III Study Design</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>24 Week Treatment Period</strong></td>
</tr>
<tr>
<td>5 week Run-in</td>
</tr>
<tr>
<td>Omalizumab Q2W or Q4W</td>
</tr>
<tr>
<td>Placebo Q2W or Q4W</td>
</tr>
<tr>
<td>Open Label Extension</td>
</tr>
<tr>
<td>Safety Follow up</td>
</tr>
<tr>
<td>28 weeks</td>
</tr>
</tbody>
</table>

Polyps-1 and Polyps-2 trials in active enrollment.

- 24-week trials including ~120 patients with a nasal polyp score of ≥5 with a unilateral score of ≥ 2 for each nostril.
- Omalizumab administered either every 2 or 4 weeks as a subcutaneous injection.
- Primary objective to determine the efficacy and safety of omalizumab compared with placebo in adult patients with chronic rhinosinusitis with nasal polyps who have had an inadequate response to standard of care treatments.
- Planned filing in 2019

Investigational. Efficacy and safety have not been established

Fevipiprant – QAW039
(Prostaglandin D2 receptor antagonist)
Fevipiprant (QAW039): A prostaglandin D2 receptor antagonist

Fevipiprant (QAW039) is a prostaglandin D2 receptor antagonist.

- **Prostaglandin D2 (PGD2) release**
- **Th2 cells, ILC2 cells**
  - Fevipiprant inhibits binding of PGD2 to DP2 receptor
  - Downstream effects inhibited
    - IL-4, IL-5, IL-13 release
    - Migration, activation, and mediator release

**Stimuli**

**Mast cell**

**IgE**

**Eosinophils**

**Investigational. Efficacy and safety have not been established**

DP2 = D prostanoid receptor 2; ILC2 = Type 2 Innate Lymphoid Cells; PGD2 = Prostaglandin D2; Th2 = Type 2 T helper cells

Previously reviewed

A2208: Effect on sputum eosinophils

Patient population
- Asthma patients receiving ICS
- ACQ ≥1.5 or ≥1 severe exacerbation in prior 12 months*

Primary endpoint
- Sputum eosinophils after 12 weeks of treatment
- Sputum eosinophils ≥2%

• 3.5-fold reduction in sputum eosinophils vs placebo (p=0.0014)
• Clinically and statistically significant improvement in ACQ vs placebo (-0.56 point difference; p=0.046)
  - Observed in pre-specified subgroup with uncontrolled asthma at baseline (ACQ ≥1.5; n=40/61)

Investigational. Efficacy and safety have not been established

*Severe exacerbation defined as requiring an increase in systemic corticosteroid therapy for ≥3 days

Ongoing Phase 3 studies

Effect of Fevipiprant on Lung Function in Moderate-to-Severe Asthma
12-week, multicenter, randomized, double-blind, placebo-controlled studies to assess the efficacy and safety of QAW039 when added to standard-of-care asthma therapy in patients with uncontrolled asthma

Effect of Fevipiprant on Exacerbations in Severe Asthma
52-week, multicenter, randomized, double-blind, placebo-controlled studies to assess the efficacy and safety of QAW039 when added to standard-of-care asthma therapy in patients with uncontrolled asthma

Long-term Safety of Fevipiprant in Moderate-to-Severe Asthma
A 2-treatment period (52-week, 104-week), randomized, placebo-controlled, multicenter parallel-group study to assess the safety of QAW039 when added to existing GINA steps 3, 4, and 5 asthma therapy in patients with uncontrolled asthma

Investigational. Efficacy and safety have not been established
CJM112
(Anti-IL17A antibody)
CJM112: Anti-IL17A in T2-low Asthma

• Studied in uncontrolled moderate-to-severe asthma with low IgE and low serum eosinophils (T2-low)
  • Not eligible for biologics developed for T2-high (allergic/eosinophilic) asthma
  • Phase 2 randomized, subject/investigator blinded, placebo-controlled multi-dose study
  • Primary endpoint: Change in FEV1, Day 92
  • Secondary endpoints include Asthma Control Questionnaire (ACQ) and AEs, Day 92

• Patients (N=110)
  – 18-75 yrs with moderate-to-severe asthma
  – FEV1 40-90% predicted
  – Symptomatic (ACQ ≥1.5)
  – IgE <150 IU/mL and serum eosinophils <300/microliter

• Status: Ongoing, estimated study completion Sept 2019

1. Clinicaltrials.gov. NCT03299686

Investigational. Efficacy and safety have not been established
CSJ117
(Inhaled anti-TSLP antibody fragment)
CSJ117: Inhaled Once Daily Anti-TSLP in Asthma

• Studied in mild stable atopic asthma
  • Phase 1 randomized, subject/investigator blinded, placebo-controlled multi-dose study
  • Primary endpoint:
    – AEs, SAEs, 12 wks
    – Late asthmatic response based on AUC for time adjusted percent decrease in FEV1 after allergen inhalation challenge, 12 wks
    – Late asthmatic response as measured by the maximum percentage decrease in FEV1 after allergen inhalation challenge, 12 wks
  • Secondary endpoints include early asthmatic response based on the above mentioned measures and PK, 12 wks
  • Patients (N=55)
    – 18-60 yrs with mild stable atopic asthma
    – Must exhibit an early and late asthmatic response to a common inhaled allergen during the screening allergen inhalation challenge

• Status: Ongoing, estimated study completion July 2019

Investigational. Efficacy and safety have not been established

TSLP = Thymic stromal lymphopoietin
Clinicaltrials.gov. NCT03138811

Novartis
QBW251
(CFTR Potentiator)
QBW251: CFTR Potentiator in Bronchitic COPD

• Studied in GOLD II-III COPD with chronic bronchitis

  • Phase 2 randomized, double blind, placebo-controlled study
  • Primary endpoint: Change in lung clearance index (LCI), Day 29
  • Secondary endpoints include change in FEV1 and other spirometric measures and PK, Day 29

• Patients (N=92)
  – 18-75 yrs
  – GOLD stage II-III COPD with chronic bronchitis, severe emphysema excluded
  – Current smoker or ex-smoker with ≥10 pack-year smoking history

• Status: Completed

CFTR = Cystic fibrosis transmembrane conductance regulator protein; COPD = Chronic obstructive pulmonary disease; GOLD = The Global Initiative for Chronic Obstructive Lung Disease . Clinicaltrials.gov. NCT02449018

Investigational. Efficacy and safety have not been established