Monoclonal Antibody Solutions for Critical Infections
Clinical stage company developing novel mAbs to prevent and treat the most critical infectious diseases with the greatest unmet need

ASN100 is in a **Phase 2 superiority study** for the prevention of *S. aureus* pneumonia in high-risk, mechanically ventilated patients, with results expected in 2018

- ✔ Addresses the **number one cause of pneumonia** in mechanically ventilated patients, a condition with a **30% mortality rate** even with best-available care

- ✔ Standard-of-care biomarker diagnostic **precisely identifies target patients**

- ✔ **Best-in-class** product targets all 6 cytotoxins implicated in pneumonia pathogenesis

- ✔ Robust pre-clinical data package, Phase 1 safety, PK/PD modeling, and real-world epidemiology data in target patient population support **high probability of success**

- ✔ **White-space market opportunity with a $2B+ worldwide sales forecast**
Mechanically ventilated patients are at risk of acquiring *S. aureus* pneumonia, a critical infection that costs time, money, and lives.

**Colonization & Toxin Production**

- **Infection superhighway:** *S. aureus* colonizes the endotracheal tube
- Pathogenic cytotoxins destroy the epithelial and immune cells, increasing risk of pneumonia
- There are **no approved pneumonia prevention agents**

**Pneumonia**

- ~1/3 of heavily-colonized patients progress to pneumonia
- Despite novel, potent anti-staph antibiotics to treat pneumonia, outcomes are poor

+Weeks on Ventilation, in ICU, in Hospital

<table>
<thead>
<tr>
<th>S</th>
<th>M</th>
<th>T</th>
<th>W</th>
<th>T</th>
<th>F</th>
<th>S</th>
</tr>
</thead>
</table>

$50K Incremental Cost

30% Mortality

$50K
ASN100 is a novel targeted solution to the problem of *S. aureus* pneumonia in high-risk mechanically ventilated patients

- **Proactively identify** high-risk, heavily-colonized patients using standard-of-care diagnostics
- **Pre-emptively** administer a single dose of ASN100 to provide 3 weeks of toxin-neutralizing protection against *S. aureus* pneumonia

**Clinical Benefit**
- Reduce progression to pneumonia
- Reduce mortality

**Health Economic Benefit**
- Reduce ventilation, ICU, and hospital days
- Reduce hospital cost
- Improve hospital quality ratings
- Avoid Medicare reimbursement penalties

**Stewardship Benefit**
- No contribution to resistance development
- No harm to patient microbiome
Proven management team with demonstrated research, development, and commercial success funded by top-tier investors

René Russo, PharmD BCPS, President & Chief Executive Officer
Cubist, Bristol-Myers Squibb

Eszter Nagy, MD, PhD, Co-Founder & Chief Scientific Officer
Intercell, University of Vienna

David Mantus, PhD, Chief Development Officer
Cubist, Seres, Sention, Shire

Chris Stevens, MD, Chief Medical Officer
Cubist, Millennium / Takeda, Alnara, Circe, Altus

Michael Gray, MBA, CPA, Chief Financial Officer & Chief Business Officer
Curis, Reprogenesis, E&Y LLP
Deep pipeline of novel mAbs that address the most critical infectious diseases

**ASN100**
*Staphylococcus aureus*
Prevention of pneumonia in high-risk mechanically ventilated patients

**ASN200**
*Escherichia coli*

**ASN300**
*Klebsiella pneumoniae*

**ASN400**
*Streptococcus pneumoniae*

**ASN500**
Respiratory syncytial virus (RSV)
Recent grant from the Bill & Melinda Gates Foundation to Advance Novel Anti-Viral Program with Global Unmet Need

Arsanis and Adimab Enter Into License Agreement to Target Respiratory Syncytial Virus (RSV) With Monoclonal Antibodies

Arsanis awarded up to $9.3 million from the Bill & Melinda Gates Foundation to advance RSV antibody program towards the clinic
ASN100
Phase 2 for the prevention of *S. aureus* pneumonia in high-risk mechanically ventilated patients, with results expected in 2018
S. aureus pneumonia is a preventable infection that costs hospitals time, money, and lives.

**Time**

1 to 2 incremental weeks on ventilator, in the ICU, and in the hospital.

**Money**

~$50K Incremental Cost

Incremental days for ventilated patients with pneumonia over ventilated patients without pneumonia¹

**Lives**

~30% Mortality Rate

Hospital cost incurred for ventilated patients with and without pneumonia¹

Recent prospective epidemiology study in ASN100 target patient population confirms burden of disease literature

Increased burden of disease in mechanically-ventilated, heavily colonized patients with pneumonia over those without pneumonia

+5 days of mechanical ventilation

<table>
<thead>
<tr>
<th></th>
<th>Without Pneumonia</th>
<th>With Pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without Pneumonia</td>
<td>9</td>
<td>14</td>
</tr>
<tr>
<td>With Pneumonia</td>
<td>14</td>
<td>14</td>
</tr>
</tbody>
</table>

+7 days in hospital

<table>
<thead>
<tr>
<th></th>
<th>Without Pneumonia</th>
<th>With Pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without Pneumonia</td>
<td>17</td>
<td>24</td>
</tr>
<tr>
<td>With Pneumonia</td>
<td>24</td>
<td>24</td>
</tr>
</tbody>
</table>

55% in-hospital mortality

<table>
<thead>
<tr>
<th></th>
<th>Without Pneumonia</th>
<th>With Pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without Pneumonia</td>
<td>19%</td>
<td>55%</td>
</tr>
<tr>
<td>With Pneumonia</td>
<td>55%</td>
<td>55%</td>
</tr>
</tbody>
</table>
**S. aureus pneumonia: mechanism of disease**

*S. aureus* produces an arsenal of cytotoxins to invade human tissue and destroy immune cells.

**6 cytotoxins (Hla + 5 leukocidins)** are critical to the development of *S. aureus* pneumonia.

The ideal agent for protection against *S. aureus* pneumonia addresses both mechanisms of cytotoxin-induced damage:

1) Protect lung epithelial cells to prevent *S. aureus* penetration

2) Protect immune cells to allow for *S. aureus* elimination via opsonophagocytosis
ASN100 is a combination of 2 fully human monoclonal antibodies (mAbs) that together neutralize the 6 *S. aureus* cytotoxins critical to the development of *S. aureus* pneumonia.

**ASN100**

- **ASN-1:** a broadly cross-reactive mAb that neutralizes alpha-hemolysin (Hla) plus 4 of the 5 *S. aureus* leukocidins.
- **ASN-2:** highly potent mAb that is uniquely able to inactivate the fifth *S. aureus* leukocidin, LukGH.

Irreversible binding neutralizes toxins and prevents disease. This is a proven MOA - antitoxin antibodies (e.g. *C. difficile*).
ASN100 is the only mAb in development that protects lung epithelial cells and phagocytes *in vitro*

ASN-1 protects human lung cells as effectively as Hla-only mAbs...

... but only ASN-1 neutralizes leukocidins to protect human phagocytes

ASN100 mAbs act synergistically to provide complete protection of human phagocytes \textit{in vitro}

Both mAbs (ASN-1 and ASN-2) are needed to neutralize all 5 leukocidins and provide complete protection across a diversity of strains and toxin expressions.

![Bar chart showing survival of human phagocytes exposed to MRSA in the presence of ASN-1, ASN-2, and ASN100. The chart indicates that ASN100 provides complete protection, while neither ASN-1 nor ASN-2 alone are sufficient. Both mAbs are required across >20 different strains of \textit{S. aureus}.]
Unlike Hla-only mAbs, ASN100 provides complete protection in prophylactic pneumonia model

ASN100 provides 100% protection when tested using the 4 most virulent, clinical strains of *S. aureus* (MSSA & MRSA)

Robust epidemiology data in target patient population informs Phase 2 study design

2. Kabak et al. unpublished

Mechanically Ventilated Patients

High-Risk Heavily-Colonized Patients

ASN100 Targets

S. aureus Pneumonia Patients

<table>
<thead>
<tr>
<th>Study Type</th>
<th>% of Mechanical Ventilated Patients at High-Risk</th>
<th>% of High-Risk Patients Who Progress to Pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrospective study1 (n~230)</td>
<td>17%</td>
<td>39%</td>
</tr>
<tr>
<td>Prospective study2 (n~240)</td>
<td>16%</td>
<td>30%</td>
</tr>
<tr>
<td>Phase 2 assumptions</td>
<td>20%</td>
<td>25%</td>
</tr>
</tbody>
</table>

2. Kabak et al. unpublished
Definitive Phase 2 superiority trial with results expected in 2018

Study Design

- Double-blind, placebo-controlled, ASN100 (3,600 mg) vs. placebo
- Superiority design and conservatively powered based on 25% placebo rate and 50% reduction in ASN100 arm
- ~350 patients; 60 sites in US and Europe
- Interim analysis for conditional power planned at ~150 patients

Key Inclusion Criteria

- Patients on mechanical ventilation
- Patients with heavy *S. aureus* colonization
- Concomitant antibiotics allowed

Endpoints

Primary: Incidence of *S. aureus* pneumonia at 21 days

Other: Length of hospital stay
- Days on mechanical ventilation
- All cause mortality

Timeline

<table>
<thead>
<tr>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1</td>
<td>Q1</td>
</tr>
<tr>
<td>Q2</td>
<td>Q2</td>
</tr>
<tr>
<td>Q3</td>
<td>Q3</td>
</tr>
<tr>
<td>Q4</td>
<td>Q4</td>
</tr>
</tbody>
</table>

Phase 2

Initiated Q4 2016

Interim
ASN100 Commercial Overview

$2 Billion white-space opportunity for a novel indication with high unmet need and no approved drugs
ASN100 provides a simple, elegant, and responsible solution to the problem of *S. aureus* pneumonia in high-risk mechanically ventilated patients

Using standard of care diagnostics, clinicians can proactively identify heavily-colonized high-risk mechanically ventilated patients and administer a single dose of ASN100 to provide three weeks of protection against *S. aureus* pneumonia

---

**ASN100 Aspires to**

- Safely reduce progression to pneumonia
- Improve health economics
  - Reduce ventilation, ICU, and hospital days
  - Reduce hospital cost
  - Reduce mortality
- Support stewardship efforts by reducing inappropriate antibiotic use
- Improve hospital quality ratings and reduce Medicare reimbursement penalties

**ASN100 Will Not**

- Contribute to the development of antibiotic resistance
- Harm the patient’s microbiome
- Break the hospital budget; incremental drug acquisition cost will be offset by lower total cost of care
Everybody wins with ASN100

“Monoclonal antibodies are exciting. There is the advantage that these are independent of resistance.”

“It definitely makes sense to target high-risk patients and give them an extra something, these are the patients we really worry about.”

“Less pneumonia always means fewer problems for us and for the patients.”

“The burden of pneumonia on patients is huge. Less means substantially decreasing a ventilated patient’s risk of mortality, risk of developing complications...it’s a long list.”

“I like this because it means there is less pneumonia in my ICU. For me that means the patients aren’t getting staph pneumonia as often, and are at lower risk for complications. For the hospital, and for P&T it means less treatment expenditure, no mortality costs. Everybody wins.”
Clinical stage company developing novel mAbs to prevent and treat the most critical infectious diseases with the greatest unmet need

ASN100 is in a **Phase 2 superiority study** for the prevention of *S. aureus* pneumonia in high-risk, mechanically ventilated patients, with results expected in 2018

✓ Addresses the **number one cause of pneumonia** in mechanically ventilated patients, a condition with a **30% mortality rate** even with best-available care

✓ Standard-of-care biomarker diagnostic **precisely identifies target patients**

✓ **Best-in-class** product targets all 6 cytotoxins implicated in pneumonia pathogenesis

✓ Robust pre-clinical data package, Phase 1 safety, PK/PD modeling, and real-world epidemiology data in target patient population support **high probability of success**

✓ **White-space market opportunity with a $2B+ worldwide sales forecast**