Jefferies 2015
Health Care Conference

June 2\textsuperscript{nd}, 2015

Jon Stonehouse, \textit{President \& Chief Executive Officer}
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Building BioCryst – Oral drugs for rare diseases

Revolutionizing the treatment of hereditary angioedema (HAE) and other rare diseases with oral small molecules

- FDA Approved
- Stockpiling
- Seasonal sales
- Completing Phase 1
- US gov’t funded
- Stockpiling

**BCX4161**
- Oral kallikrein inhibitor in advanced development

**BCX7353**
- 2nd generation kallikrein inhibitor BCX7353 entering clinical development 2Q15

**BCXxxxx**
- Two rare disease targets in early discovery

Foundation of structure based drug design discovery platform generating potent and specific enzyme inhibitors
BioCryst’s steps toward revolutionizing HAE treatment

**Revolutionary step 1: BCX4161**
- OpuS-1 proof of concept efficacy/safety
- OpuS-2 enrolling
- Improving formulation pre- and post-approval
- Building commercial & medical affairs capability
- Anticipate 2017 NDA filing
- First to market oral prophylactic
- Launch in key markets upon approval

**Revolutionary step 2: 2nd Gen**
- Target profile: 1 pill, once a day, wipe out attacks
- Initial BCX7353 PK indicates potential to meet our target profile
- Preclinical development complete
- Initiating Phase 1 during 2Q15
- Worldwide launch upon approval

Retain worldwide rights to our broad oral kallikrein inhibitor portfolio
HAE is significantly undertreated and underdiagnosed. In spite of approved treatments, disease burden remains high.

Survey of 186 patients in Spain, Germany and Denmark

- 59% of patients reported an attack at least once a month
- 67% reported moderate-to-severe pain during an attack
- 74% reported moderate-to-severe swelling during an attack
- Duration of swelling lasted 12-24 hours in patients who treated an attack within 1 hour of symptoms
- Anxiety regarding future attacks significantly reduces quality of life in moderate to severe HAE patient population

Global prevalence ~ 140,000 people

~15,000 people with HAE in US + EU-5 + Japan

Burden of Illness Study in Europe

- Survey of 186 patients in Spain, Germany and Denmark
- 59% of patients reported an attack at least once a month
- 67% reported moderate-to-severe pain during an attack
- 74% reported moderate-to-severe swelling during an attack
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2. Grouping based on UN World Population Prospects: The 2012 Revision
Academic investigation indicates that HAE patients with more severe disease have lower levels of endogenous kallikrein inhibitor [functional C1INH]¹

- Plasma samples from 115 patients with HAE, taken at the time of diagnosis, and 64 healthy controls
- Standardized functional C1INH (C1INHf) level assays
- Significantly lower levels of functional C1INH in plasma in patients with progressively more severe disease (overall p=0.0003)
- Disease score integrates frequency of attacks, attack severity, and need for medical intervention²

1. Kelemen Z, Moldovan D, Mihaly E, et al. Baseline level of functional C1-inhibitor correlates with disease severity scores in hereditary angioedema. Clin Immunol 2010;134(3):354-358 (Figure reproduced under license by permission of the publisher.)

Similarly, academic investigators have shown that HAE patients with more frequent attacks have increased activation of the contact pathway\(^1\)

- Plasma samples from 162 patients with HAE, taken in routine clinic visits (ie not during an angioedema attack), and 81 healthy controls
- Standardized kininogen fragment (cleaved HK) assays
- Significantly higher levels of cleaved kininogen in plasma in patients with progressively more frequent attacks

1. Suffritti C, Zanichelli A, Maggioni L, et al. High-molecular-weight kininogen cleavage correlates with disease states in the bradykinin mediated angioedema due to hereditary C1-inhibitor deficiency. *Clin Exp Allergy 2014* (Figure reproduced under license by permission of the publisher.)
OPuS-1 Efficacy and safety results supported promotion of BCX4161 into advanced development

- OPuS-1 was a randomized placebo-controlled crossover study in 24 HAE patients with high baseline attack rates
  - The primary endpoint was met, p < 0.001
- A significant improvement in health-related quality of life (AeQoL) weighted total score was observed after 4 weeks of BCX4161 administration, p=0.004
- Disease activity (AAS28) was reduced over 4 weeks of BCX4161 administration, p=0.022
- The safety and tolerability profile of BCX4161 was similar to placebo

<table>
<thead>
<tr>
<th>Adjudicated attacks</th>
<th>BCX4161 period n=24</th>
<th>Placebo period n=24</th>
<th>Difference (95% CI)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Least Squares Mean Attack rate per week</td>
<td>0.82</td>
<td>1.27</td>
<td>-0.45 (-0.67, -0.23)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Analysis was performed using a mixed effect model including sequence, period and treatment as fixed effects, and subjects within sequence as a random effect. Sequence and period were not significant.
Advanced development of BCX4161 is targeting NDA in 2017

**OPuS-2: Randomized placebo-controlled 12-week study of BCX4161 in HAE**

- Primary endpoint: mean acute angioedema attack rate (same as in OPuS-1)
- n= 32 per arm
- 100 mg soft gel capsule dosage form

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**Completion of Advanced Development of BCX4161**

- Commercial formulation development
  - Initial NDA/MAA: goal of three capsules per dose
  - sNDA: target further improvement to two capsules per dose
- Complete NDA/MAA requirements for clinical efficacy, clinical safety, nonclinical safety and commercial manufacturing
Patients with less-frequent attacks should show proportionally greater treatment benefit compared to those with more attacks.

**Illustrative data**

- **Normal range, attack-free**
- **1.6 attack / mo improvement**: > 70% relative reduction
- **1.6 attack / mo improvement**: > 40% relative reduction

- **Infrequent attacks**: 1.6 attack / mo improvement
- **Frequent attacks**: 4 attacks / month improvement
- **Very frequent attacks**: 2.4 attacks / month improvement

- **Attack frequency - Attacks per Month**
  - 0
  - 1
  - 2
  - 3
  - 4

- **Kallikrein inhibitory activity**
  - 0%
  - 25%
  - 50%
  - 75%
  - 100%
  - 125%
BCX7353 2nd generation oral plasma kallikrein inhibitor: Superior PK compared to BCX4161

Rat BCX7353

NHP (BCX7353 & BCX4161) and Human (BCX4161)
Rapivab® (peramivir injection)  
First BioCryst discovered drug approved in U.S.

- **Indication**: for the treatment of acute uncomplicated influenza in patients 18 years and older who have been symptomatic for no more than 2 days

- First and only one dose i.v. treatment approved in the U.S.

- Adverse events observed in clinical trials were similar to placebo and mild, with the most common adverse reaction being diarrhea (8% Rapivab vs. 7% placebo)

- **Make available this flu season**: High margin return on sales, revenue generation contributes to funding HAE program

- BioCryst will work during 2015 to secure a U.S. Government procurement contract

- **Full prescribing information available at** [www.rapivab.com](http://www.rapivab.com)
Stockpiling potential allows for lower cost of capital

**Precedent flu antiviral stockpiling**

- Over 107 million treatment courses of influenza antiviral drugs in the national inventory [FY2014, PHSSEF budget]

- During 2009 H1N1 pandemic, BCRX supplied 10,000 5-day courses of peramivir under a contract to procure up to 40,000 courses

- Continued support for pandemic influenza preparedness in FY2015 HHS budget

**Precedent highly pathogenic countermeasures**

<table>
<thead>
<tr>
<th>Product</th>
<th>Pathogen</th>
<th>Company</th>
<th>Doses</th>
<th>Cost ($M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BioThrax vaccine</td>
<td>Anthrax</td>
<td>Emergent BioSolutions</td>
<td>29M</td>
<td>$691</td>
</tr>
<tr>
<td>Raxibacumab antitoxin (CY ’13)</td>
<td>Anthrax</td>
<td>GSK</td>
<td>60K</td>
<td>$193</td>
</tr>
<tr>
<td>AbThrax antibody</td>
<td>Anthrax</td>
<td>HGS (now GSK)</td>
<td>65K</td>
<td>$326</td>
</tr>
<tr>
<td>Botulinum antitoxin</td>
<td>Botulism</td>
<td>Cangene</td>
<td>200K</td>
<td>$427</td>
</tr>
<tr>
<td>MVA vaccine</td>
<td>Smallpox</td>
<td>Bavarian Nordic</td>
<td>20M</td>
<td>$505</td>
</tr>
<tr>
<td>ACAM2000 vaccine (CY ‘08)</td>
<td>Smallpox</td>
<td>Acambis</td>
<td>&gt;72M</td>
<td>$425-660</td>
</tr>
<tr>
<td>ST-246 antiviral</td>
<td>Smallpox</td>
<td>Siga</td>
<td>1.7M</td>
<td>$433</td>
</tr>
</tbody>
</table>

1. FY2014 Budget for Public Health and Social Services Emergency Fund, pg 116
BCX4430 is the *only* single treatment to show improved survival in NHP experimental models of two different filovirus infections.

BARDA awarded BioCryst an advanced development contact 3/31 worth up to $35m.

**Marburg Virus cynomolgus macaque study**

**Ebola Virus Rhesus macaque study**


Right panel, BioCryst data on file. Study conducted at USAMRIID and funded by NIH/NIAID under contract HHSN272201300017C.
# Cash position & 2015 guidance (in millions)

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash &amp; investments at March 31, 2015</td>
<td>$111.3</td>
</tr>
<tr>
<td>Q1 2015 operating cash utilization</td>
<td>$3.8</td>
</tr>
</tbody>
</table>

## 2015 Guidance

<table>
<thead>
<tr>
<th>Description</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating cash utilization&lt;sup&gt;+&lt;/sup&gt;</td>
<td>$65 – 80</td>
</tr>
<tr>
<td>Operating expenses&lt;sup&gt;#{}&lt;/sup&gt;</td>
<td>$75 – 95</td>
</tr>
<tr>
<td>Cash runway from December 31, 2014</td>
<td>Beyond mid-2016</td>
</tr>
</tbody>
</table>

<sup>+</sup>Excludes hedge adjustments & other non-routine cash flows.

<sup>#{}</sup> Excludes equity-based compensation.
Value creating milestones in 2015

- Commence Phase 1 study of BCX7353 (2nd generation) oral kallikrein inhibitor (2Q:15)
- Complete BCX4430 Phase 1 development program (3Q:15)
- Complete BCX7353 Phase 1 study (3Q:15)
- Report results from OPuS-2 HAE trial (YE:15)
- Secure advanced development funding for BCX4430 (March)
- Initiate 2nd Gen HAE Phase 2 proof of concept trial (YE:15)
- Obtain U.S. Government RAPIVAB procurement contract (YE:15)