Revolutionizing the Treatment of Infectious Diseases with Defensin-Mimetics
Disclaimer and Safe Harbor

**Forward-looking statements**
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Developing drugs is risky, expensive, and time-consuming. All timelines and projections are based on data currently available. Advancement to each next step of development is contingent on positive data from previous work supporting such progress. Additional required experiments and studies can add significant time and cost. Substantial delays and additional costs typically occur in drug development, and should be expected. You should consider these risks carefully before making any investment. This discussion is permitted by the Private Securities Litigation Reform Act of 1995.
PolyMedix Overview

Rational Drug Design + Rational Business Model

❖ **Novel drugs for serious acute disorders**

❖ **Two products in Phase 2 clinical trials –**
  - Infectious Disease: *Novel Antibiotic – Defensin-Mimetic PMX-30063*
  - Acute Cardiovascular: *Anticoagulant Reversing Agent PMX-60056*

  - *Large market opportunities, major unmet medical needs*
  - *Straightforward clinical endpoints*
  - *Acute dosing – efficient, inexpensive development paths*

  - Efficacy and safety demonstrated in 8 clinical trials

❖ **Proprietary computational drug discovery platform –**

  - Internally discovered pipeline of innovative, first of their kind drugs
PMX-30063 – Competitive Advantages
*The first and only defensin-mimetic*

- New Class of Antibiotic – **Defensin-Mimetic** – *small molecule mimic of host-defense proteins*
  - **Unique mechanism of action** - designed to make bacterial resistance unlikely
    - Unlikely to encounter a non-responsive strain
    - Unlikely for resistance to develop in the future
- Gram+ and Gram- activity
- Bactericidal
- Anti-inflammatory
- Anti-biofilm properties
- Potential shorter course of therapy & monotherapy
- Phase 2 – 215 patients completed enrollment
  - **Interim analysis from ~ 80 patients indicates all dosing arms are safe + 93% clinical success by day 2-3**
The Antibiotic Market Today...

Biochemical Approach

- Beta-lactams
- Glycopeptides
- Cell wall synthesis
- Lipopeptides
- Cell membrane depolarization
- Aminoglycosides
- Macrolides
- Tetracyclines
- Ribosomes
- Fluoroquinolones
- Sulfonamides
- DNA
Resistance a risk for **all** of them

**Biochemical Approach**

- Beta-lactams
- Glycopeptides
  - Cell wall synthesis
- Lipopeptides
  - Cell membrane depolarization
- Aminoglycosides
- Macrolides
- Tetracyclines
- Fluoroquinolones
- Sulfonamides
- Ribosomes
- DNA

>70% of infections are now drug resistant
Learning from Evolution to Solve the Problem:
*Mimicking host-defense proteins*

**Biochemical Approach**
- Beta-lactams
- Glycopeptides
- Cell wall synthesis
- Aminoglycosides
- Macrolides
- Tetracyclines
- Ribosomes
- Fluoroquinolones
- Sulfonamides
- DNA

**Biophysical Approach**
- Lipopeptides
- Cell membrane depolarization

**PMX-30063**

*Directly disrupts cell membrane*

First synthetic, *small-molecule* mimetic of host-defense proteins
- Imitates body’s natural defense system
- Selective for bacteria
- Bacterial resistance has not developed despite millions of years of evolution
- Active against hundreds of resistant strains
Direct Membrane Disruptive Mechanism
Unique Mechanism of Action Among Systemic Antibiotic Drugs

SEM’s of drug effects on *E. coli* bacteria, 30-60 min time kill

**PMX-30063 is bactericidal and has the same membrane disruptive mechanism of action as the natural human defensin proteins**
PMX-30063 – Resistance Unlikely to Develop

Even after up to 20 passages, no bacterial resistance was seen with PMX-30063
PMX-30063 Mimicks the Mechanism of Action of Human Defensin Proteins

The biological activities of host defense proteins depend on an *amphiphilic helix*:

Novel approach: *imitate nature with small molecule mimetics* of host defense proteins
Selective for Bacteria

**Human Cells**

- Antimicrobial peptide
- Hydrophobic interactions
  - Outer leaflet
  - Inner leaflet

**Bacterial Cells**

- Electrostatic and hydrophobic interactions
  - Prototypic plasma membrane of a multicellular animal (erythrocyte)
  - Bacterial cytoplasmic membrane

- Cholesterol
- Zwitterionic phospholipids
- Acidic phospholipids
**PMX-30063 is active against vancomycin, daptomycin, and linezolid resistant strains**

*Broad spectrum activity against drug-sensitive and resistant strains of S. aureus, S. epidermidis and S. hemolyticus*

<table>
<thead>
<tr>
<th></th>
<th>Drug-suscept.</th>
<th>OXA-R</th>
<th>VRSA/VISA OXA-R</th>
<th>LZD-NS OXA-R</th>
<th>DAP-NS OXA-R</th>
<th>VRSA/VISA DAP-NS OXA-R</th>
</tr>
</thead>
<tbody>
<tr>
<td>isolates</td>
<td>217</td>
<td>161</td>
<td>7</td>
<td>5</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>30063 MIC range</td>
<td>0.25 - 1</td>
<td>0.25 - 2</td>
<td>0.5 - 1</td>
<td>0.5 - 1</td>
<td>0.5 - 2</td>
<td>0.5 - 1</td>
</tr>
</tbody>
</table>

OXA-R: oxacillin-resistant  
VISA: vancomycin intermediate S. aureus  
VRSA: vancomycin resistant S. aureus  
LZD-NS: linezolid non-susceptible  
DAP-NS: daptomycin non-susceptible

Data Presented at IDSA, October 2011
**PMX-30063 - Safely Administered in Healthy Subjects**

**Completed 3 Phase 1 studies in 123 subjects**

<table>
<thead>
<tr>
<th>Phase</th>
<th>n</th>
<th>Dose (mg/kg)</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A</td>
<td>26</td>
<td>2.5</td>
<td>1</td>
</tr>
<tr>
<td>1B</td>
<td>77</td>
<td>0.6 (3.0 total dose)</td>
<td>5-10</td>
</tr>
<tr>
<td>1B</td>
<td>20</td>
<td>1.0 load + 0.35/day (5.5 total dose)</td>
<td>Up to 14</td>
</tr>
</tbody>
</table>

**Combined Results:**

- Side effects prevalent with other antibiotics **not observed**
- **No** gastrointestinal, metabolic, respiratory, renal, or blood chemistry effects
- Dose-limiting adverse effects were transient, self-limiting, and fully reversible without treatment
- Supported advancing into Phase 2

Data Presented at ECCMID, May 2011
PMX-30063 Phase 2 Study -- Design

Objective: Safety and Efficacy

- Trial conducted in Canada & Europe (Russia, Ukraine)
- 7 days of dosing (5 days on PMX-30063 + 2 days placebo; 7 days for daptomycin); 1x/day IV infusion
- 200 patients, 4 arms, 50 patients per arm
- Interim analysis completed after first 80 patients
### Overall Clinical Success - *Pooled results across all four dose groups*

<table>
<thead>
<tr>
<th>Clinical Success</th>
<th>Day 2-3 On Therapy</th>
<th>Day 7-8 End of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average (all groups)</td>
<td>93%</td>
<td>92%</td>
</tr>
<tr>
<td>Range</td>
<td>87% - 100%</td>
<td>87% - 100%</td>
</tr>
</tbody>
</table>

- Consistent efficacy across all groups
- Potential for shorter dosing regimens

**Safety:**
- All treatment arms were safe and generally well-tolerated
- No deaths
- No arm(s) discontinued as a result of SAE’s or premature treatment discontinuations
- Transient sensations of mild “tingling” was most frequent observed side effect
Skin Infection (ABSSSI) & Clinical Response from Phase 2 Study

Pre-treatment

Post-treatment (Day 7)
PMX-30063 Phase 2 – Next Steps

- Enrollment completed - 215 patients
- Data analysis underway
- Full study results for all patients expected in 1H 2012
- FDA discussions planned
- Additional efficacy study planned for 2012
  - Potential shorter dosing regimen
# Competitive Positioning: PMX-30063 vs. Leading MRSA Antibiotics

<table>
<thead>
<tr>
<th></th>
<th>Azithromycin (macrolides)</th>
<th>Vancomycin (glycopeptides)</th>
<th>Linezolid (oxazolidinones)</th>
<th>Daptomycin (lipopeptides)</th>
<th>PMX-30063 (Defensin-mimetic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Mechanism/Class of Antibiotic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Short Dosing Schedule</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Bactericidal Activity</td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
<td>✓ ✓</td>
</tr>
<tr>
<td>Gram+ and Gram–Activity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Long post-antibiotic effect</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td>Anti-inflammatory &amp; anti-biofilm properties</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td>Resistance unlikely</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>
PMX-30063 Antibiotic
Additional opportunities

**Other indications for current i.v. formulation:**
- Bacteremia
- Endocarditis
- Pneumonia

**Other indications for current solution formulation:**
- Topical application – oral musositis in cancer patients
- Topical application – ophthalmic infections

**Oral formulation:**
- *Clostridium difficile*
- Crohns Disease/Irritable Bowel Syndrome

**Other defensin-mimetics - >300 lead compounds:**
- Gram-negative pathogens
- Fungal infections
- Tuberculosis
Cancer Oral Mucositis

- Oral ulcerative mucositis common, painful, dose-limiting toxicity - can lead to reduction/cessation of radiation and chemotherapy for cancer
- **Appx. 450,000 patients/year in U.S. alone**
- The risk of septicemia is increased 4-fold in oral mucositis
- **62% of patients require hospitalization for oral mucositis**
- **70% of patients with Grade 3 or 4 require gastric feeding tubes**
- Adds an average of **$18,515 to the cost of treatment**
- 1-point increase results in **$25,405 in additional hospital costs**
- Only 1 approved agent – Kepivance- narrow indication – $9,900/cycle

---

1 S. Sonis
Oral Mucositis

Courtesy Dr. Stephen Sonis, Brigham and Women’s Hospital, Harvard Medical School
PMX-30063 significantly reduces duration of mucositis in animal models

Number of days of mucositis > Grade 3:

- Placebo: > 40%
- PMX-30063: < 3%

92%-94% reduction in oral mucositis
Clinical Predictability of the Hamster Oral Mucositis Models  
*Studies by Dr. Stephen Sonis, Harvard*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Effect in animal model</th>
<th>Effect in Clinic</th>
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<tbody>
<tr>
<td>ActoGenix</td>
<td>33%</td>
<td>30%</td>
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<tr>
<td>AG013 (HTF-1)</td>
<td>33%</td>
<td>30%</td>
</tr>
<tr>
<td>SciClone SCV-07</td>
<td>33%</td>
<td>30%</td>
</tr>
<tr>
<td>Velafermin (hFGF-20)</td>
<td>37%</td>
<td>51%</td>
</tr>
<tr>
<td>PMX-30063</td>
<td>94%</td>
<td></td>
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</tbody>
</table>
PMX-60056 Heptagonist

- Improve anticoagulant management of bleeding complications
- Specific reversing agent for heparin, LMWH
- Acute care, single-dose, short-term follow-up
- Efficacy and safety demonstrated in in 4 P1/P2 clinical studies
- Two Phase 1B/2 clinical trial underway

Pentasaccharide sequence on all heparin, LMWHs

PMX-60056 heptagonist

PolyMedix®
Challenges with Anticoagulation Therapy
*Balancing clotting and bleeding*

- **Heparin** (LMWH, Bivalirudin)
  - Coronary artery bypass graph
  - Angioplasty
  - Stent replacements
  - Deep vein thrombosis
  - Orthopedic surgery
  - Cancer
  - Hip & Knee replacements
  - General surgery
  - Abdominal surgery

Prevent blood clots

Maintain adequate supply of blood

Reduce risk of bleeding
Potential Applications & Estimated Patient Populations Worldwide

- PCI - 2.5 mm
- CABG - 800 K
- Heart Valve - 200 K
- Pacemaker - 400 K
- LMWH Major Bleed - 600 K
- LMWH Non-major Bleed - 2.4 mm

Around 7 million potential patient uses/year worldwide
PMX-60056 – Anticoagulant Reversing Agent
Rationally designed to reverse heparin, LMWHs

- **Heparin**
  - Synthetic, small-molecule
  - Binds to the pentasaccharide sequence
  - Prevents interaction with antithrombin
  - Reverses drug effects

- **LMWH**
**Potential Indications/Uses**
- PCI
- Heart Valve Replacements
- CABG
- LMWH-associated bleeding

**Clinical Outcomes**
- Reduce incidence of bleeding (surgery)
- Treat bleeding (LMWH)
- Allow optimal anticoagulation

**Targeted Results**
- Save lives
- Save money
Heparin Reversal
Individual Subjects – No variation

Data Presented at AHA, 2010
Total PMX Dose to Near Baseline vs Protamine Requirement

\[ y = 0.4295x \]

\[ R^2 = 0.963 \]

Data Presented at ASH, 2010
PMX-60056 Ongoing Clinical Trials

**Phase 2 PCI Trial - Ongoing**
- Open label
- Up to 40 patients
  - Undergoing Percutaneous Coronary Intervention (PCI)
  - Received heparin
- Acute i.v. administration
- 14 day follow-up
- Endpoint: Safely and rapidly reverse heparin in PCI patients with PMX-60056

**Phase 1B/2 Trial – Ongoing**
- Reverse enoxaparin – dose-response study
## Full Pipeline

*Created internally with proprietary drug discovery technology*

<table>
<thead>
<tr>
<th>Product</th>
<th>Indication</th>
<th>Pre-Clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
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<tbody>
<tr>
<td><strong>Infectious Disease</strong></td>
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<td><strong>PMX-30063</strong></td>
<td>Skin Infections (ABSSSI)</td>
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<td>Blood Stream Infections*</td>
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<td>Lung infections*</td>
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<td>Cancer Oral Mucositis</td>
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<tr>
<td><strong>Next-generation PMX defensin- mimetics (&gt;300)</strong></td>
<td>Gram-negative infections</td>
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<td></td>
<td>Anti-fungal</td>
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<td>Biodefense – anthrax, plague</td>
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<td></td>
<td>Malaria</td>
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<td></td>
<td>Tuberculosis</td>
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<td><strong>Supported by 15 grants</strong></td>
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<td><strong>Cardiovascular</strong></td>
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<tr>
<td><strong>PMX-60056</strong></td>
<td>Angioplasty, Stents (PCI)</td>
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<td>Heart Surgery (CABG)*</td>
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<td>Emergency Care*</td>
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<td><strong>Antimicrobial Materials</strong></td>
<td>Biomaterials Applications</td>
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<tr>
<td><strong>PolyCide®</strong></td>
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* Phase 1 data support other IV uses.
Commercialization

- Retain rights to market certain hospital products in North America

- Out-license select products –
  - International rights
  - Primary care, oral applications

- PMX-30063 antibiotic –
  - Systemic i.v. – ABSSSI, pneumonia
    - Pivotal trials possible in 2013 – 2x appx. 700 patients
  - Cancer oral mucositis – topical oral rinse
  - Favorable pharmacoeconomics possible
## Financial Summary (as of September 30, 2011)

<table>
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<tr>
<th>Category</th>
<th>Details</th>
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<tbody>
<tr>
<td>Cash &amp; Investments:</td>
<td>$25.0M</td>
</tr>
<tr>
<td>Common Stock:</td>
<td>106M</td>
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<tr>
<td>Options:</td>
<td>18.1M ($1.22 weighted average strike)</td>
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<td>Warrants:</td>
<td>50.6M ($0.99 weighted average strike)</td>
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<td>Total Fully Diluted Shares:</td>
<td>174M</td>
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<td>Recent Institutional Investors:</td>
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<tr>
<td>Fidelity</td>
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<td>RA Capital</td>
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<tr>
<td>Perceptive</td>
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<td>Ayer Capital</td>
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<td>RCM Capital</td>
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<tr>
<td>William Harris</td>
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**Upcoming Milestones**

**PMX-30063 Defensin-Mimetic Antibiotic**
- Final results from 215 patients in Phase 2 ABSSSI trial
- Next Phase 2 efficacy study

**PMX-60056: Anticoagulant reversing agent**
- Complete Phase 2 PCI Trial
- Complete Phase 1B/2 Lovenox (enoxaparin) reversal study
## Value Proposition

### Two Novel First in Class Drugs in Phase 2

<table>
<thead>
<tr>
<th>Defensin-mimetic Antibiotic</th>
<th>Anticoagulant Antagonist</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMX-30063</td>
<td>PMX-60056</td>
</tr>
</tbody>
</table>

### Full Pipeline of Innovative Therapeutics

<table>
<thead>
<tr>
<th>Areas with Efficient, Inexpensive Development</th>
<th>Clinical Trials</th>
<th>Non-Dilutive Grants</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 clinical trials completed, 2 underway</td>
<td>15 non-dilutive</td>
<td>support drug discovery</td>
</tr>
</tbody>
</table>

### Solid Business & Scientific Foundation

<table>
<thead>
<tr>
<th>Large Market Opportunities</th>
<th>Superior Product Positioning</th>
<th>Proprietary Computational Drug Design Platform</th>
</tr>
</thead>
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PolyMedix®