BUILDING A HEALTHY FUTURE FOR ALL

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Eugene J. Choi, Ph.D.
Executive Director
ejchoi@vcu.edu

Website:
www.medicines4all.vcu.edu
Twitter: @medsforall
Instagram: medicines4all
What Motivates Us?

- 36.7 million people worldwide live with HIV
- 53% receive antiretroviral treatments
- 4 million people die annually from HIV, tuberculosis, malaria, viral hepatitis, and other neglected tropical diseases
Democratize Pharmaceutical Manufacturing by open sourcing low cost processes to drive price reductions in the marketplace

Reinvent Medicine Supply Chain via vertical integration of advanced starting materials prepared from commodity chemicals & leveraging of flexible manufacturing methodologies that enable direct-to-consumer

Create the Next Generation of Global Scientists by instilling principles and foundations that drive accessibility & self-sustainability
The State of Pharmaceuticals Manufacturing

Primary Cost Drivers in Today’s Active Pharmaceutical Ingredient (API) Manufacturing

- Raw Materials
- Solvent Consumption
- Inflexible Processing Technologies

Lack of Access to Affordable Critical Medicines
Fragile Supply Chain
API Costs

Patented Drug Cost Components

- Limited window for optimization
- Time to market is key driver

Generic Drug Cost Components

- Must establish equivalency
- World Health Organization drugs similar to generics landscape

Consequences for Global Health Generics:
- Constrained manufacturer margins (supply chain risk)
  - New, low-volume treatments kept off market
  - Reduced access to critical meds

API costs drive 40-70% of the selling price for generic drugs
The Opportunity

Replace inefficient processes with streamlined production of critical medicines

- Reduce API costs so it is a minimal driver of medication price (esp. for generics)
- Develop a process optimization model that is translatable to:
  - High volume and low volume medications
  - Drugs in market and in development
- Develop novel manufacturing platforms to facilitate manufacturer AND market uptake
- Generate less waste with “greener” processes

Delivering Chemistry Innovation and Enabling Manufacturing Innovation

To Improve Access to, and Enhance Security of Supply of, Existing and Emerging Global Health Treatments
M4ALL Process Optimization & Implementation Approach

M4ALL Process Optimization
(for priority drug targets)

- Chemistry & Yield Optimization
- Solvent & Reagent Selection
- Commodity Starting Materials
- Process Consolidation
- Batch & Continuous Process

Manufacturing & Market Implementation

Address primary cost drivers in existing API manufacturing processes

Tech transfer partners enable manufacturer uptake of M4ALL processes & tracking of pricing reduction in market
M4ALL Outcomes: Nevirapine

M4ALL Nevirapine Process

Generic Manufacturers

M4ALL Improvements to Nevirapine Production

- Raw Material Costs: 40% down to 53%
- Yield: 91% increase
- Process Efficiency: 2x increase
- Solvent Changes: 5x decrease
- Waste-to-Product: 14x decrease

Total Price Decrease: 9%
2015 Savings: $7.8M
# M4ALL’s Portfolio of Targets

<table>
<thead>
<tr>
<th>HIV</th>
<th>Anti-Malarials</th>
<th>Antibiotics/Antimicrobials</th>
<th>Future plans to pursue</th>
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<tr>
<td>Nevirapine</td>
<td>Artemisinin</td>
<td>Ciprofloxacin</td>
<td><strong>Tuberculosis drugs</strong></td>
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<td>Tenofovir</td>
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<td>Fluconazole</td>
<td><strong>Oncology drugs</strong></td>
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<td>Dolutegravir</td>
<td>Future plans to pursue new targets</td>
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<td><strong>Opioid antagonists</strong></td>
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<td>Emtricitabine (in progress)</td>
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<td>Darunavir</td>
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<td>Lamivudine (3TC) (Planned)</td>
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Open Sourced Processes + Distributed Manufacturing

M4ALL Continuous Process for Nevirapine


Stage 1: Formation of CYCLOR (7)
Stage 2: Ring closure to nevirapine (1)

• Suite of COTS & bespoke platforms enables scalability at any level
Distribute Medicines Anywhere

- Reduces need for stockpiling
- Smaller footprint provides distribution flexibility
- Empowers regional & in-country (i.e. independence)
Anticipated Regulatory Science Challenges

- More players entering the market for global health drugs, including those that are developing continuous capabilities
- Altered, contaminated, and counterfeit products an ongoing global issue
- No reliable, simplified QA/QC for process or products

2015 Pharma Partnerships in Global Health

2017 Pharma Partnerships in Global Health

Source: IFPMA
Potential Solutions for Product & Process

Capability to analyze & control quality of reactants & products online:

• Innovative reactor platform capable of developing new chemistry pathways for fast process optimization and control

• Relies on effective measurement technologies, to determine critical process attributes to quickly optimize reaction parameters

• Integrated control of all reactor parameters in a smart systems approach allows for fast screening of reaction space with real-time measurement to provide an agnostic platform for chemical development, optimization, and production

On-line measurement technologies provide feed stock quality & reactor control resulting in quality API products
Potential Solutions for Supply Chain

Safe & Secure Tracking of Medicines via Blockchain

**Raw Materials Supplier**
- Date of birth
- Supplier name
- Supplier departure date

**Manufacturer**
- Date & confirmation of receipt of raw materials
- Process specs
- Batch lot specs & validation

**Blockchain**
- Transparent record of every modification without ability to tamper

**Distributor**
- Date & confirmation of receipt of medicines
- Batch lot specs & validation
- Packaging & labeling location
- Product expiration date

**Internet of Things/Cloud Based Monitoring & Data Collection**

**Consumer**
- Scan QR codes on medicine packaging to view data from each step of the process
Acknowledgements