



do more
feel better
live longer

Pharmaceutical Manufacturing Innovation

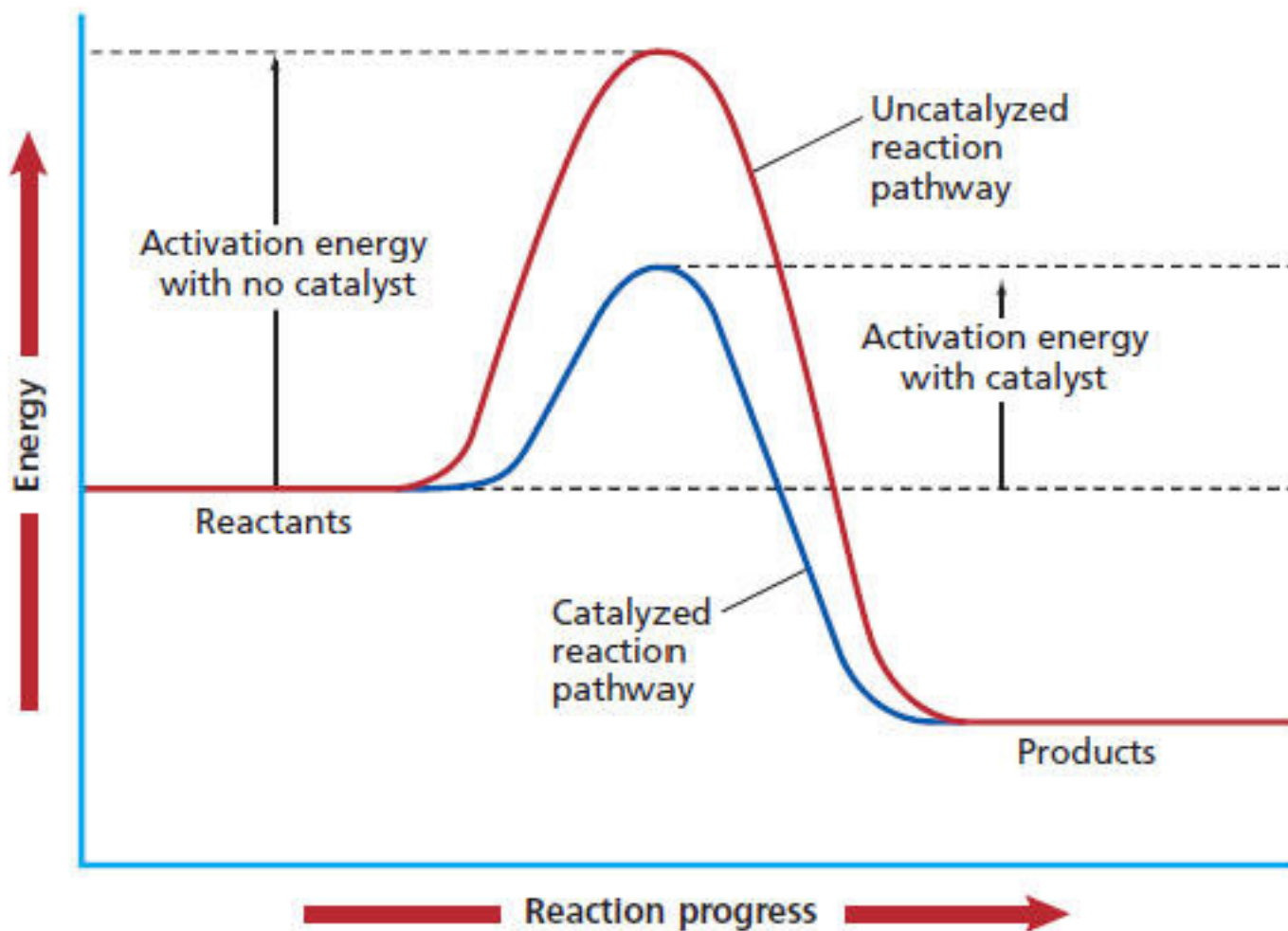
Opportunities and Challenges

CCR 2015 Annual Meeting
Douglas Mans

Chemical Reaction Kinetics



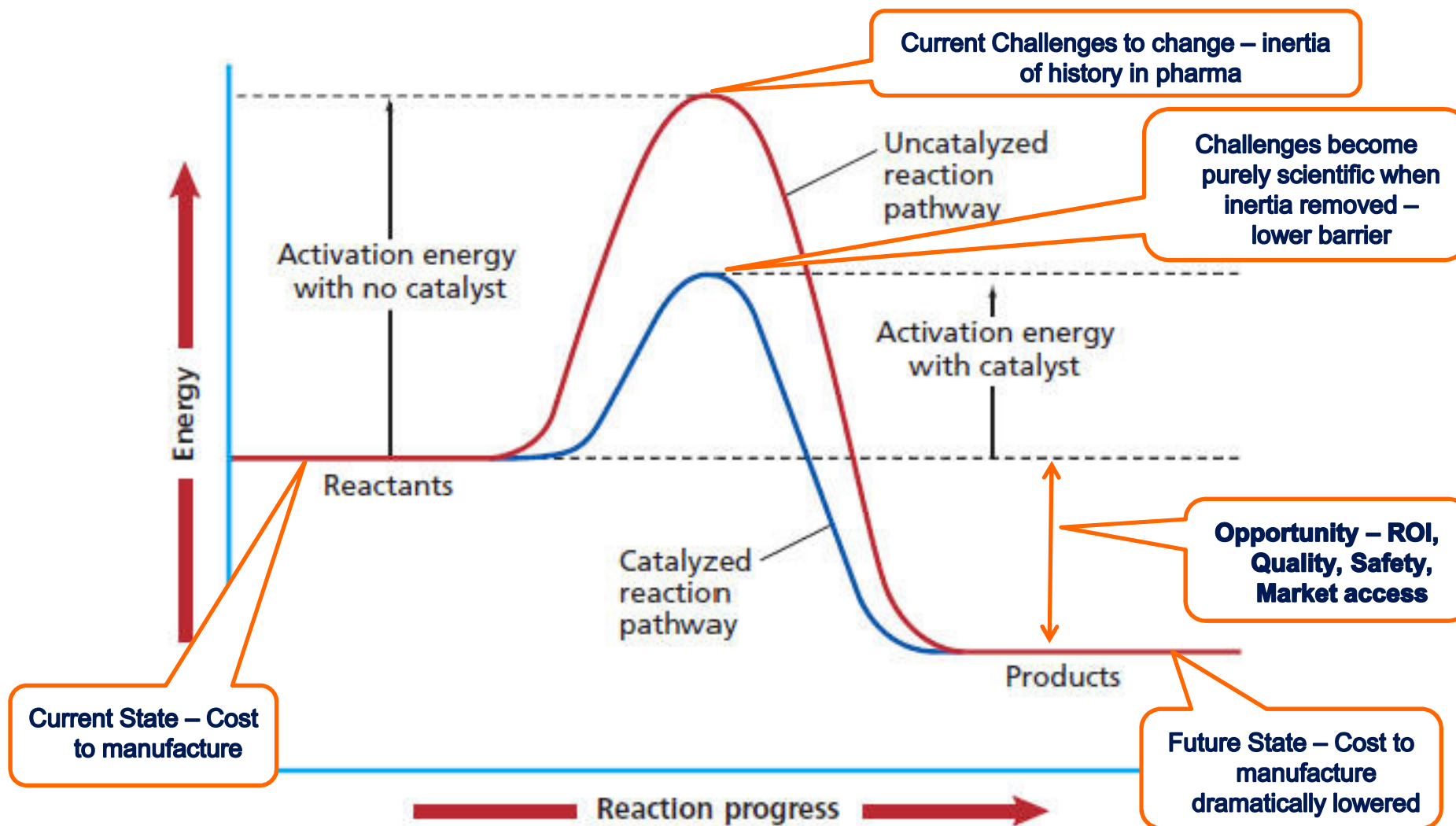
A framework for Pharmaceutical Manufacturing Innovation



Chemical Reaction Kinetics



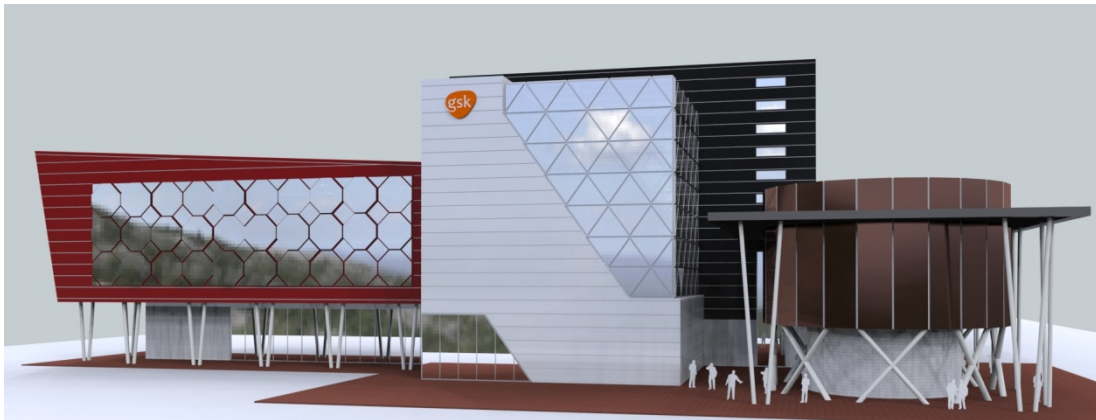
A framework for Pharmaceutical Manufacturing Innovation



Future State - GSK is pursuing an ambitious manufacturing technology vision and roadmap



In our vision of the **Future State**, GSK will have a more agile and responsive supply chain that delivers higher quality and more affordable products to patients at the point of need



- Small high-tech facilities
- Interconnected
- Flexible and responsive
- Low Inventory
- Low CAPEX
- Intuitive
- High Quality
- Visual performance
- Low Carbon



Flexible spaces that can evolve rapidly as manufacturing technology advances



Modular (continuous) manufacture



Smart intensive standard platforms

What Science and Technology is driving the *Opportunity*?



“The Third Revolution: The Convergence of Life Sciences, Physical Sciences and Engineering”

This Third Revolution is driving innovations in:

- Big data and signal detection
- Synthetic biology
- Augmented reality
- Automation and autonomous robotics
- Particle templating
- Additive manufacturing and self-assembly
- Functional surfaces
- Novel drug delivery strategies

GSK are applying these innovation to pharma manufacturing

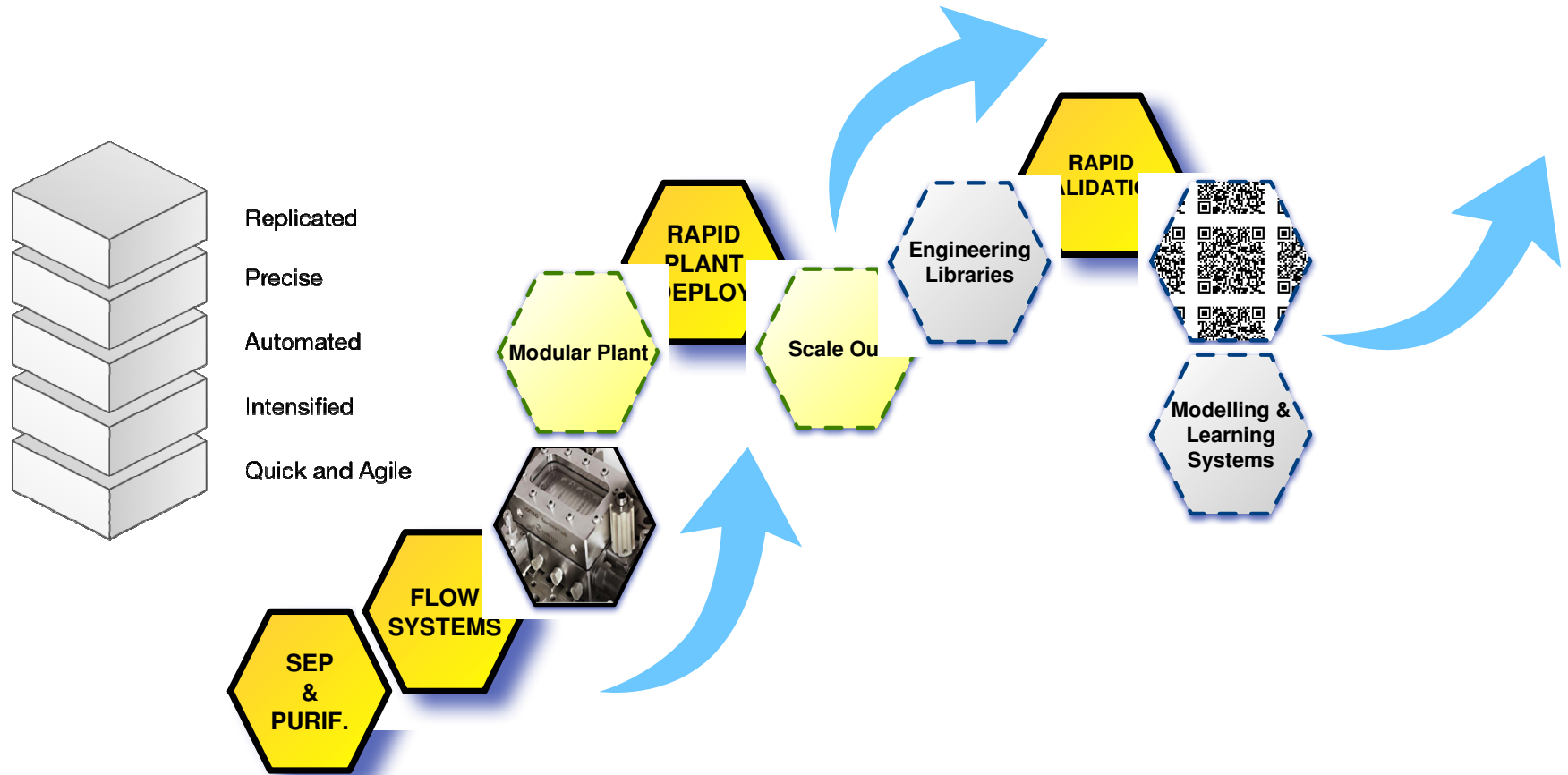


“The Third Revolution: The Convergence of Life Sciences, Physical Sciences and Engineering”, MIT White Paper, January 2011

Continuous Primary (API Manufacture)



The Technology Tree Replicated Sub Component. Assembled to execute a Recipe



Continuous Primary (API Manufacture)



What do we need to be good at?

Chemistry/Physical Chemistry

Heterogeneous Systems (including feed)

Separation Technologies (to glue chemical steps together)

Mixing

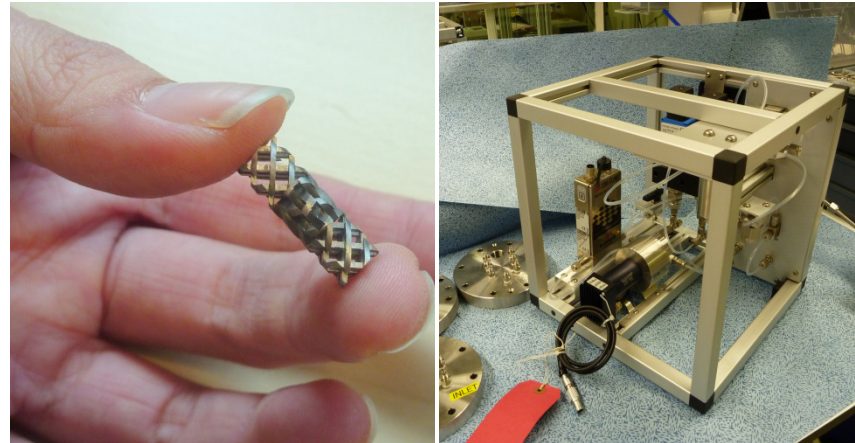
Pumping and Metering

Controlling & Measuring at small scale

Simplifying Use (Validation, Operating Decisions)

Standardising of Equipment and Training

Process Economics



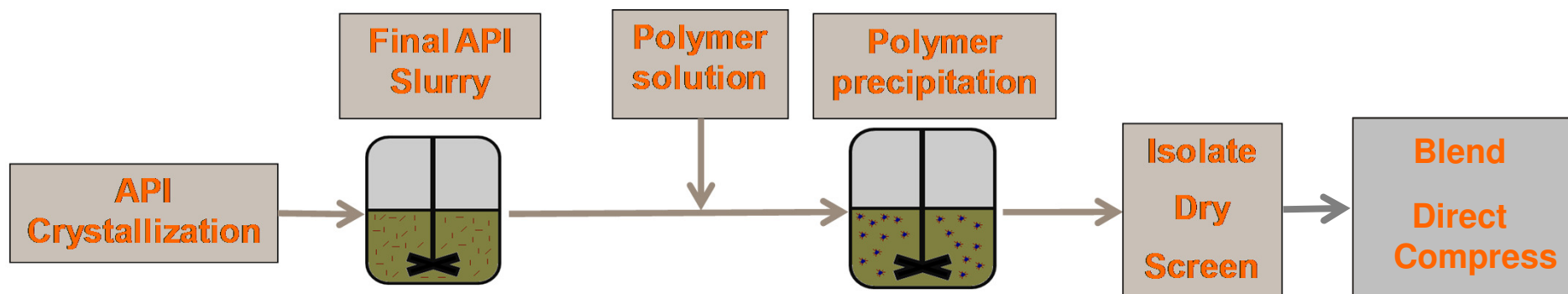
Continuous Secondary (Drug Product Formation)

Precipitated Polymer High Value Constructs



Objectives

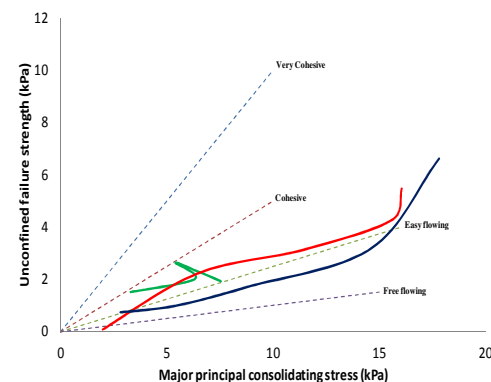
- Investigate the use of polymer additives to induce agglomeration on GSK compounds, develop a methodology to screen assets, and identify key process parameters and analytical techniques for control.
- **Improved flow properties allow the potential for simple formulations (blend and direct compress / capsule fill)**



Bulk density: 0.103 g/ml



0.237 g/ml



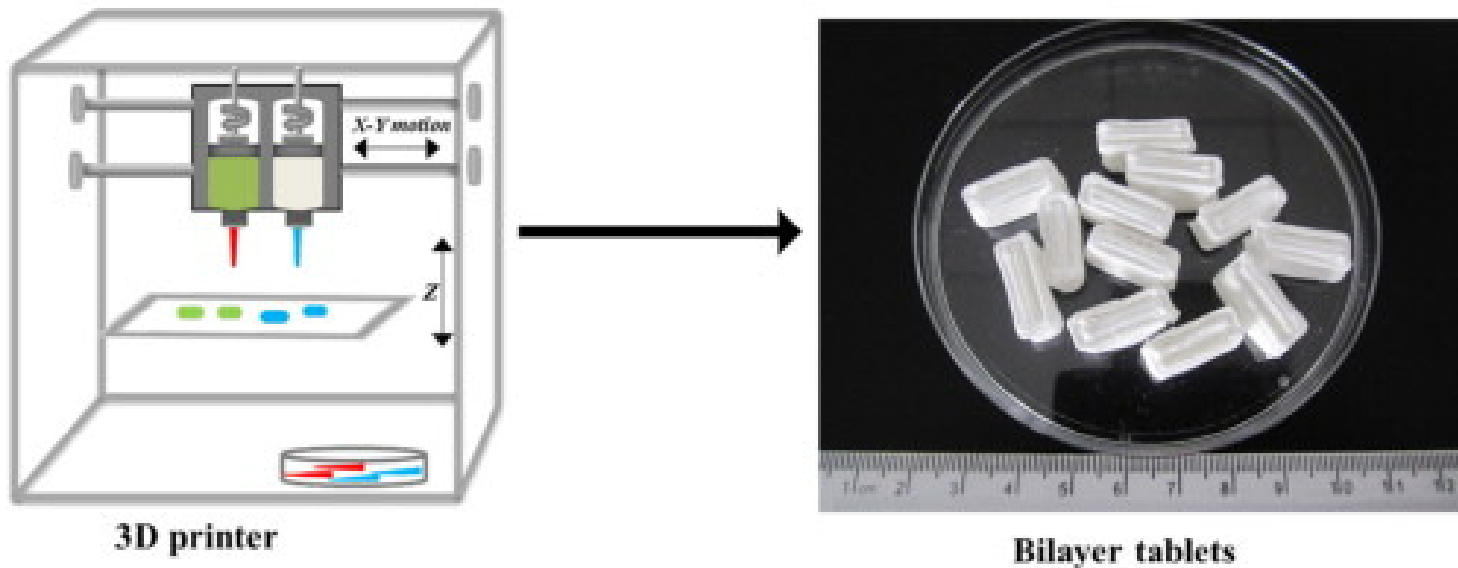
Improved flow via shear cell test:
green = poor flow,
red and blue = improved flow

Continuous Secondary (Drug Product Formation)



3D Printing of Oral Solid Doses

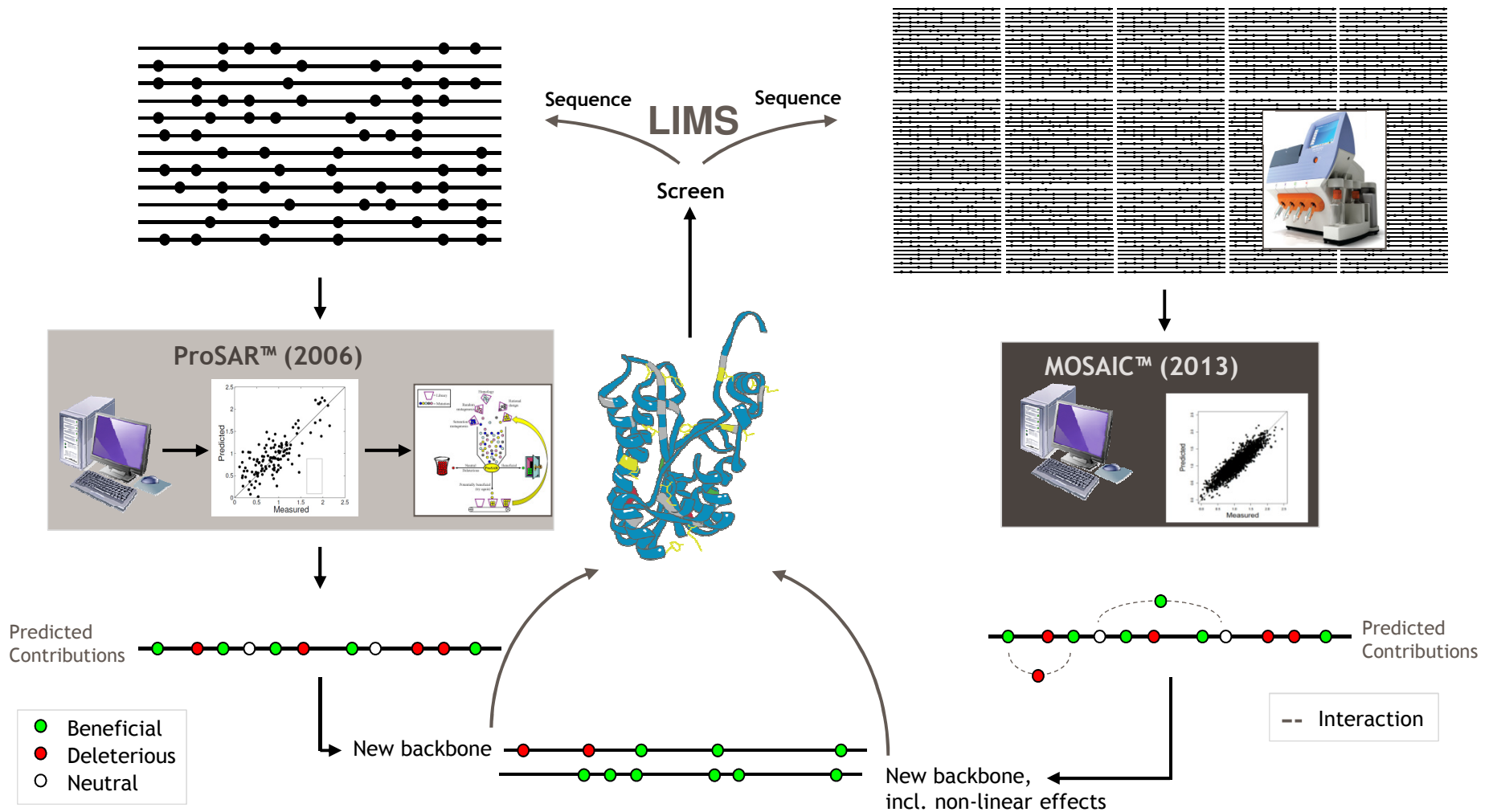
- Potential for distributed manufacture of patient-specific tablets at specialty pharmacies
- Explore opportunities to reduce pill burden through variable dose API combinations
- May achieve complex release without a complicated manufacturing process
- Opportunities to simplify the supply chain



* Shaban A. Khaled, Jonathan C. Burley, Morgan R. Alexander, Clive J. Roberts, "Desktop 3D printing of controlled release pharmaceutical bilayer tablets ", International Journal of Pharmaceutics 461 (2014) 105– 111

Synthetic Biology

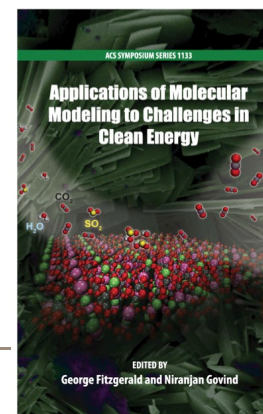
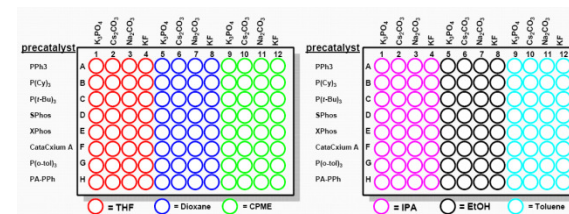
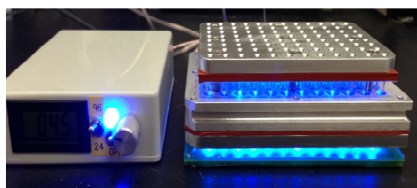
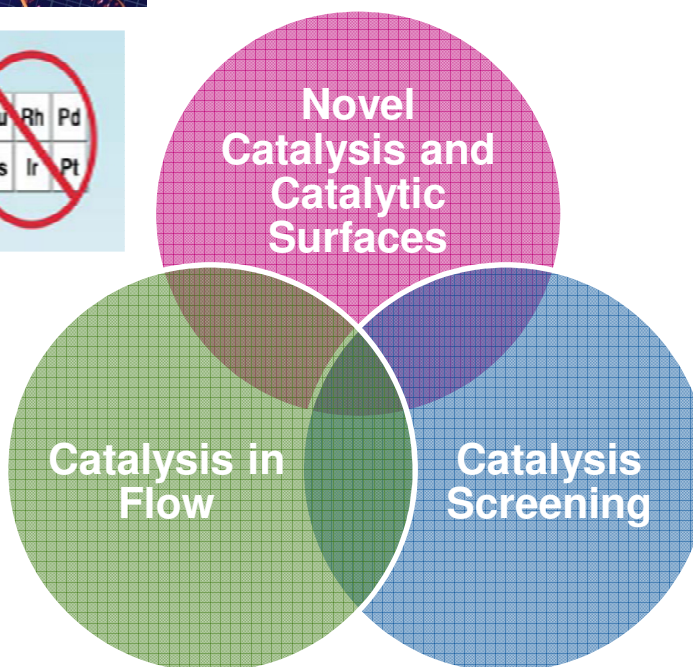
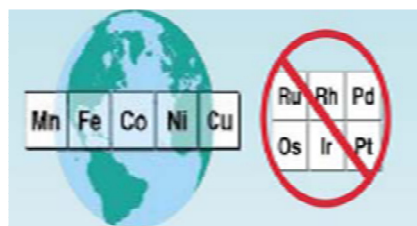
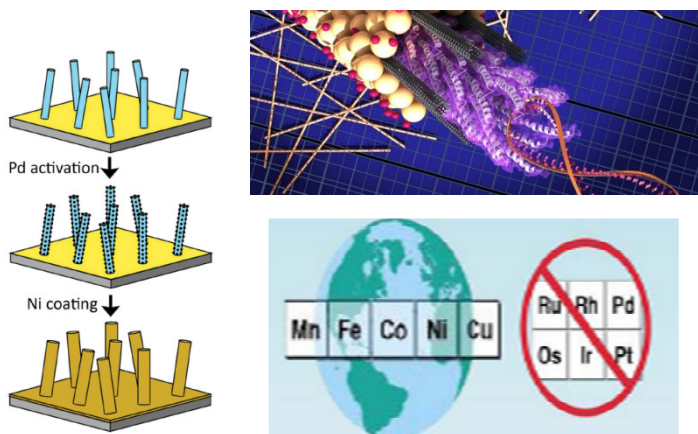
CodeEvolver®: Staying At The Forefront Of Protein Engineering



Chemical Catalysis and Novel Methods



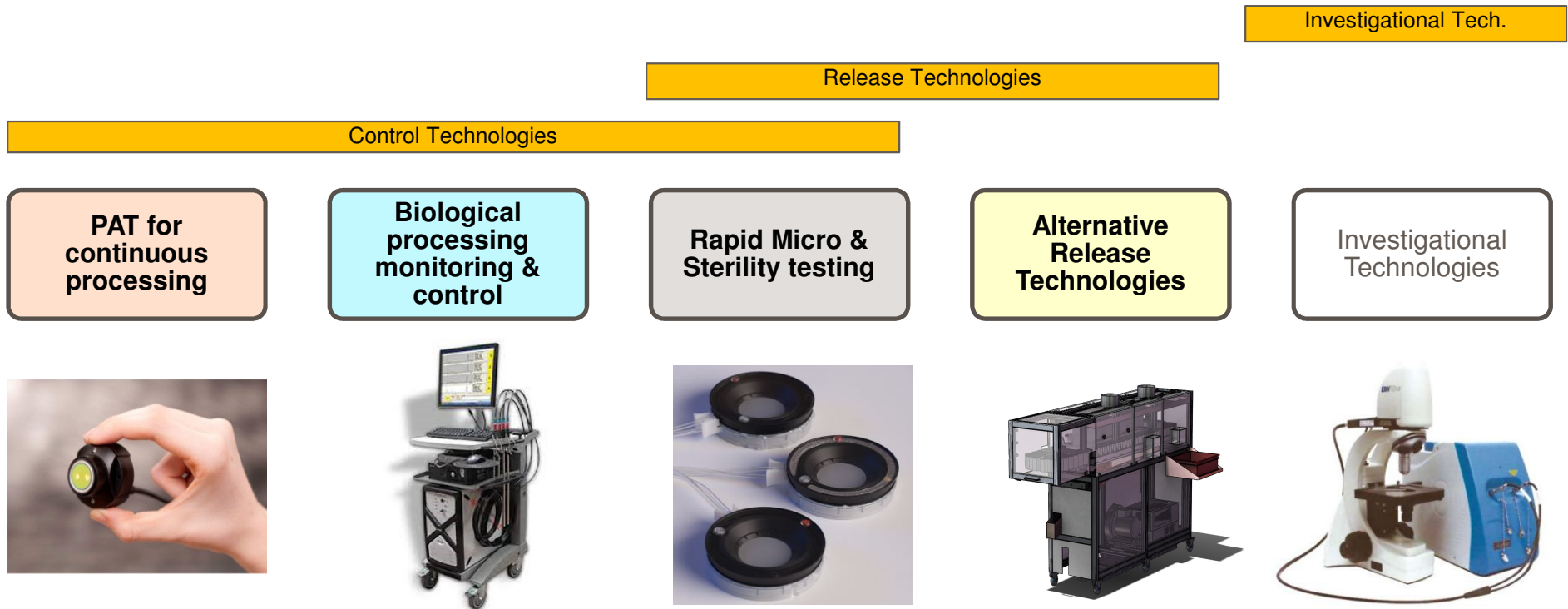
Areas of Interest



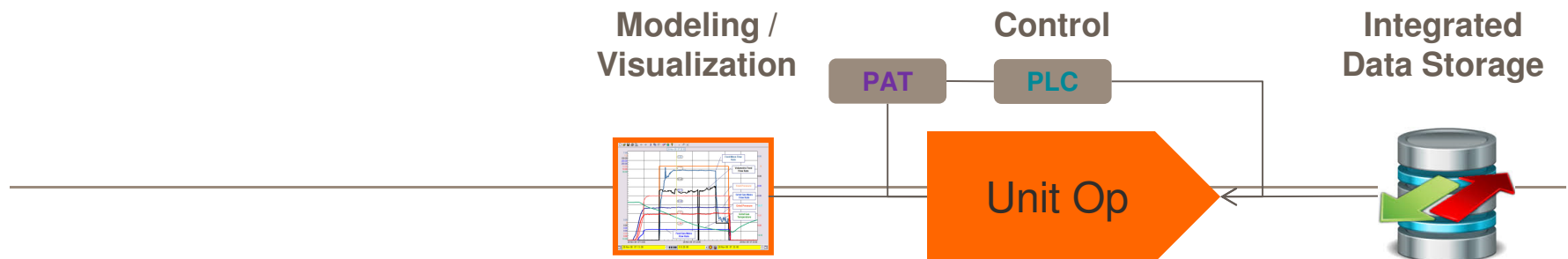


Future Analytical & Control Technologies

Areas of Interest



➔ Embed analytics, Informatics and automation to improve product quality and reduce waste

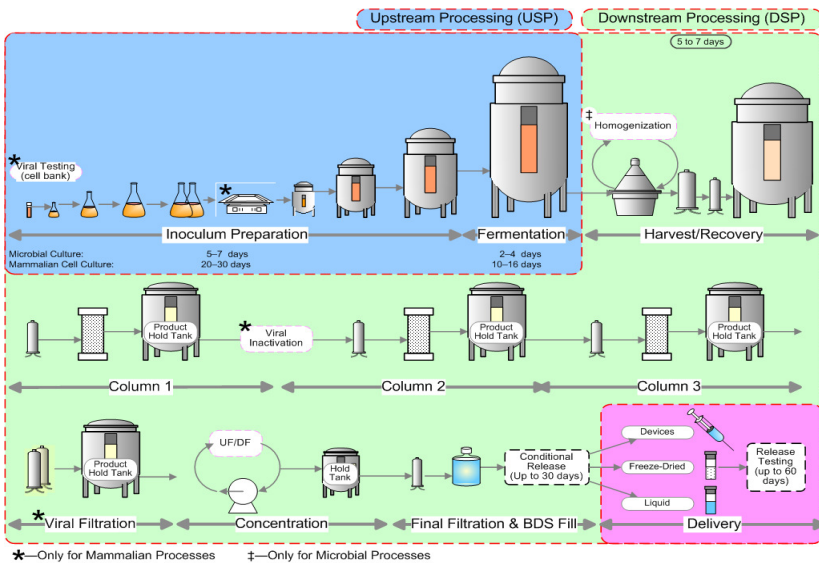


Biopharmaceuticals

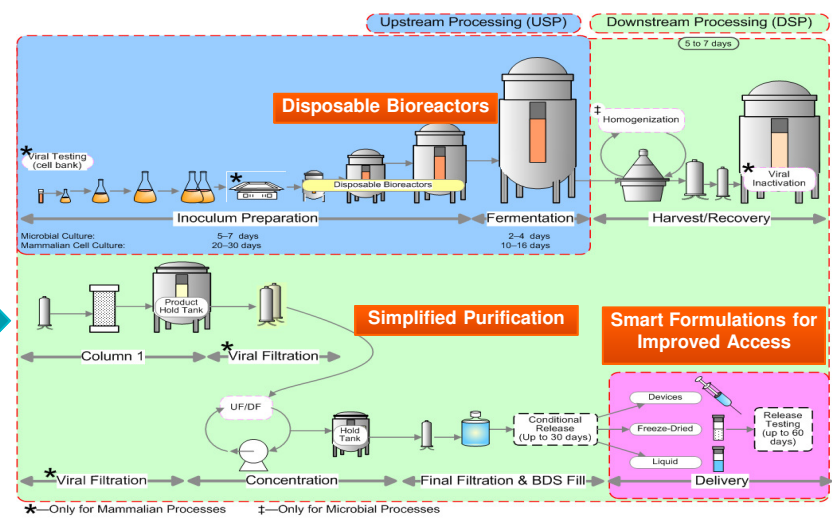
Areas of Interest



Current Manufacturing Platform for a Biopharmaceutical



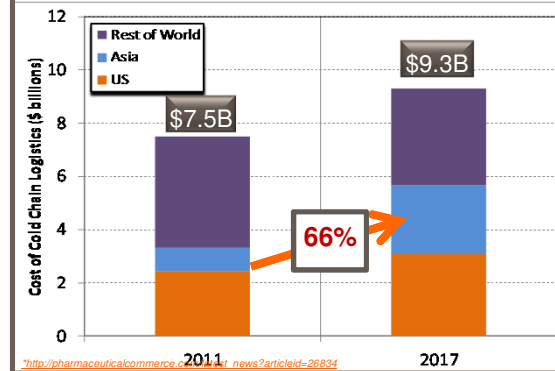
Future Manufacturing Platform for a Biopharmaceutical



Improve Patient Experience and Access by:

- ↓ Cost of Goods
- ↓ Cost and time of Drug Development
- ↑ Patient Access by Transforming Drug Delivery

Reduce Dependence on cold chain to increase patient access*



Achieving the *Future State* represents a significant *Opportunity* for all stakeholders



Patients

- Increased access and availability to medicines driven by lower cost and increased supply chain security and reliability
- Higher quality (and more customised product design – personalized medicines)



Regulators

- Less oversight and inspection to safe guard patient interest driven technology enable Quality by Design and robust manufacturing



Reimbursement Agencies

- More cost effective and economically sustainable healthcare driven by increased efficiency of manufacturing



Industry

- Reduced risk profile based on more reliable manufacturing and more agile and responsive supply chains
- Enhanced economic efficiency (less inventory, lower capital, reduced cost of poor quality)

Two philosophical questions

Over-coming the activation energy



Should we pursue novel manufacturing technologies through the NCE portfolio or through post-launch life cycle?

Does Technology Strategy drive Manufacturing Strategy or *vice versa*?



NCE Portfolio

- Challenges
 - **Attrition**
 - New technology risk and the reluctance to combine technology risk and clinical risk
 - **Perceived regulatory risk**
 - New technologies invariably require additional development effort
 - **Existing skills and capabilities not aligned to new technologies**
- Mitigation
 - Purposeful and proactive mapping of new technology onto portfolio
 - Proactive internal and external regulatory engagement and advocacy
 - Investment in ring-fenced resources to create head-room
 - Proactive skills and capability build

Post-launch Lifecycle

- Challenges
 - **Write-off of existing capital investment**
 - Timeline to implement and specific timeline for full world-wide regulatory approval
 - **Disruption to existing operations – Supply Chain Establishment**
 - **Limited and late visibility of opportunity window – technology development timeline cannot meet operational or commercial timeline**
 - **Existing skills and capabilities not aligned to new technologies**
- Mitigations
 - Stop or challenge investment in old technologies
 - Proactive engagement and planning with operations and supply chain strategy functions
 - Transparent supply chain and lifecycle strategies
 - Prioritisation of opportunities
 - Proactive skills and capability build

What progress is GSK making thus far?



The current landing wave...

– **Continuous tableting**

- Installed an integrated high-shear wet granulation unit in Ware NPI facility
- Planned investment in continuous blend and direct compression in new Indian OSD facility

– **Novel secondary technology**

- Candidate selected with particle templating technology

– **Flow Chemistry**

- Preparing to file and commercialise one late life-cycle 3 stage flow process
- Building a portfolio of NCE and commercial product flow opportunities from single stage niche chemistries to multi-stage processes

– **Biotransformations**

- Significant investment in enzyme evolution capability through strategic partnership with Codexis
- Successfully filed and commercialising one late life-cycle enzyme process with a second readying for filing as well.
- Active portfolio of NCE and commercial product opportunities

– **Informatics**

- Deploying more advanced and automated product attribute trending systems – Ellipta data trending apps deployed

Where could the next wave come from?



Blue Sky Areas of Interest/Investment

- Novel separation technologies – capture and release technologies
- Templated particles – exquisite control of particle formation
- Cell factories – cascades of reactions within a single host system
- Novel analytical techniques – non-destructive **real time** analysis
- Catalysis – novel materials and functional surfaces
- Informatics – big data integration and decision making in **real time**
- Operator-machine interface – augmented reality systems



Discussion and questions