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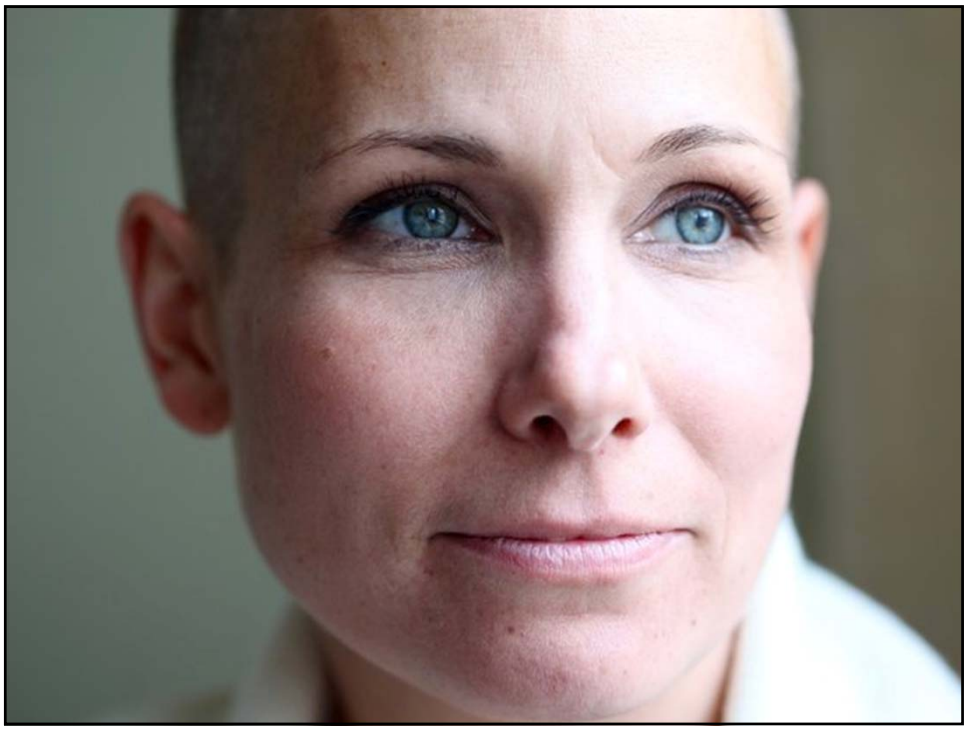
Opportunities for Distributed Manufacturing of High-Quality Biopharmaceuticals

J. Christopher Love
Chemical Engineering
Koch Institute at MIT
April 27, 2017

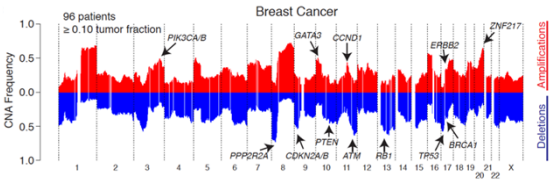


Pinpoint precision for discovery in human disease

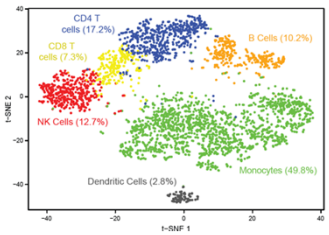
Blood
- Cells
- cfDNA
- Exosomes

Tissue
- FNA's
- CSF
- Biopsy

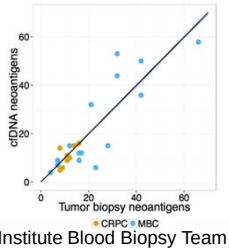
Whole-exome sequencing of ctDNA



Single-cell RNA-seq



Neoepitopes from blood



Adalsteinsson *et al*., Broad Institute Blood Biopsy Team
Gierahn, Hughes, Wadsworth, Shalek et al., Seq-Well (*Nature Methods*)

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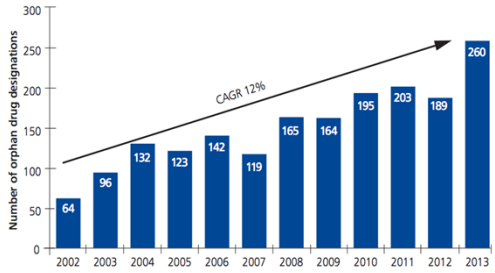
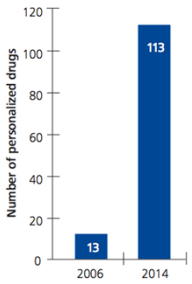
Accelerated discovery is improving identification and stratification of disease



Source: Evaluate-Pharma, "Orphan Drug Report 2014," October 2014, 15



Source: Personalized Medicine Coalition, "The Case for Personalized Medicine," First and Fourth Editions, 2006 and 2014

"Advanced Biopharmaceutical Manufacturing: An Evolution Underway", Deloitte 2015

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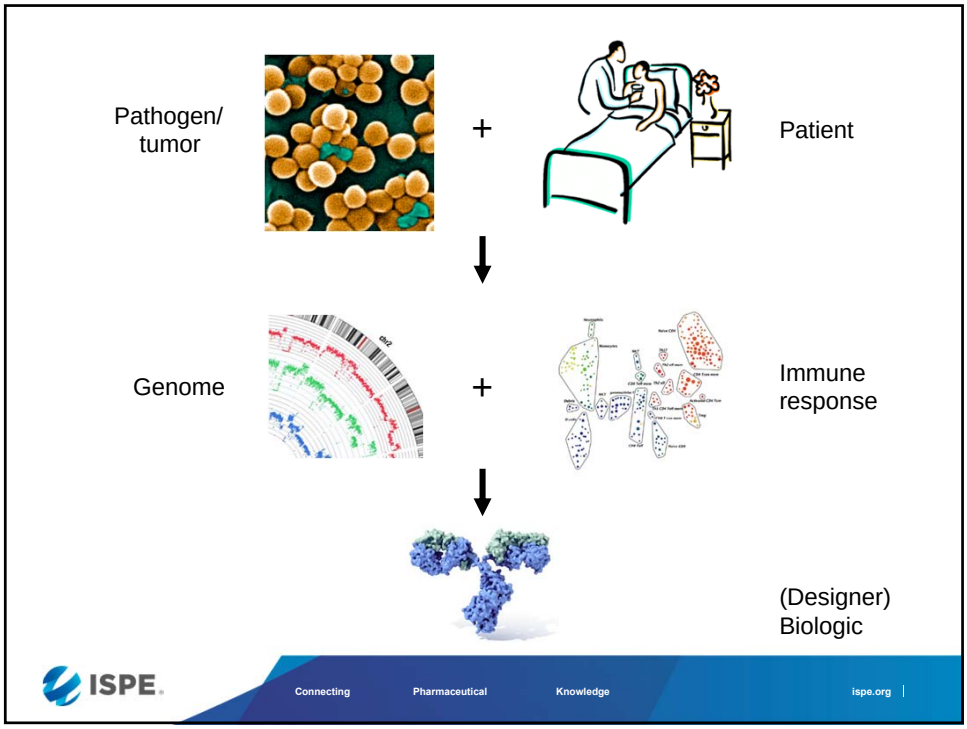
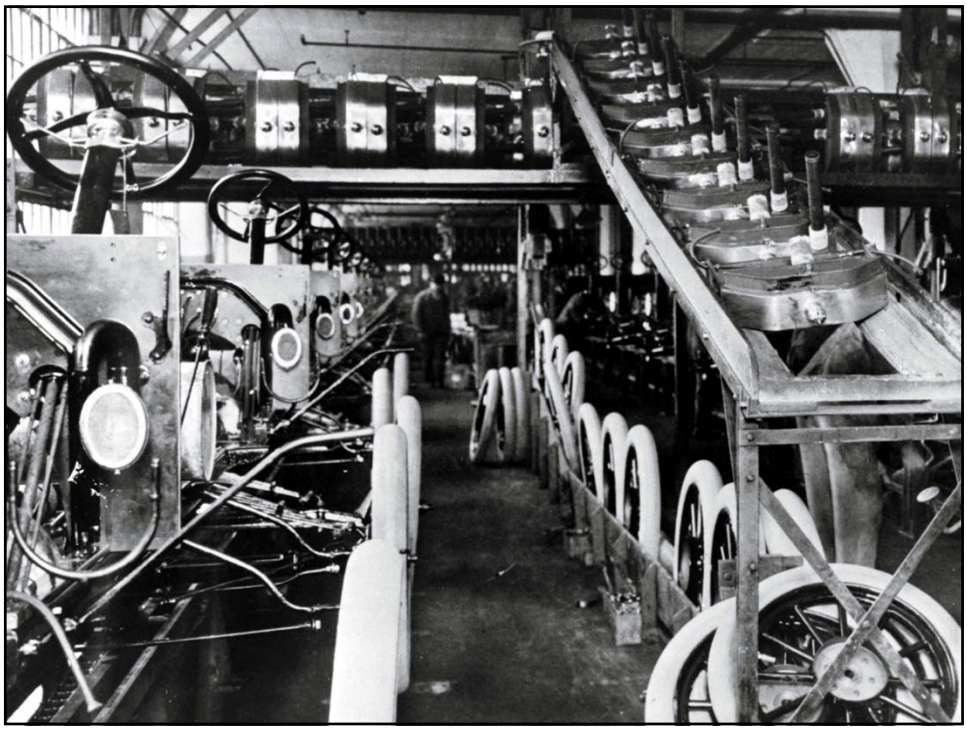
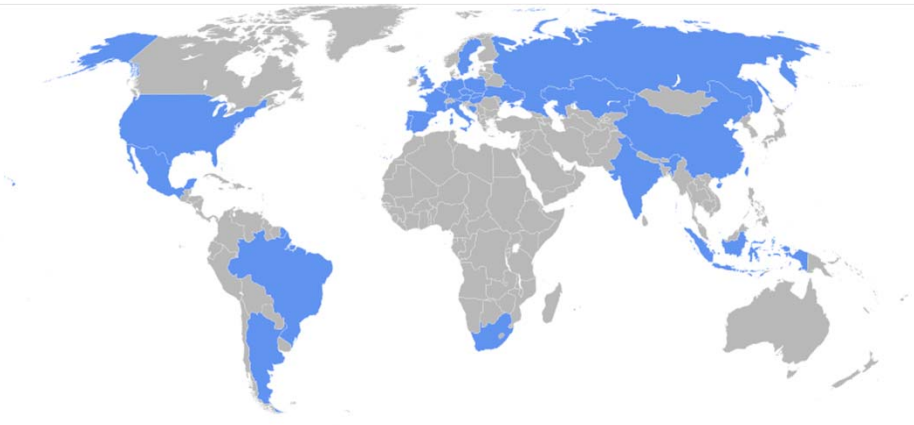


- **Cycle of target discovery and drug development for human disease accelerating**
- **Refining disease indications are becoming smaller and more precise**
- **Technologies and analytics advancing for tracking disease status (e.g., liquid biopsy)**

Is today's manufacturing strategy ready?



Volkswagen Group Factories (circa 2010)



By EOZyo - Based on en:Image:World locations of Volkswagen Group factories actualized.PNG.PNG, Public Domain, https://commons.wikimedia.org/w/index.php?curid=5768152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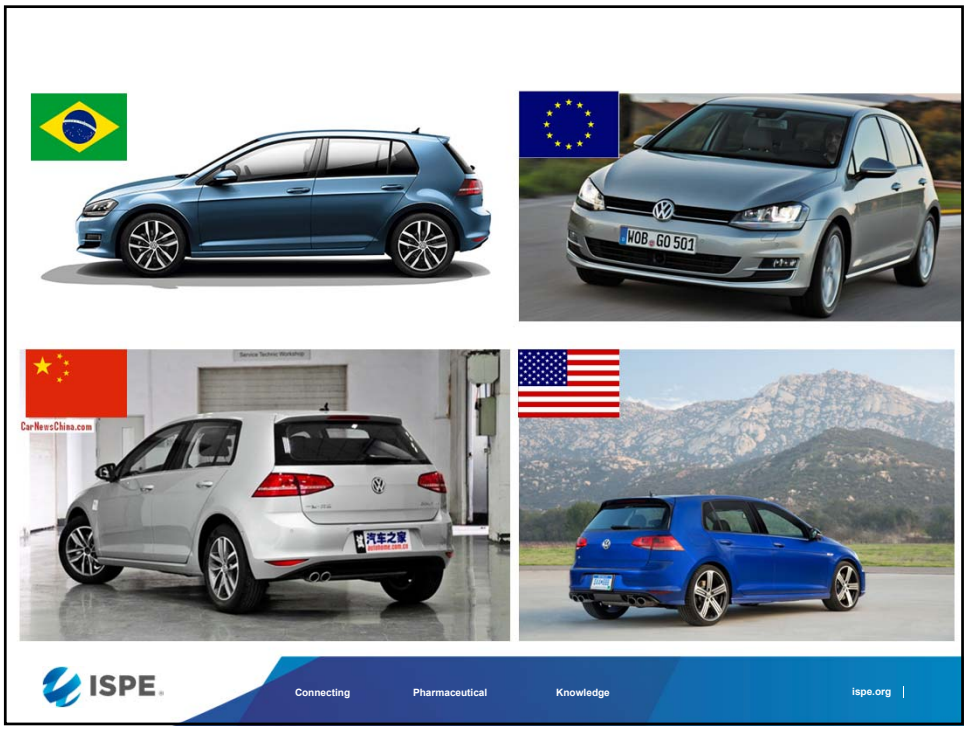
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Global Market, Regional Manufacturing: Why?

Local requirements

- National regulations on safety and design
- Durability and environment (road conditions)

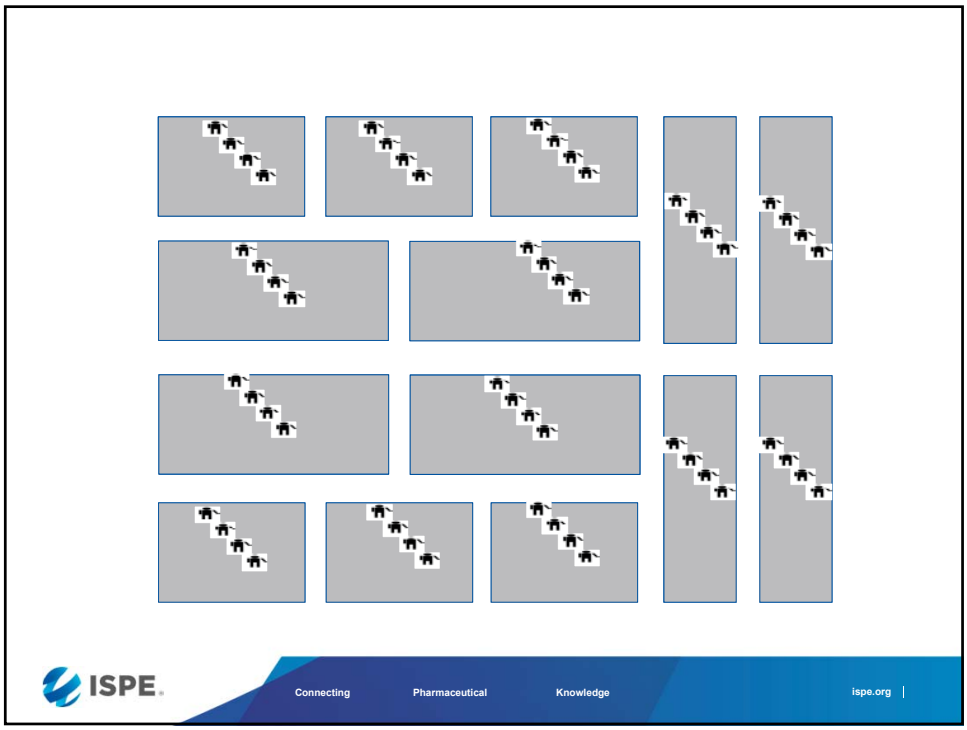
Local expectations

- Engine size and fuel
- Cost vs. luxury

Solution: Universal, cost-effective architectures tailored to regional supply chain, labor and facility

http://www.fiercepharma.com/manufacturing/pfizer-building-modular-biologics-plant-china


http://www.gereports.com/pfizer-will-use-ges-modular-factory-to-make-next-generation-drugs-in-china/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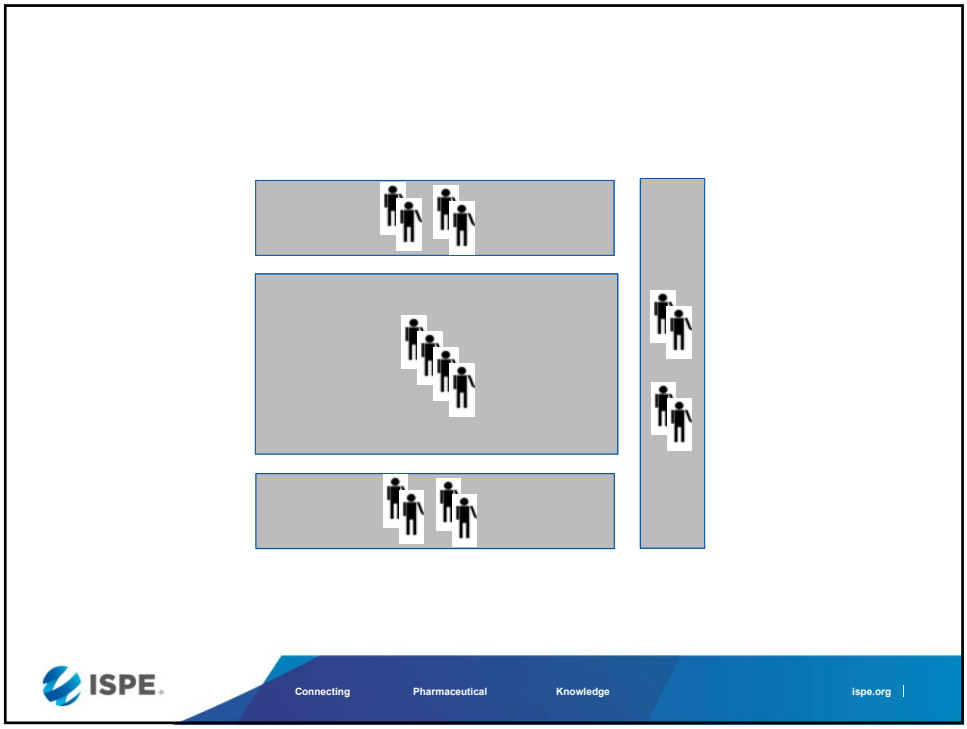
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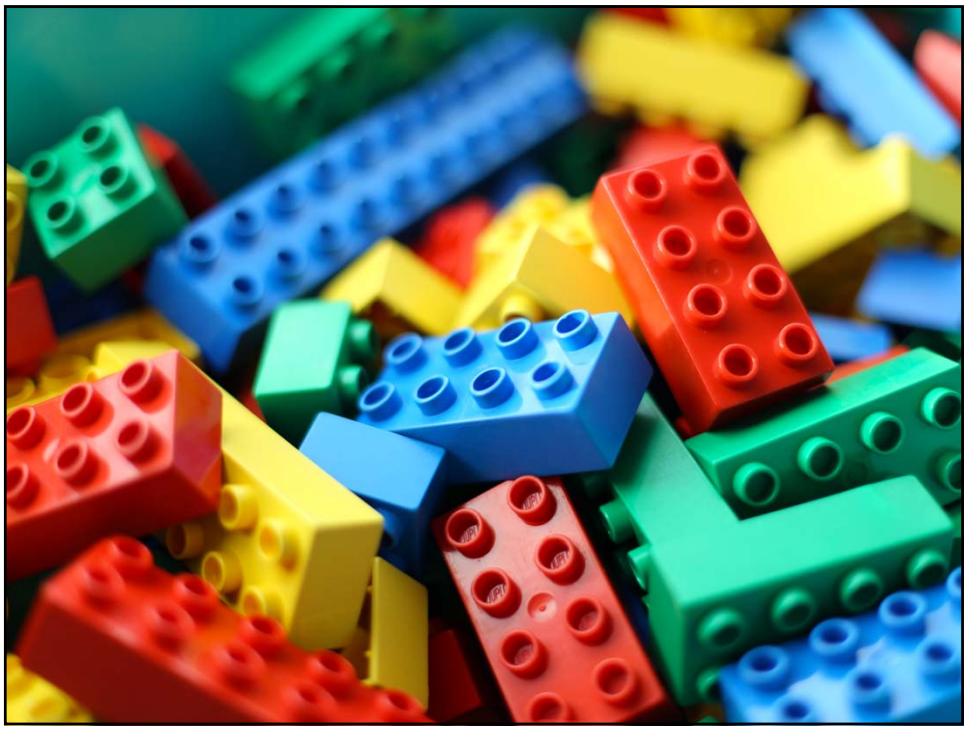

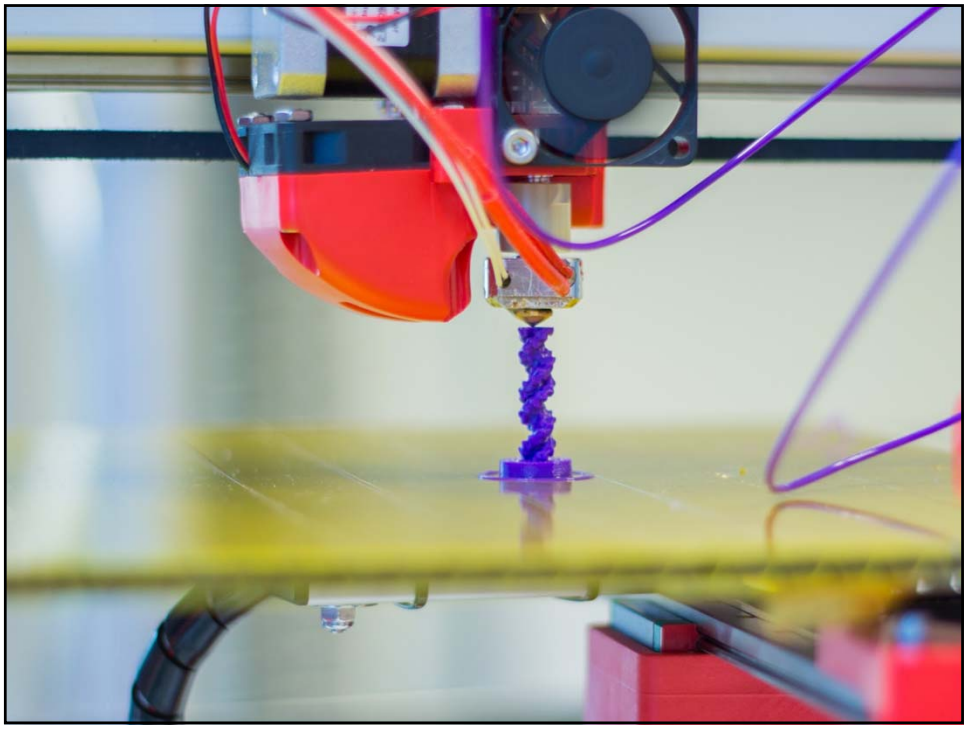

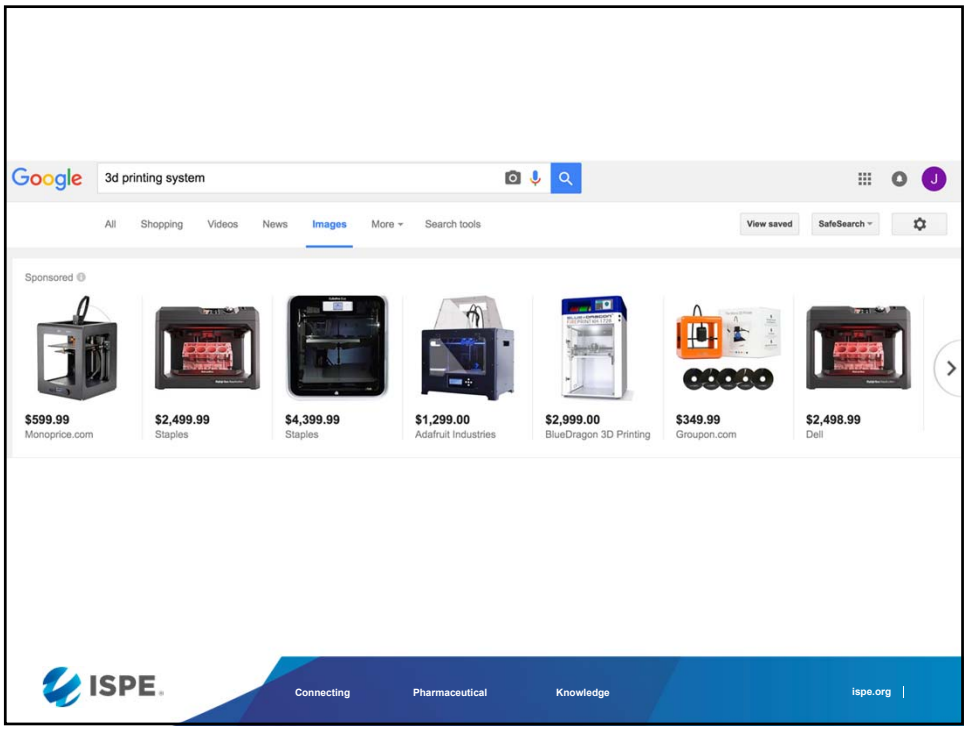
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Lessons from Democratizing Part Manufacturing

Generates global competition

Enables open innovation

Broadens access to differentiated solutions

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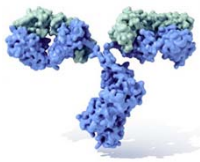

What if we could promote rapid cycles of innovation in drug development and supply for biopharmaceuticals?

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InSCyT

A small-scale prototype manufacturing system for fast production of high-quality drug substance

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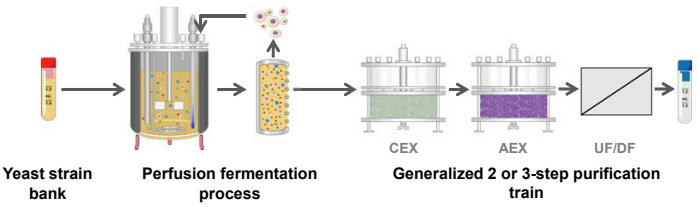
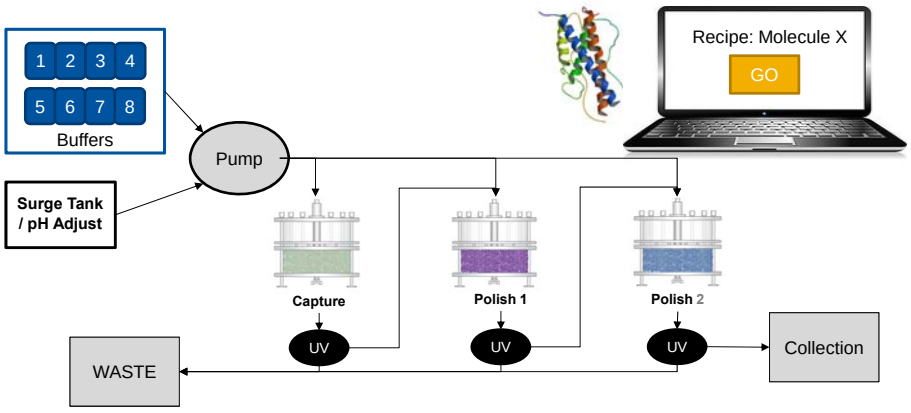
InSCyT benchtop biologics manufacturing system

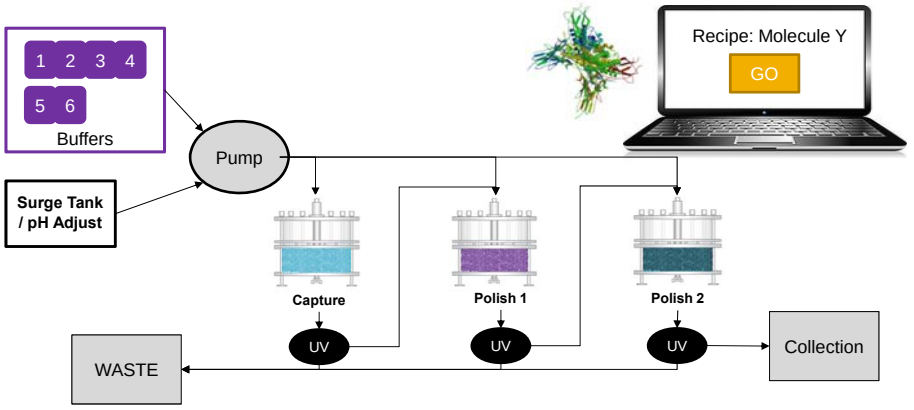


(William Hancock (NEU), Steve Cramer (RPI), Richard Braatz (MIT), Kerry Love, and Team)

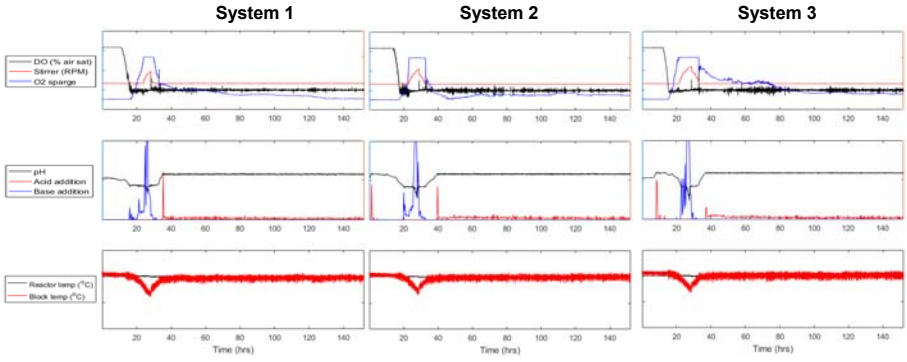
Simple, automated purification of Molecule X



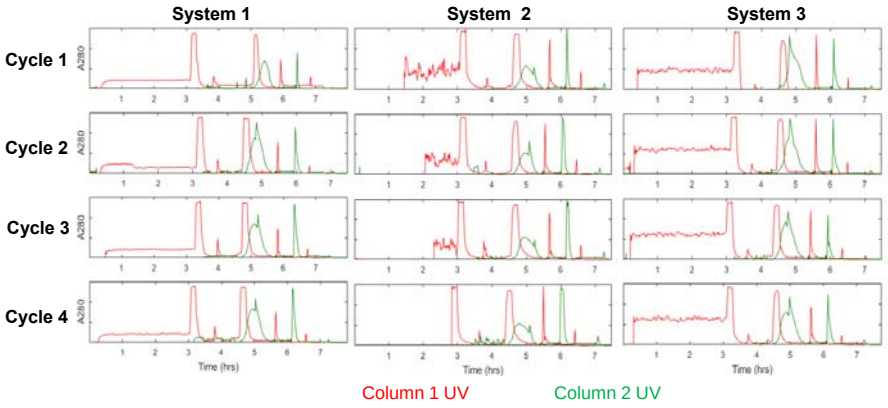
Simple, automated purification of Molecule Y



Bioreactors perform consistently across multiple systems

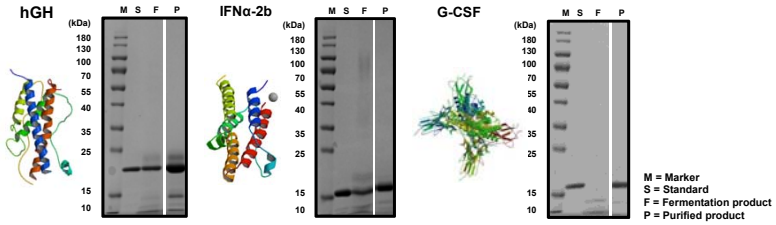


Purification is consistent across multiple cycles and multiple systems



Column 1 UV Column 2 UV

"Plug and play" manufacturing: Production of 3 model biologics (hGH, IFNα-2b, & G-CSF)



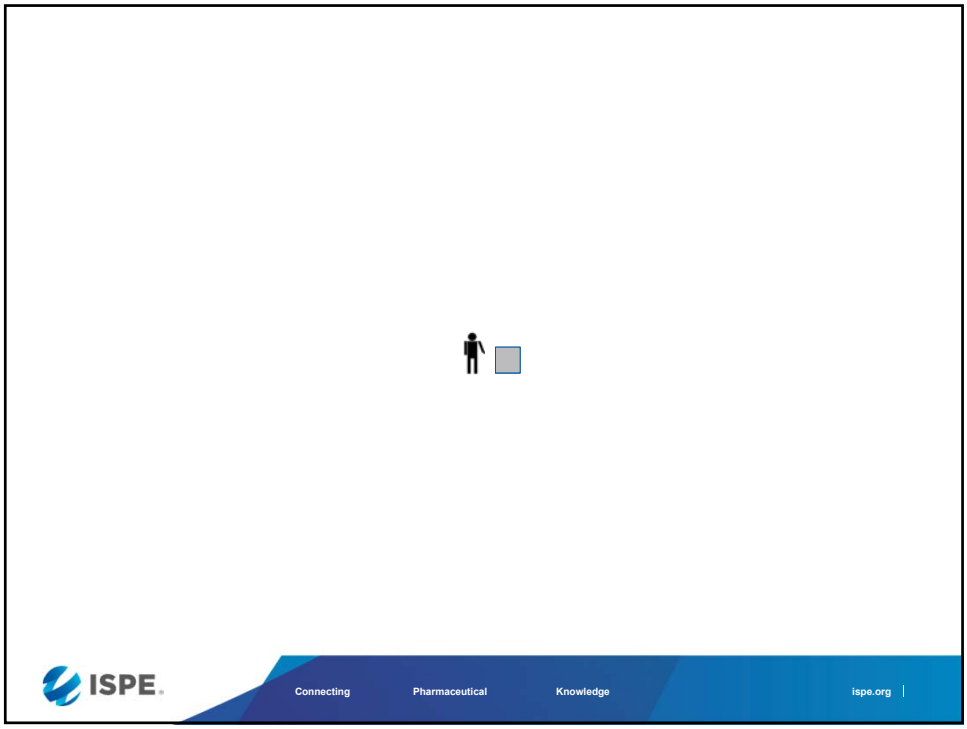
M = Marker
S = Standard
F = Fermentation product
P = Purified product

Drug	BDS	Aggregate	Other Impurities	Bioactivity
hGH	95.1%	0%	4.9%*	Matches WHO Std
IFNα-2b	93.4%	2.1%	4.5%#	Pending
G-CSF	97.6%	0.2%	2.2%	Matches Reference

* Proteolyzed variants not clinically relevant
# N-terminal variants

100's to 1,000's of doses in < 6 days on the bench

(William Hancock, Steve Cramer, Richard Braatz, Kerry Love and Team)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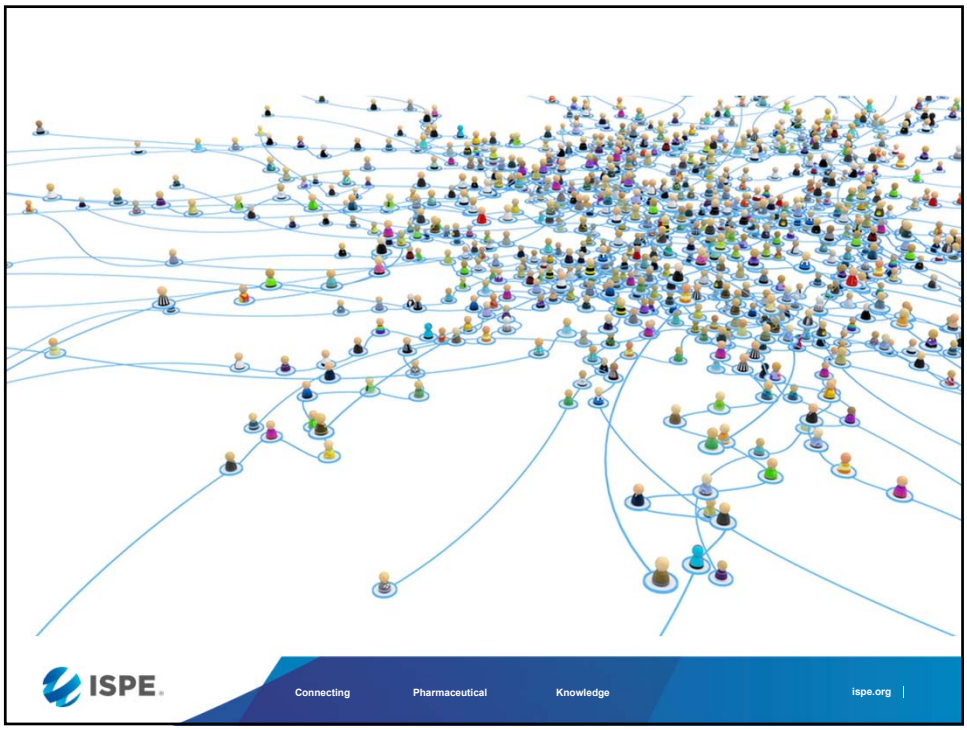
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Potential Benefits for Distributed Drug Manufacturing

Access to global talent and science

Flexible management of capacity and logistics to meet market demand

Reduced inventory and stock (less waste)

Small capital investment – more innovation

Financial and moral support of local economies

Challenges for Distributed Manufacturing

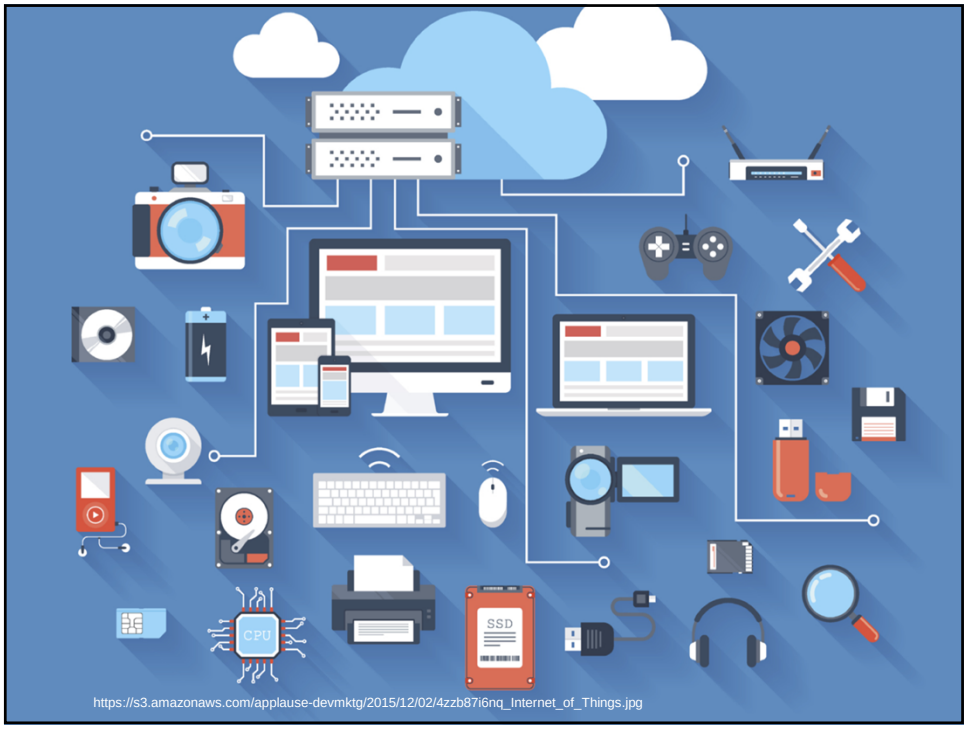
Robustness

Quality Control and Assurance

- Regulations
- Risk vs. patient benefit

Supply chain models

- Agile production and qualification
- Expanded network of suppliers
- Logistics and security



https://s3.amazonaws.com/applause-devmktg/2015/12/02/4zzb87i6nq_Internet_of_Things.jpg

FASTlab 2 with FDG Duo cassette image courtesy of GE Healthcare

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Vision: Small, fast & flexible manufacturing systems

Potential markets

Regional production

Fast to clinic

Rare/Orphan Disease

More patients accessing high quality drugs globally

Our InSCyT team

Massachusetts Institute of Technology

Northeastern University

PALL Corp.

Rensselaer

DARPA/SPAWAR

Any opinions, findings and conclusions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the views of the Defense Advanced Research Projects Agency (DARPA) and SPAWAR Systems Center Pacific (SSC Pacific).

Catie Bartlett
Richard Braatz
Lisa Bradbury
Joe Brady
Danielle Camp
John Clark
Noelle Colant
Steven Cramer
Laura Crowell
Aleksander Cvetkovic
Amanda Del Rosario
William Henry Doherty
Chaz Goodwine
William Hancock
Ralf Kuriyel
Di Liu
Yanjun Liu
Chris Love
Kerry Love
Amos Lu
Nicholas Mozdzierz
Alan Stockdale
Steven Timmick
Nicholas Vecchiarello
Annie Wang
Di Wu