



# **The Future of Drug R&D: How Biomedical Scientists Will Square the Circle**

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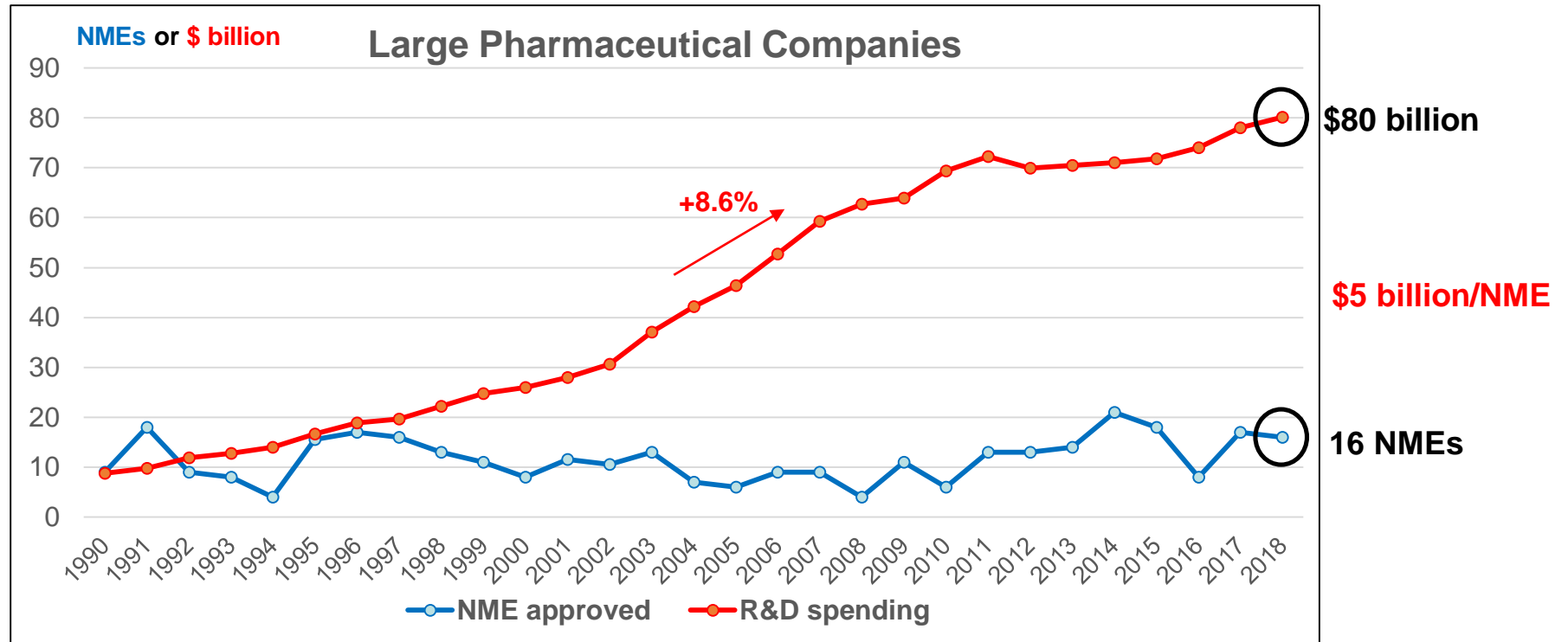
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# Pharma has a problem...

More R&D isn't yielding more drugs



Firms included: ABBV, AZN, BAY, BI, BMY, GSK, JNJ, LLY, MRK, NVS, PFE, ROC, SNY; Firms created by merger or spinoff (ABBV, AZN, GSK, NVS) include data from predecessors

Sources: Pharma R&D spending: EvaluatePharma@; NME approved: drugs@FDA

# And pharmaceutical innovation is increasingly **irrelevant** to the health of Americans

- Industry spends **\$180 billion** in R&D annually
- Yet, generics fill **95%** of prescriptions (J. Woodcock, 9/6/19)
- Health outcomes (e.g., life expectancy) keep worsening
- Science is dazzling, but million-dollar shots are not having a detectable impact on population health, yet they crush patients financially
  - **42%** of cancer patients to exhaust their savings within 2 years of diagnosis (Endpoints/J Carroll 11/26/19)

**Why spend so much if it touches so few?**

## And it's bound to get **worse**

- There are over 1 million US patients eligible for CAR-T therapy @ \$400,000 each (avg), representing a potential expenditure of **\$400 billion** to treat **0.3%** of the population
- FDA projects that by 2025 it will approve **10 to 20** gene/cell therapies each year
- Over 12 years (average patent life), that's a cohort of **~180 drugs**
- Assuming that they treat as many patients and cost as much as existing gene therapies (e.g., Luxturna, Kymriah, Zolgensma), it would translate into an annual cost of **~\$200 billion** to treat less than 100,000 patients (**<0.05%** of population)
- By comparison, the cost of treating the entire US population is now **~\$330 billion**

**Are we hurting many (by making insurance unaffordable)  
to benefit a few? Is it tenable?**

**It is not tenable, but technology will likely **rescue**,  
not doom, drug R&D**

There are three key cost drivers to drug R&D:

- The supply of drug candidates
- The cost of clinical research
- The cost of manufacturing

# The supply of drug candidates

- Innovating is getting **cheaper**
  - Big science is making once proprietary knowledge and tools available to all for **free**
  - The cost of starting a new company is **plummeting**
  - **Seed funds** have sprung up to finance bold, early science. “Valley of death” is no longer in the headlines
  - **Crowdsourcing platforms** (e.g., scientist.com) are helping firms grow without adding scale
  - What used to cost \$50 million can now be done for \$5 million or less, which no longer requires VC funding
- Cheaper innovation models are enabling a **global grassroots exploration** of new biology
  - 74% of drugs approved in 2018 came from small and mid-sized companies
  - There are > 800 gene/cell therapies in the clinic
  - FDA estimates that by 2020 we will add 200 more each year
- Translation is **accelerating**
  - Scientific breakthroughs are quickly followed by the creation of multiple, well-funded startups to exploit the new opportunities

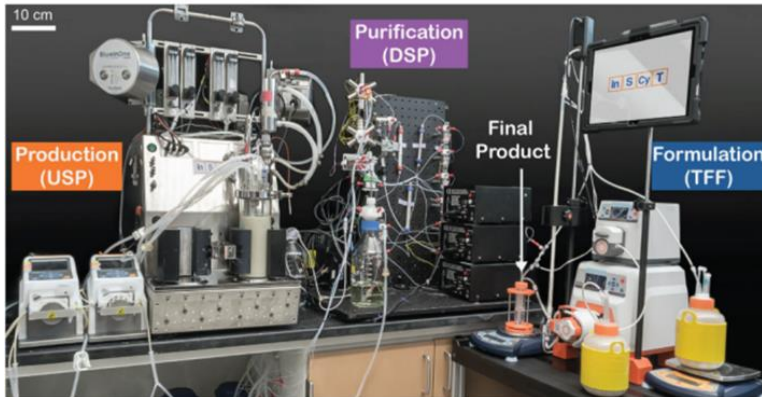
# RWE offers the opportunity to change the economics of clinical research

Risk-based monitoring	~ 5% of total clinical trial spend
Adaptive trial designs	Average saving of ~20% study subjects and up to 25% reduction in trial timeline
Platform trials	~20-40% saving of trial costs and reduction of timeline by ~25%
Highly simplified trials	~50% reduction in per site and per patient costs
Real world evidence ( <i>in lieu</i> of RCT)	Up to ~90% reduction in total trial cost and ~75% reduction in trial timeline

Source: Levy E, Presentation to Drug Forum of Nat. Acad. Of Med. 7/17/2018

# On-demand, miniature manufacturing has the potential to upend the pharmaceutical industry

## Table-top manufacturing @ MIT



Nat Biotechnol. 2018 Oct 1. doi: 10.1038/nbt.4262

"A team of researchers has engineered a miniaturized biopharmaceutical "factory" that could fit on a dining room table and produce hundreds to thousands of doses of a needed treatment in about three days... This on-demand manufacturing system is fully automated and can be readily reconfigured to produce virtually any approved or experimental vaccine, hormone, replacement enzyme, antibody, or other biopharmaceutical." *Dr. Francis Collins*

## Suitcase-sized "plant" @ UMBC



Nature 575, 274-277 (2019) | doi: 10.1038/d41586-019-03455-x

"...produce hundreds or thousands of doses of multiple drugs, all in less than 24 hours."

## 3D printing @ U of Glasgow



Science. 2018 Jan 19. doi: 10.1126/science.aa03466

"...a series of interconnected reaction vessels that carry out four different chemical reactions involving 12 separate steps"



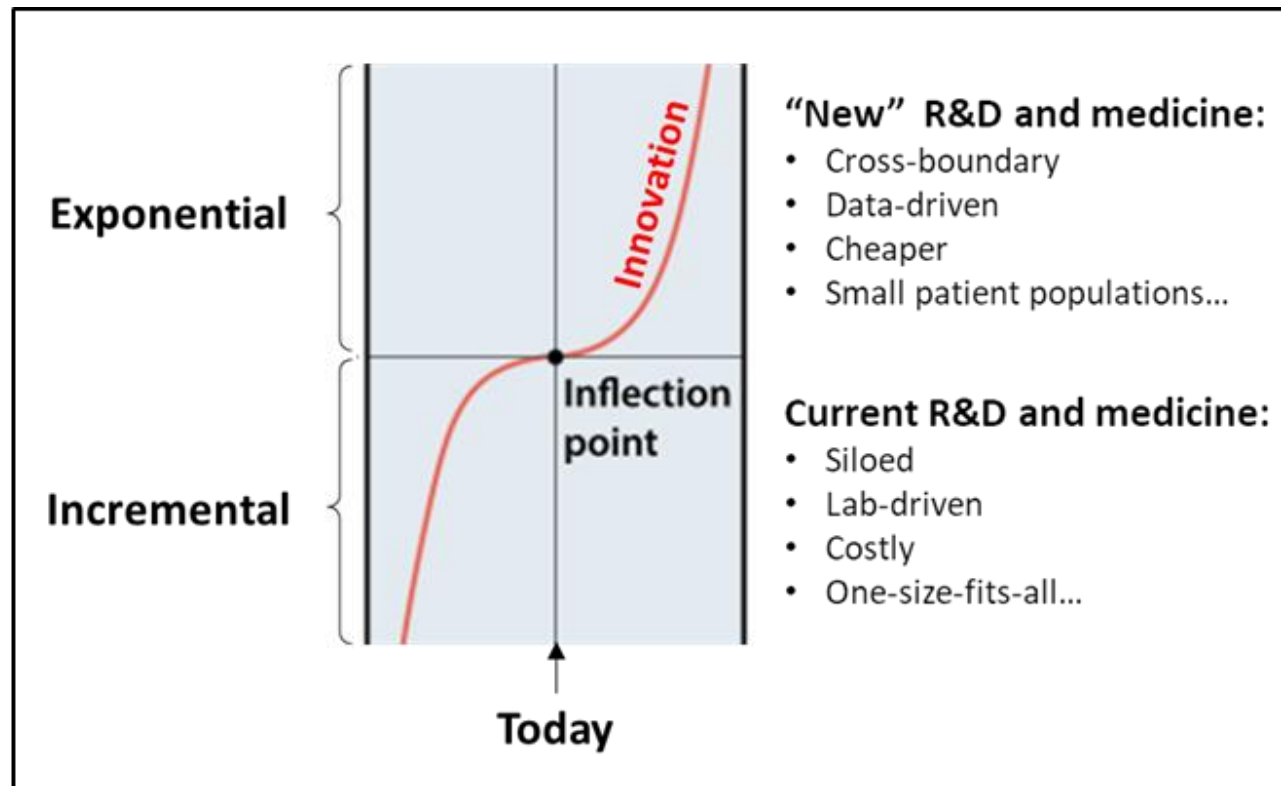
# A sense of déjà-vu?

- Flashback to the 1970s
  - Mainframe computers used to dominate data-processing
  - They were expensive: IBM 370 (500 KB RAM, 233 megabytes hard disk) rented for \$450K monthly (in 2019 \$)
  - They were costly to develop and manufacture. Only large companies did it (IBM, CDC, Honeywell, Burroughs, DEC, NCR...)
  - No way around it... “want computing power? Got to pay the price”
- Then came the 1980s
  - PCs slash costs; prices plummet; nearly all mainframe makers disappear
  - IBM goes from most-admired company to near-bankruptcy in 4 years

The arguments used to justify high drug prices echo those used to explain the high cost of mainframe computing: “it costs a lot” ... until someone finds a workaround

# Something is happening... Pharma may soon face a transformation similar to that wrought on mainframe manufacturers by PC makers 30 years ago

Most of the technologies discussed in this presentation are already in use or at an advanced stage of development



More innovation, better innovation, affordable innovation, and the promise of declining healthcare costs for all patients everywhere

**Thank You!**

# Suggested additional readings

- Friedman, J. How Biotech Startup Funding Will Change in the Next 10 Years.  
<https://blog.ycombinator.com/how-biotech-startup-funding-will-change-in-the-next-10-years/>
- Levy, E. A medicinal product developer's perspective on cost and delay. Presentation at the Drug Forum seminar on "Examining the Impact of Real-World Evidence on Medical Product Development: Application", National Academy of Medicine, 7/17/2018.  
<http://nationalacademies.org/hmd/Activities/Research/DrugForum/2018-July-17/Videos/Session-I-Videos/5-Levy-Video.aspx>
- Collins, F. How to Make Biopharmaceuticals Quickly in Small Batches  
<https://directorsblog.nih.gov/2018/10/08/how-to-make-biopharmaceuticals-quickly-in-small-batches/>
- Arnold, C. Medicines on Demand  
<https://www.nature.com/articles/d41586-019-03455-x>
- 3D Printing Drugs – The Latest Advancements Around the World  
<https://all3dp.com/2/3d-printing-drugs-the-latest-advancements-around-the-world/>