Manufacturing & Digital Day Agenda

Introduction	*Stéphane Bancel, CEO*	*1:00–1:20 PM*	*20 min*
Norwood Overview	*Juan Andres, Chief Technical Operations & Quality Officer*	*1:20–1:50 PM*	*30 min*
Q&A Session		*1:50–2:05 PM*	*15 min*
Competing in the Age of AI	*Karim R. Lakhani, Charles E. Wilson Professor of Business Administration* *Dorothy & Michael Hintze Fellow* *Harvard Business School, Laboratory for Innovation Science at Harvard*	*2:05–2:50 PM*	*45 min*
Moderna Digital Strategy	*Marcello Damiani, Chief Digital and Operational Excellence Officer*	*2:50-3:20 PM*	*30 min*
Advanced Analytics and AI @ Moderna	*Dave Johnson, PhD*	*3:20-3:50 PM*	*30 min*
Q&A Session		*3:50-4:05 PM*	*15 min*
Closing	*Stéphane Bancel, CEO*	*4:05-4:15 PM*	*10 min*

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Manufacturing & Digital Day

Stéphane Bancel

March 04, 2020

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Forward-looking statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended including, but not limited to, statements concerning: the ability of digital integration to reduce labor requirements and cycle time in our manufacturing process; the ability of our artificial intelligence platform to reduce failures and increase quality across our platform; the expected increase in speed, decrease in cost and consistency across future PCV batches; the expected manufacturing cost reductions for our CMV product; the ability of our Norwood site to support commercial launch of CMV or any other mRNA product and the number of doses per year that would be produced at our Norwood site. In some cases, forward-looking statements can be identified by terminology such as "will," "may," "should," "expects," "intends," "plans," "aims," "anticipates," "believes," "estimates," "predicts," "potential," "continue," or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. The forward-looking statements in this press release are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, many of which are beyond Moderna's control and which could cause actual results to differ materially from those expressed or implied by these forward-looking statements. These risks, uncertainties, and other factors include, among others: preclinical and clinical development is lengthy and uncertain, especially for a new class of medicines such as mRNA, and therefore our preclinical programs or development candidates may be delayed, terminated, or may never advance to or in the clinic; no mRNA drug has been approved in this new potential class of medicines, and may never be approved; mRNA drug development has substantial clinical development and regulatory risks due to the novel and unprecedented nature of this new class of medicines; despite having ongoing interactions with the FDA or other regulatory agencies, the FDA or such other regulatory agencies may not agree with our regulatory approval strategies, components of our or filings, such as clinical trial designs, conduct and methodologies, or the sufficiency of data submitted; and those risks and uncertainties described under the heading "Risk Factors" in Moderna's most recent Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission (SEC) and in subsequent filings made by Moderna with the SEC, which are available on the SEC's website at www.sec.gov. Except as required by law, Moderna disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this press release in the event of new information, future developments or otherwise. These forward-looking statements are based on Moderna's current expectations and speak only as of the date hereof.

This presentation also contains estimates, projections and other statistical data made by independent parties and by Moderna relating to market size and growth and other data about Moderna's industry. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of Moderna's future performance and the future performance of the markets in which the Company operates are necessarily subject to a high degree of uncertainty and risk.

Note Regarding Trademarks

Moderna is the owner of various U.S. federal trademark registrations ("®") of and other trademarks ("TM"). Certain other trademarks, trade names and service marks appearing in this presentation are the property of third parties. Solely for convenience, the trademarks and trade names in this presentation are referred to without the ® and TM symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

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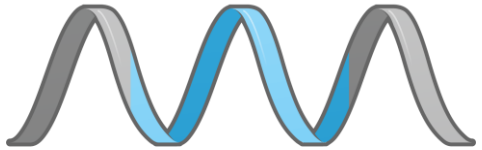
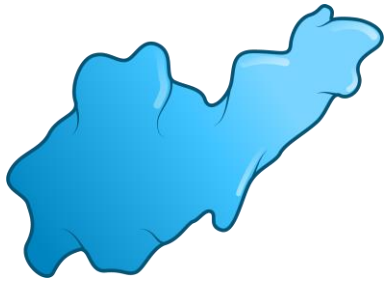
mRNA is the software of life

What if it could be turned into a drug?

Central Dogma of Molecular Biology

DNA → **messenger RNA** → **Protein**





Hard Drive

DNA stores our genetic information

Software

mRNA reads off the DNA and instructs cells to make protein

Hardware

Proteins accomplish the work in the body – structure, signaling, metabolism, etc.

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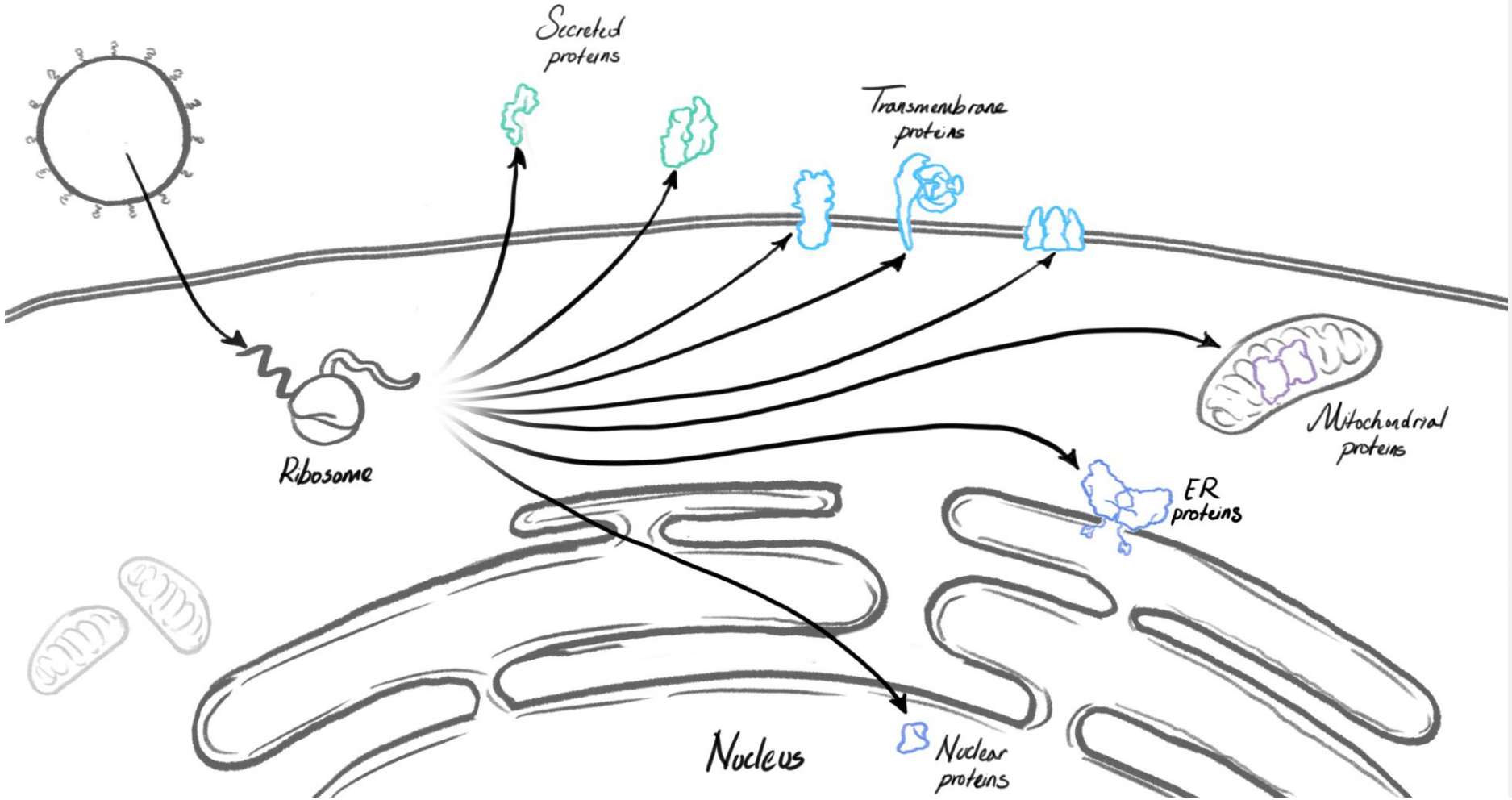
mRNA as a potential new class of medicines



1. Large product opportunity
2. Higher probability of technical success
3. Accelerated research and development timelines
4. Greater capital efficiency over time vs. recombinant technology

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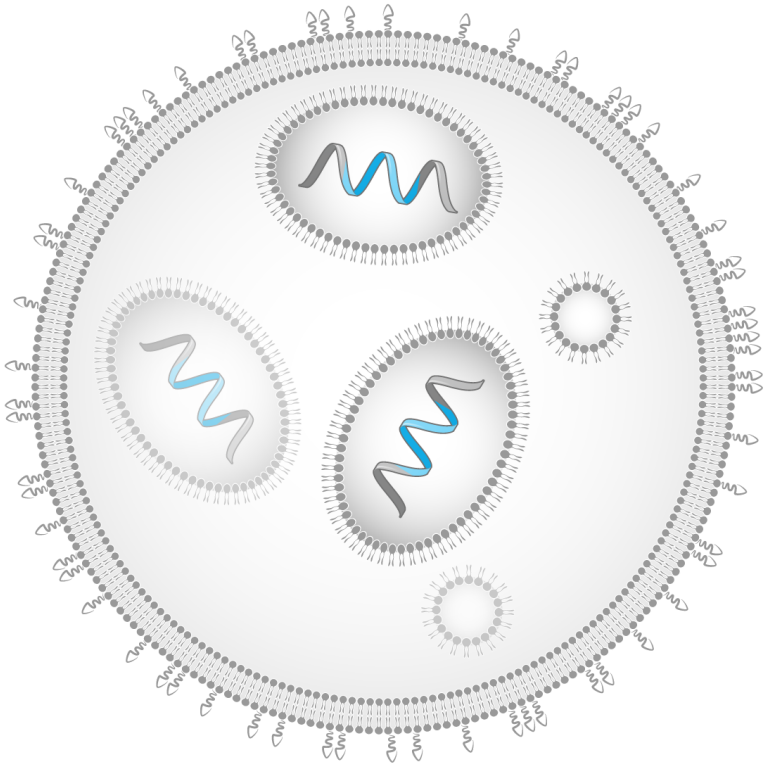
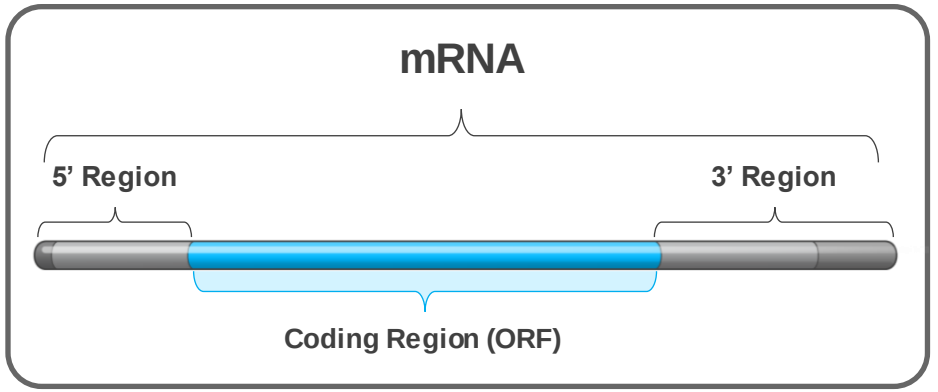
If mRNA could be a drug…it would be a platform

If you develop a solution for one program, you have a template for many programs

Formulation





If mRNA works once,
it should work over and over again for different coding regions → different proteins

And development of new mRNA drugs should be fast!

1. Large product opportunity
2. Higher probability of technical success
3. Accelerated research and development timelines
4. Greater capital efficiency over time vs. recombinant technology

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We have focused on managing risk since inception

With a focus on…

1. Technology risk
2. Biology risk
3. Execution risk
4. Financing risk

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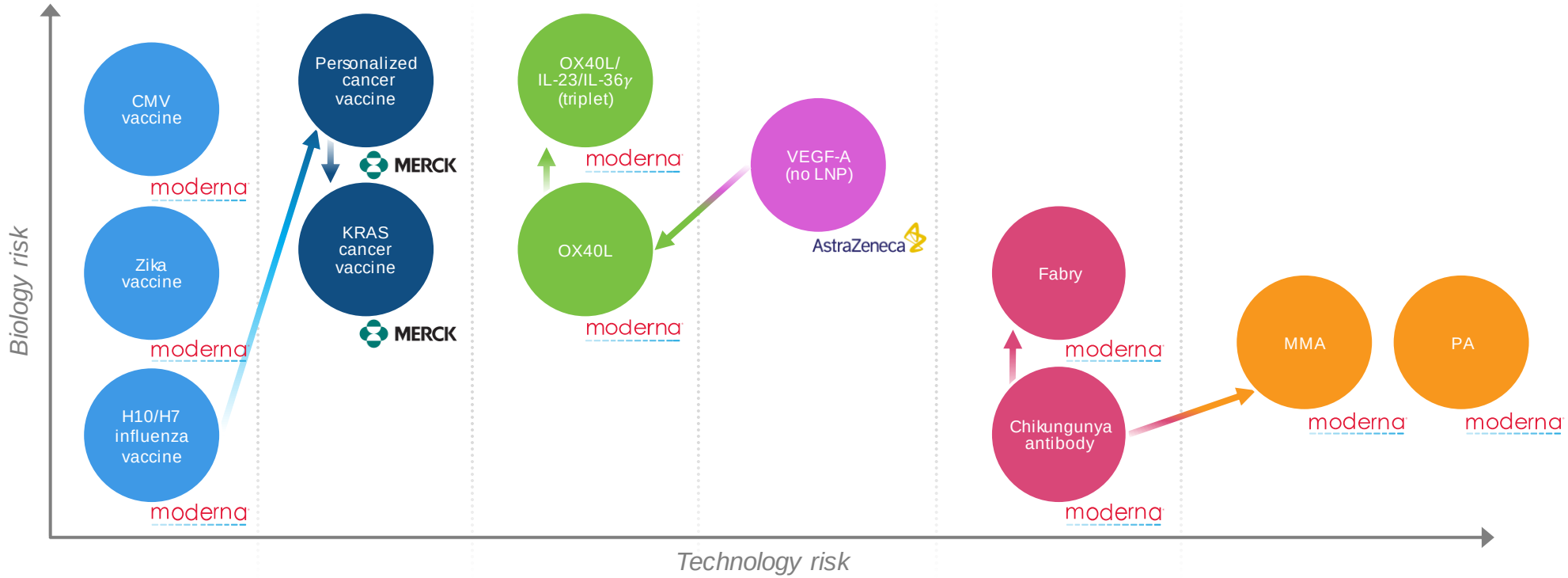
To manage technology risk we took six modalities into the clinic in parallel



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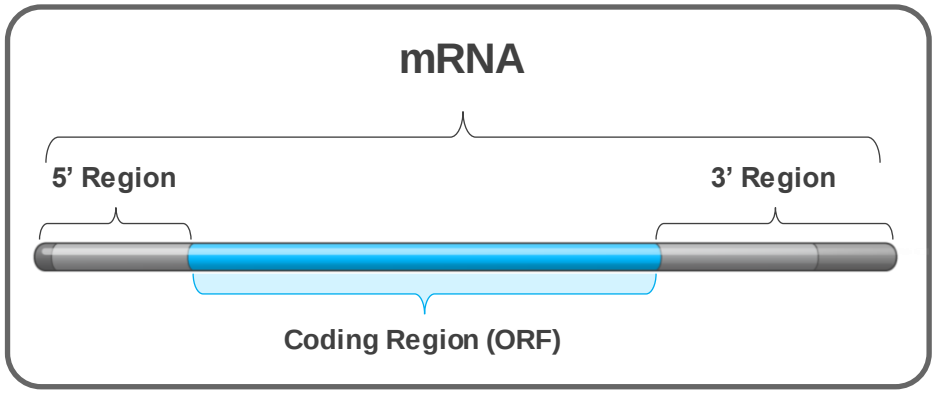
Given the breadth of the portfolio we needed to build our own, fully integrated/digital facility to reduce execution risk



If mRNA works once,
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And development of new mRNA drugs should be fast!

Single platform

↓

economies of scale

Time Cost Resources

Ability to scale-up

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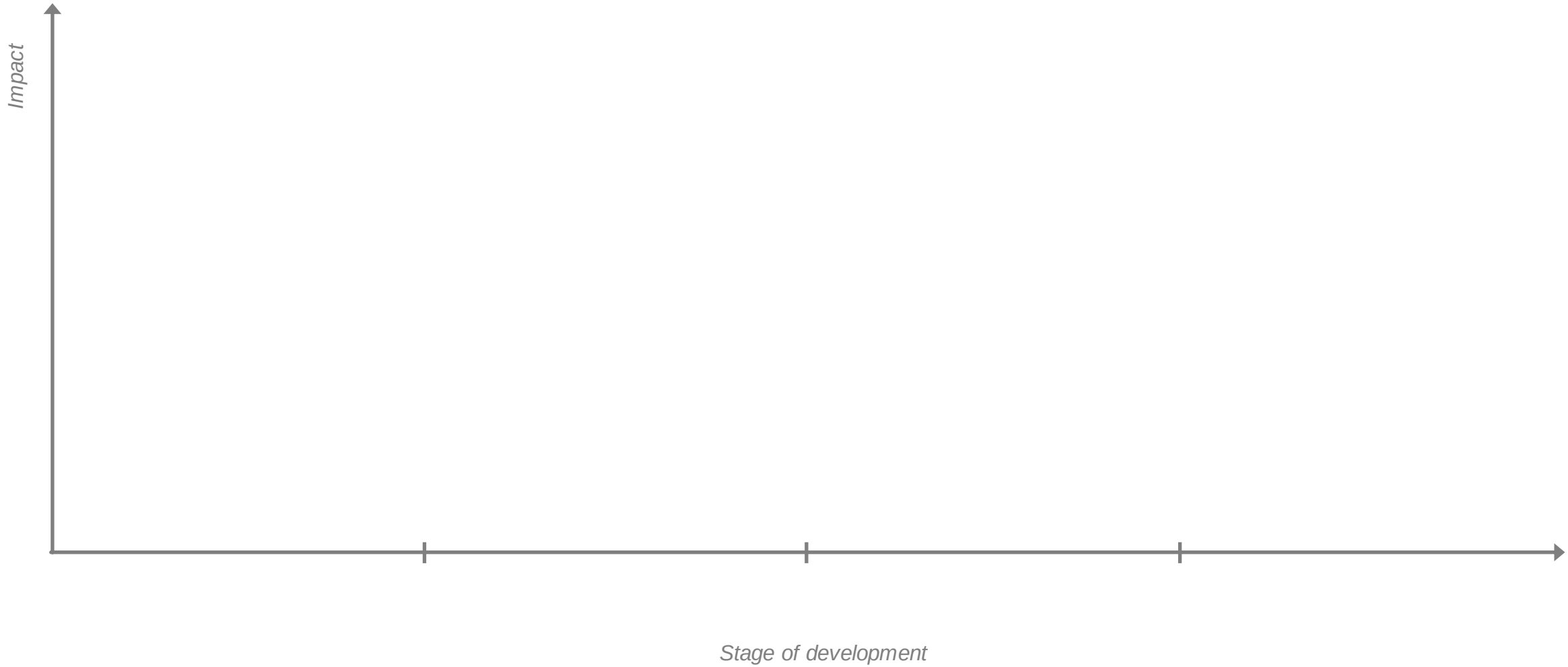
Progression towards a new class of medicines



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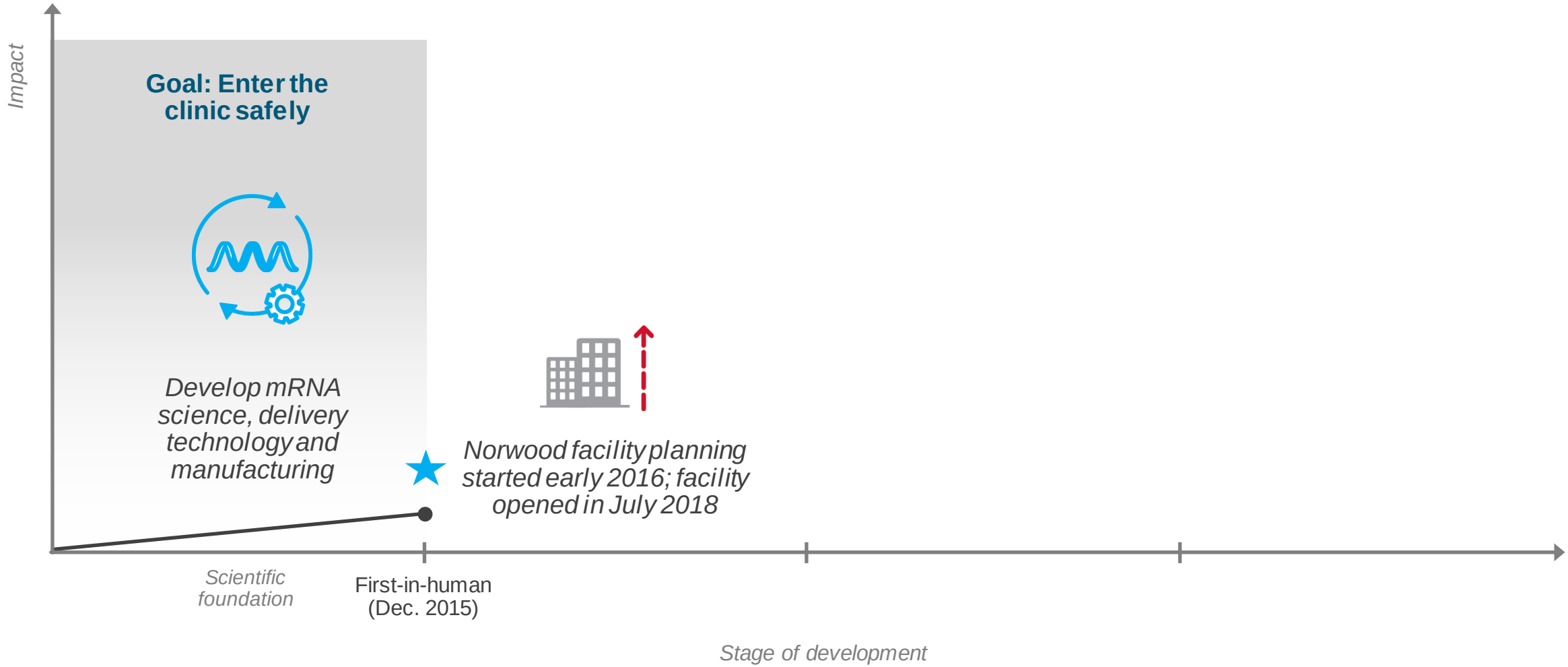
Progression towards a new class of medicines



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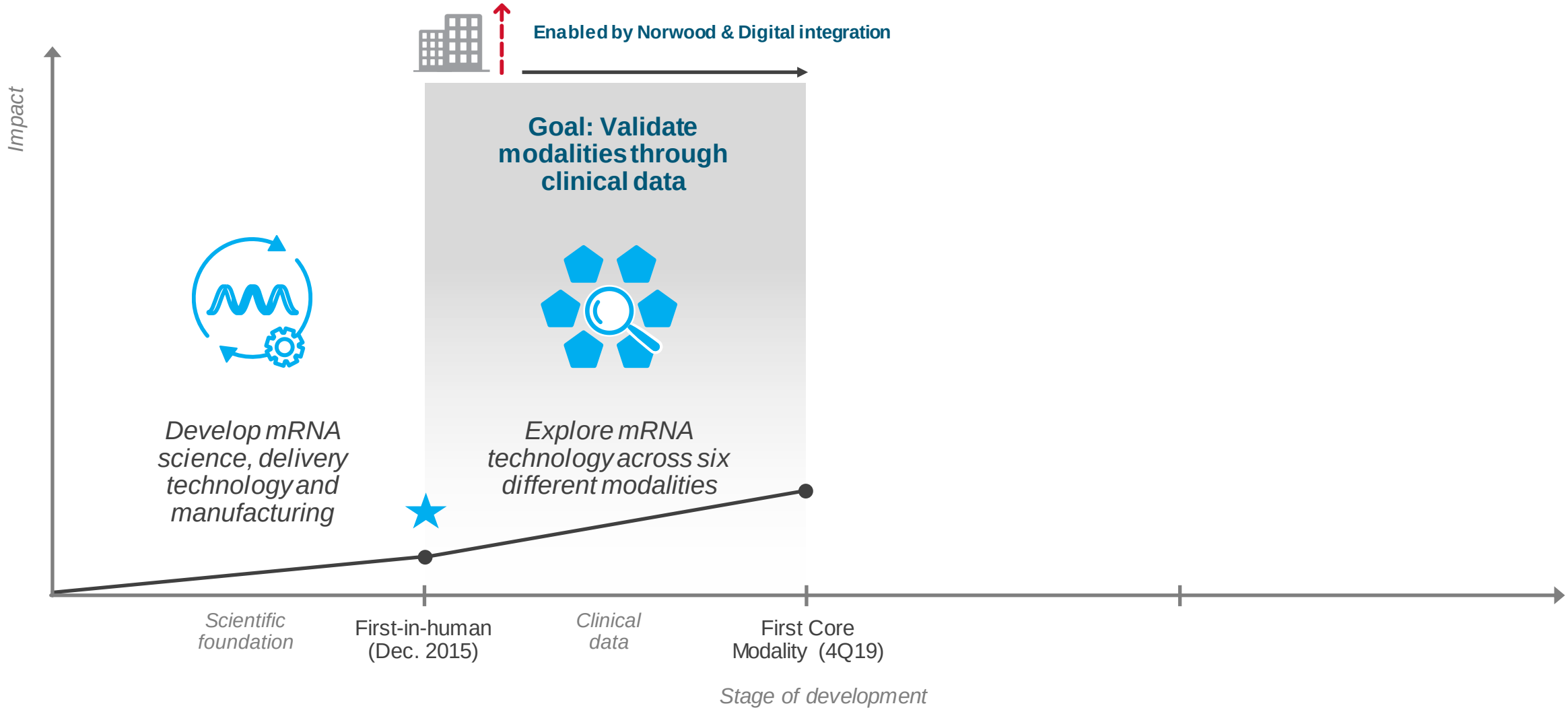
Progression towards a new class of medicines



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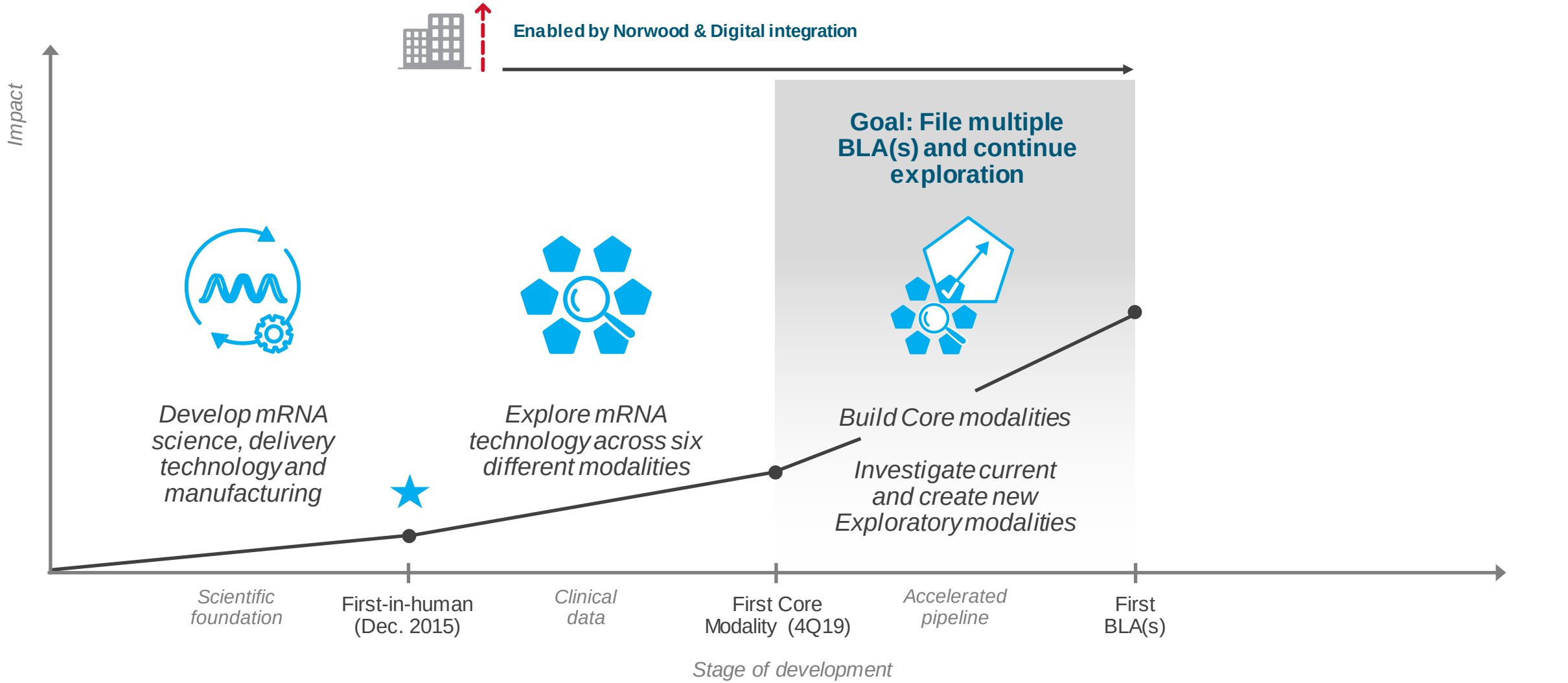
Progression towards a new class of medicines



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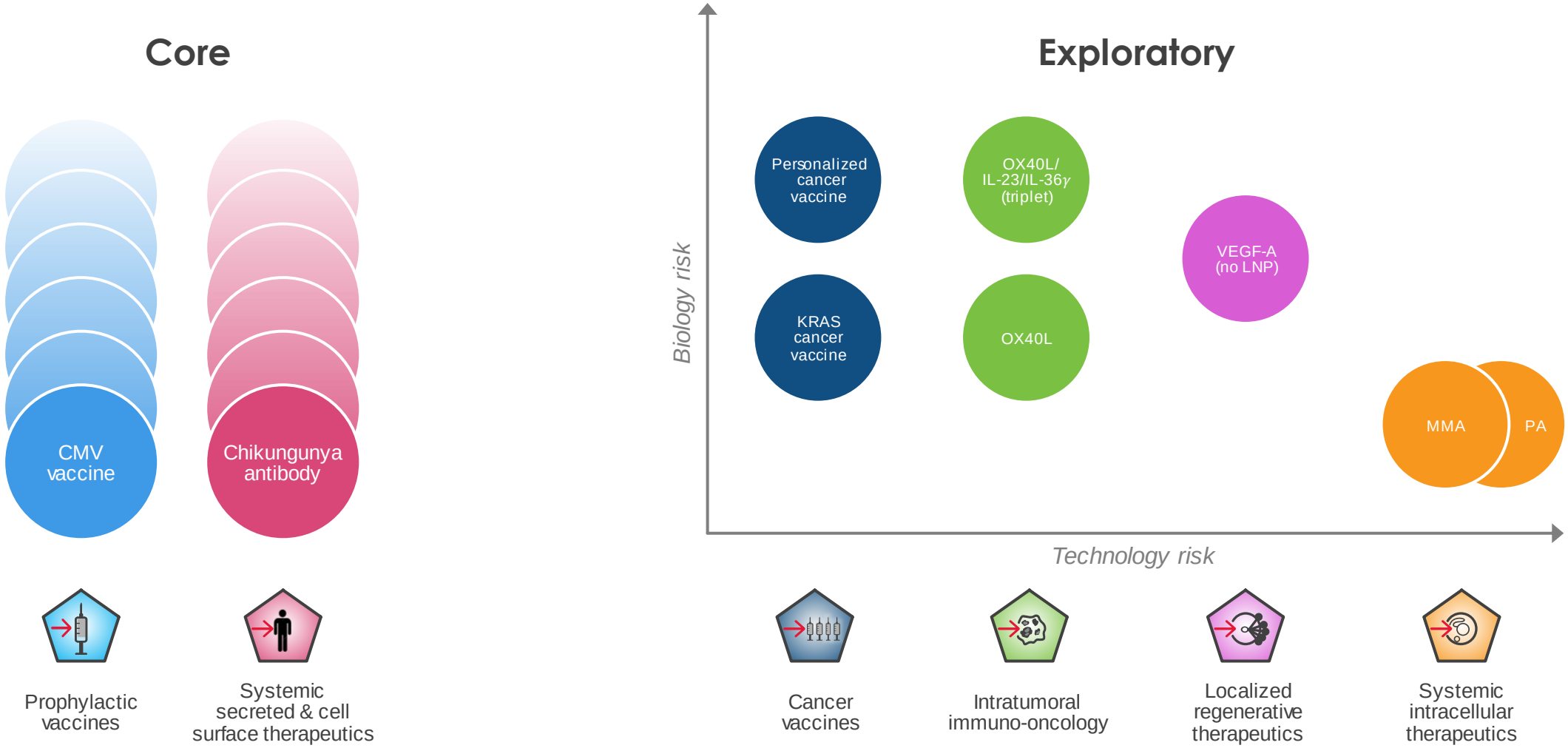
Expanding core modalities with additional development candidates



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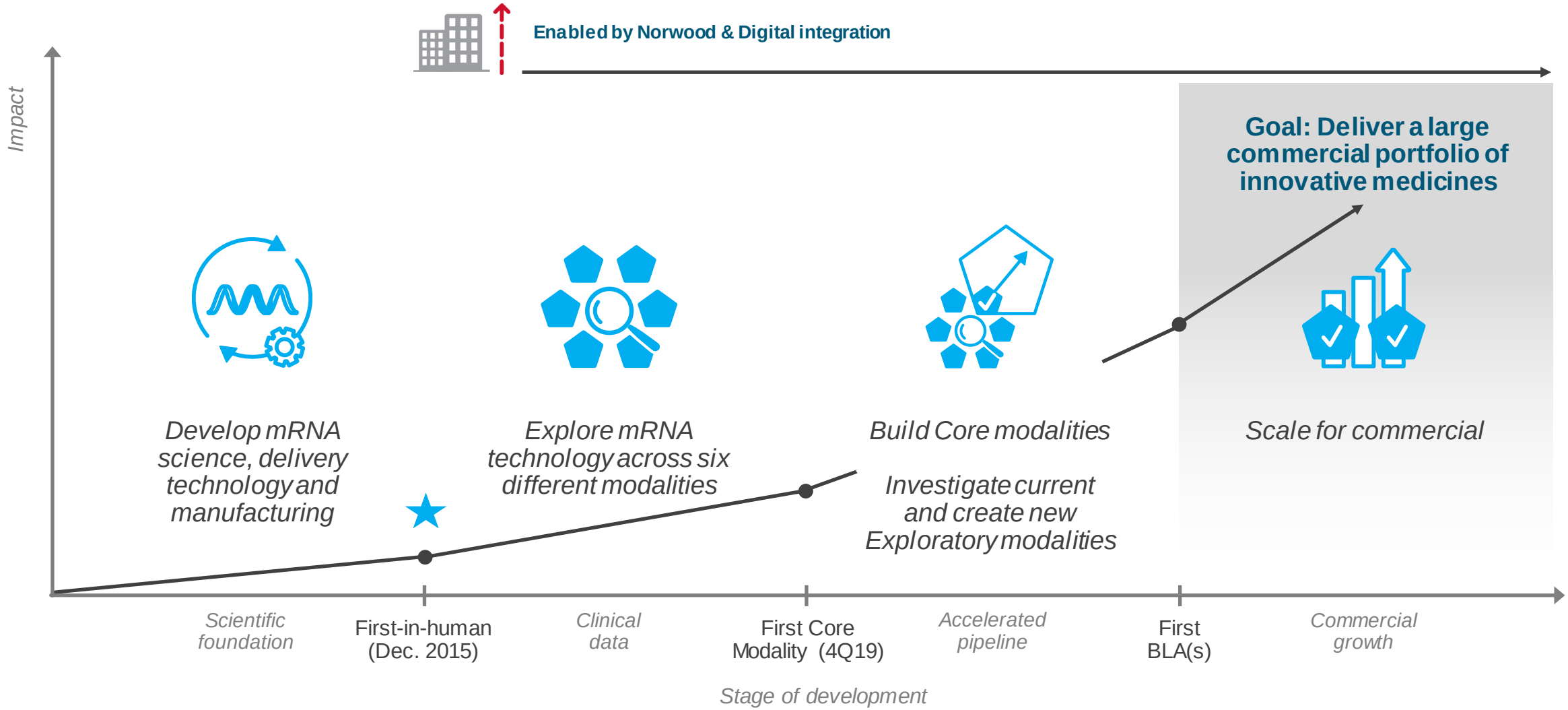
Progression towards a new class of medicines



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Norwood

Juan Andres

March 4, 2020

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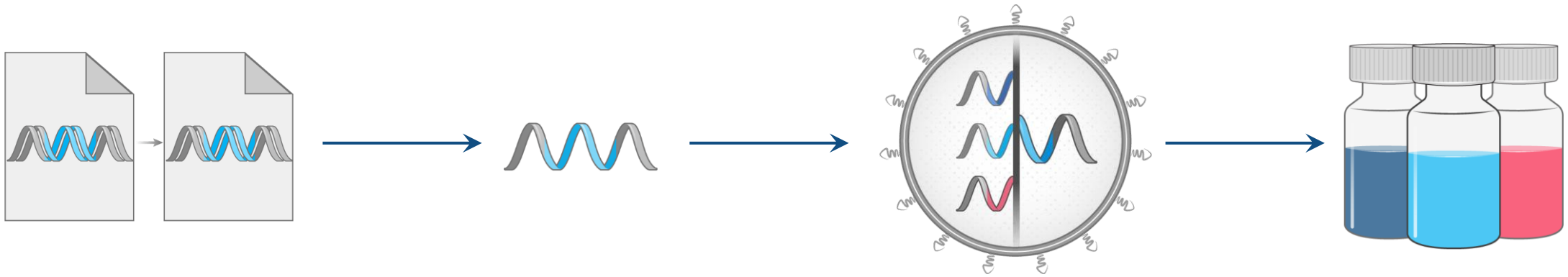
Juan Andres, Chief Technical Operations and Quality Officer

As Chief Technical Operations and Quality Officer, Juan Andres is responsible for the supply of product required for Moderna's preclinical and clinical development programs, as well as scaling the CMC (chemistry, manufacturing and controls) processes across Moderna's portfolio. Mr. Andres also will lead all CMC late-stage development and future commercialization activities.

Mr. Andres was previously the Global Head of Technical Operations (Manufacturing and Supply Chain) for over 25,000 Novartis employees across all of its divisions. Prior to Novartis, Mr. Andres worked at Eli Lilly & Co. for 18 years in a variety of manufacturing, production and quality roles in the United States, Puerto Rico, UK and Spain, most recently serving as Vice President, Pharmaceutical Manufacturing.

NEW

We are a platform…



DNA mRNA mRNA + LNP Drug product

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NEW = Learning

PLATFORM = Many

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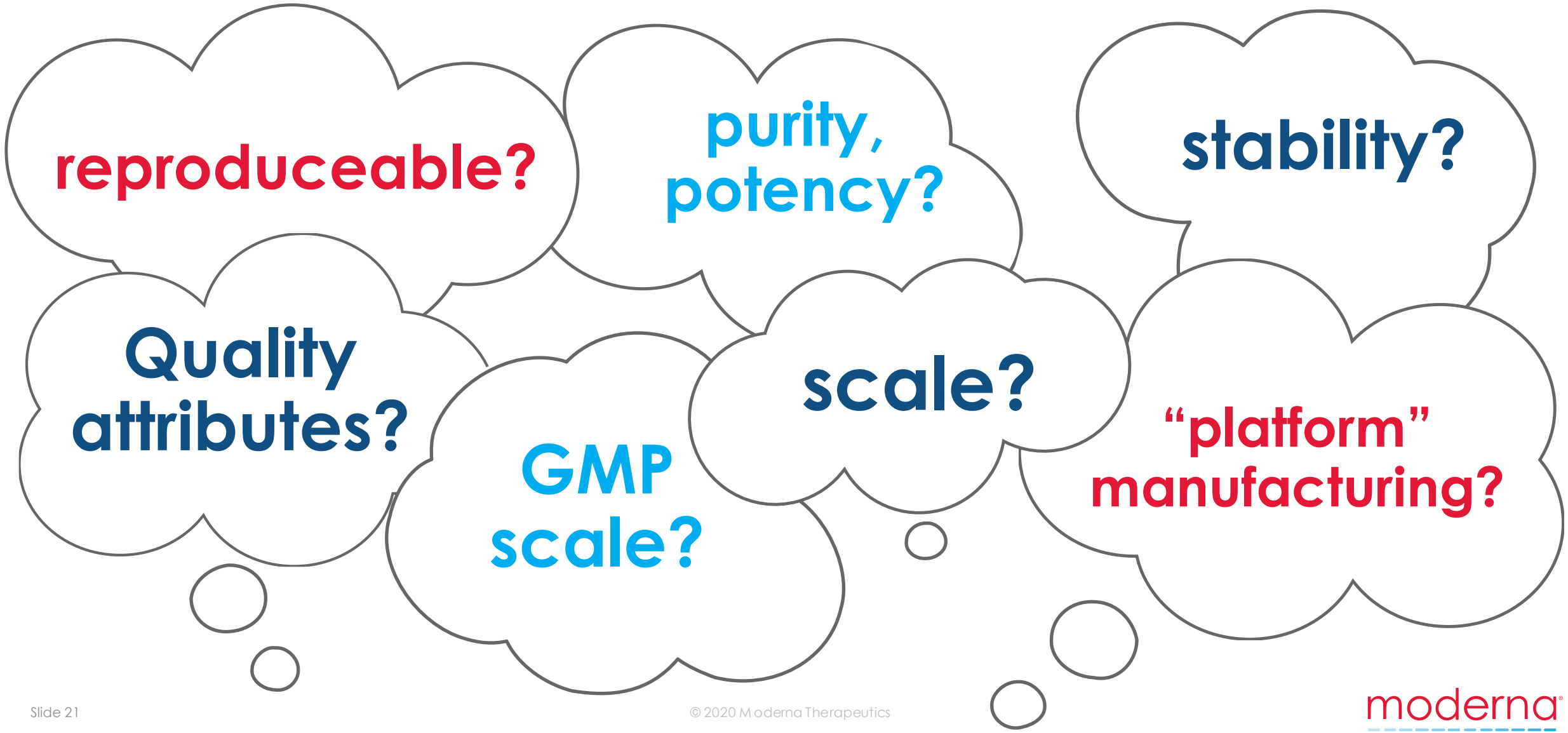
We initially had more questions than answers…



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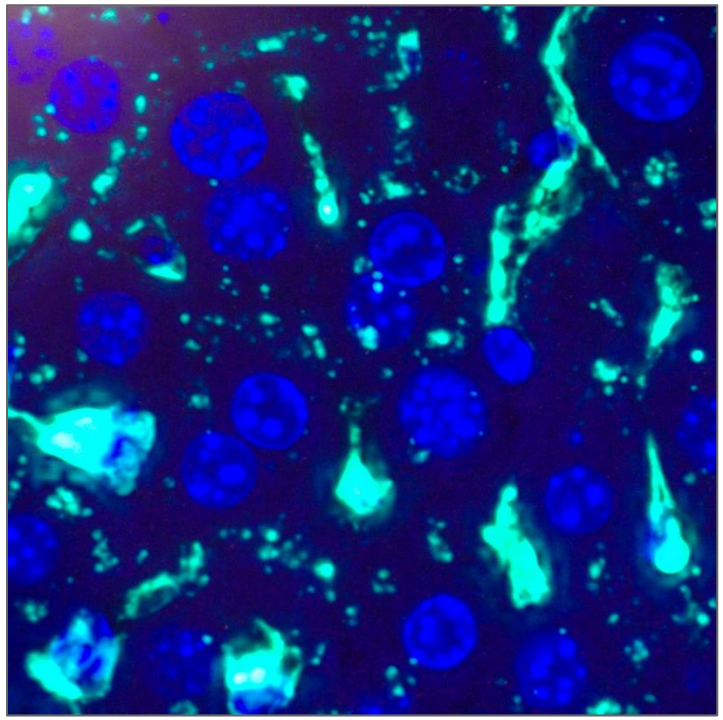
Platform research + technical development = “create”



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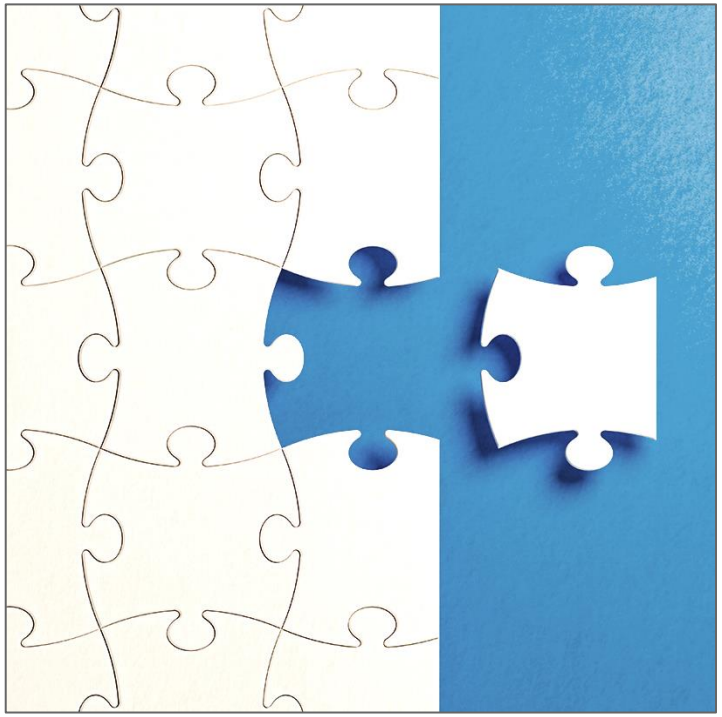

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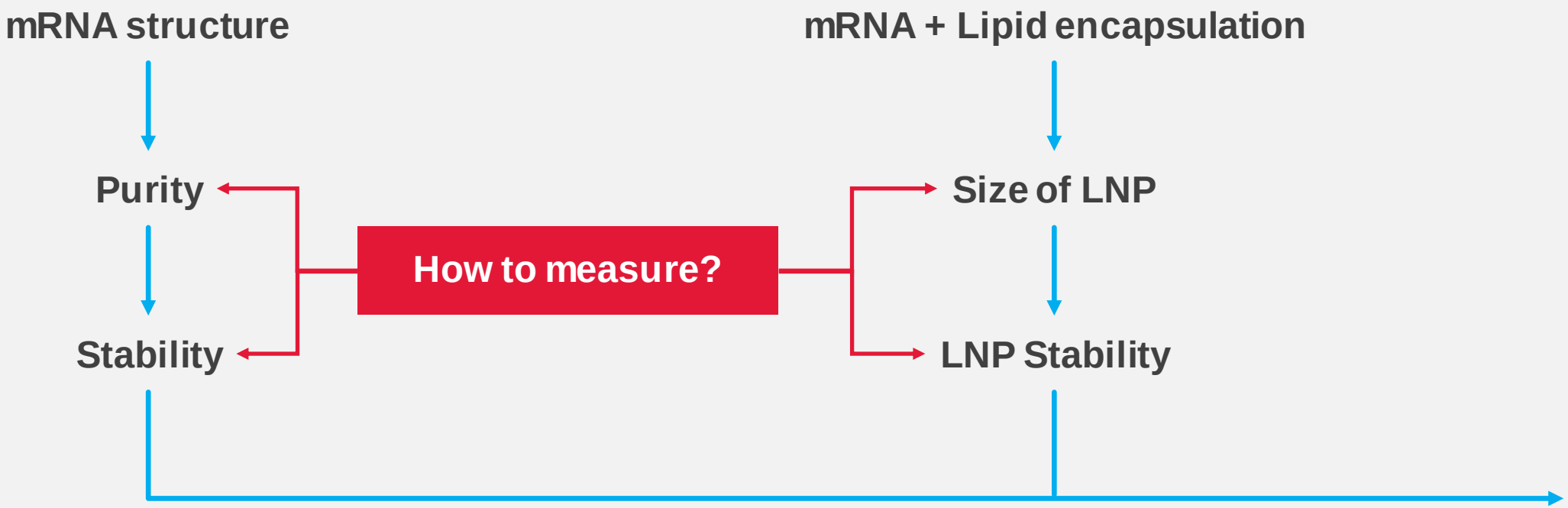
We have solved many questions



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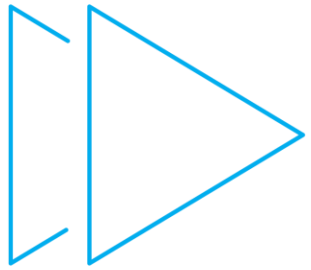
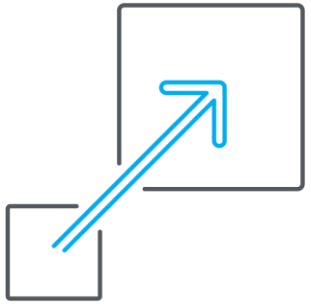
Once right…



Speed



Scale

Cost

…were engineering problems!

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Before Norwood

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Norwood is a clinical development site

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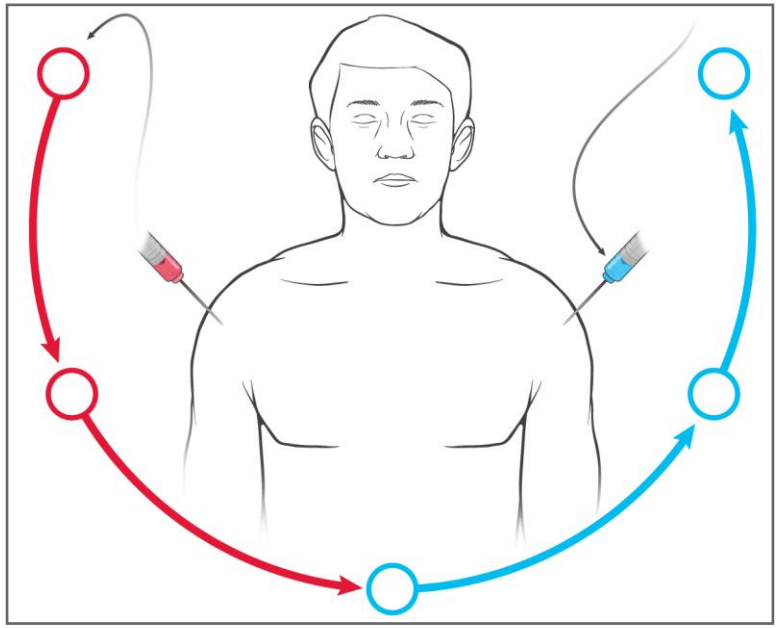
3 Engines

PRECLINICAL

PERSONALIZED VACCINE UNIT



CLINICAL

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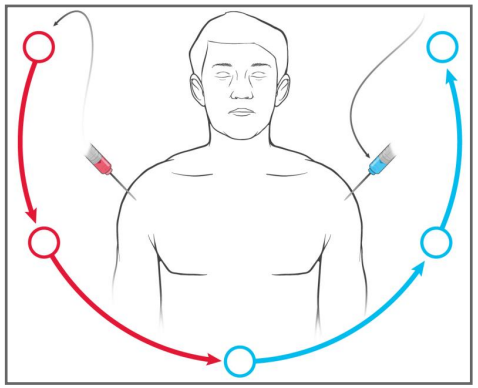
	PRECLINICAL	PERSONALIZED VACCINE UNIT	CLINICAL
Batches			
Scale	23,500	1 batch/1 patient; 90 to date	1 batch/many patients

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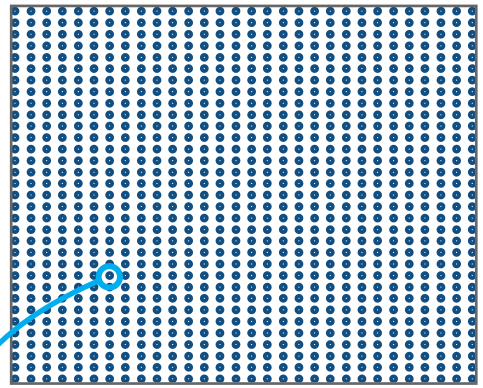
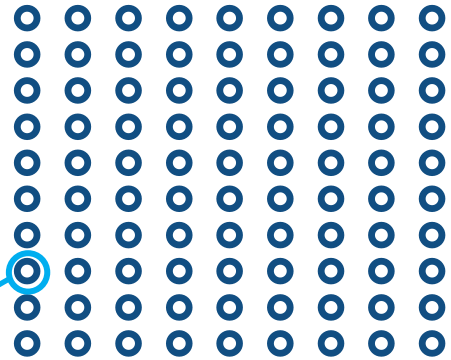
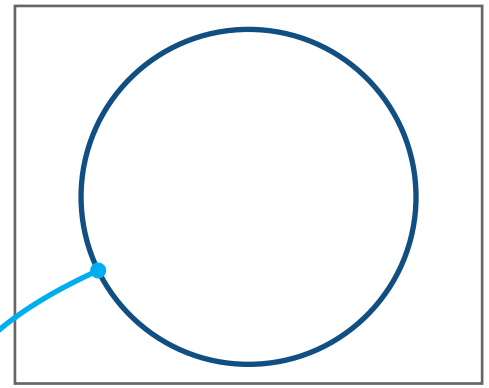
	PRECLINICAL	PERSONALIZED VACCINE UNIT	CLINICAL
Batches			
	23,500	1 batch/1 patient; 90 to date	1 batch/many patients
Scale			
	10mg	>100mg	5g-75g+

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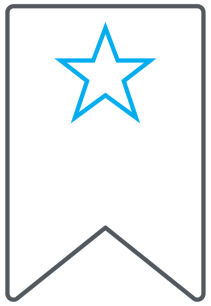
What we know now…. Platform technology

Similar processes

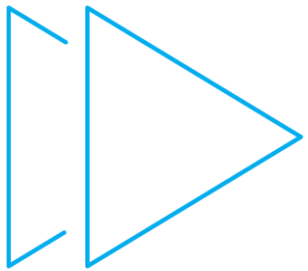
Fast process improvements

Cell-free

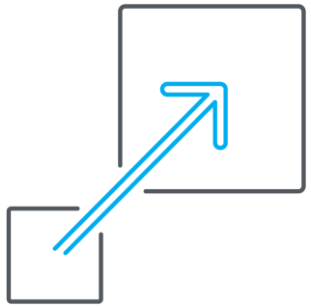
Less capital investment



Quality



Speed



Scale

Cost

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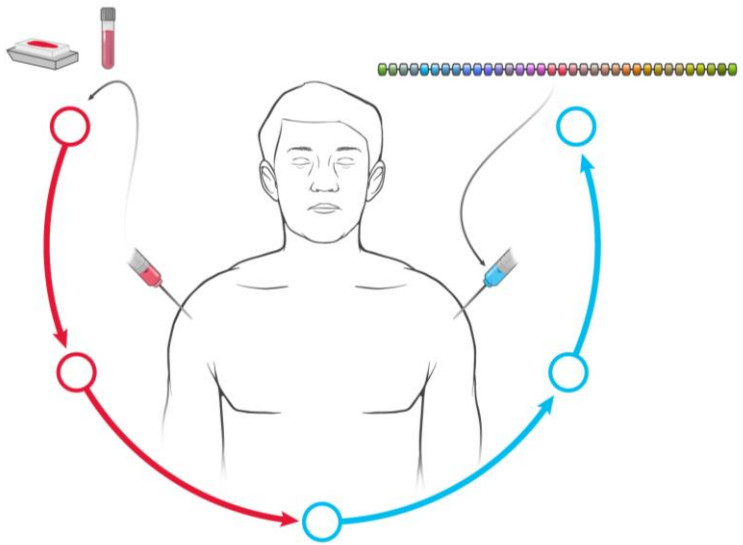
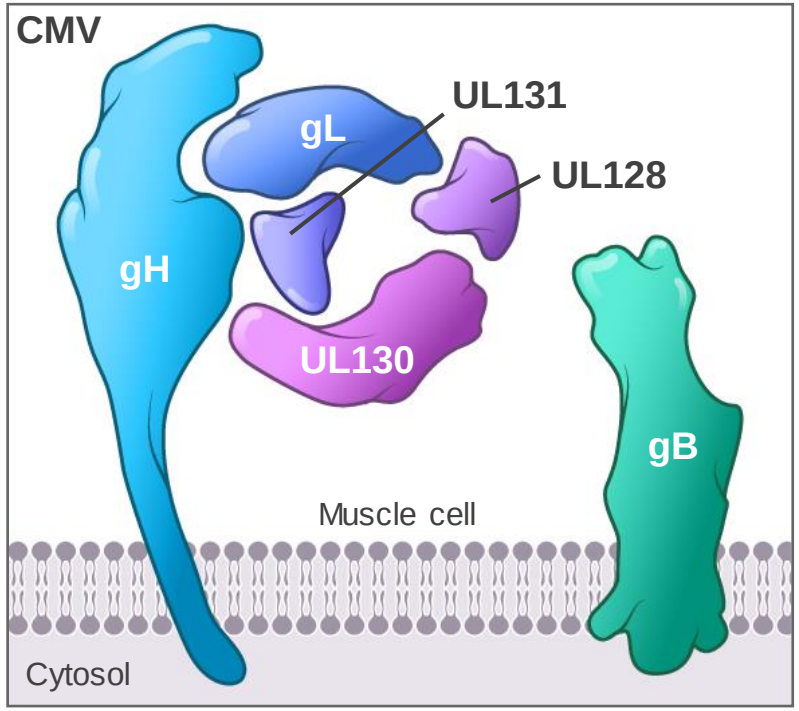
3 recent examples pave our future

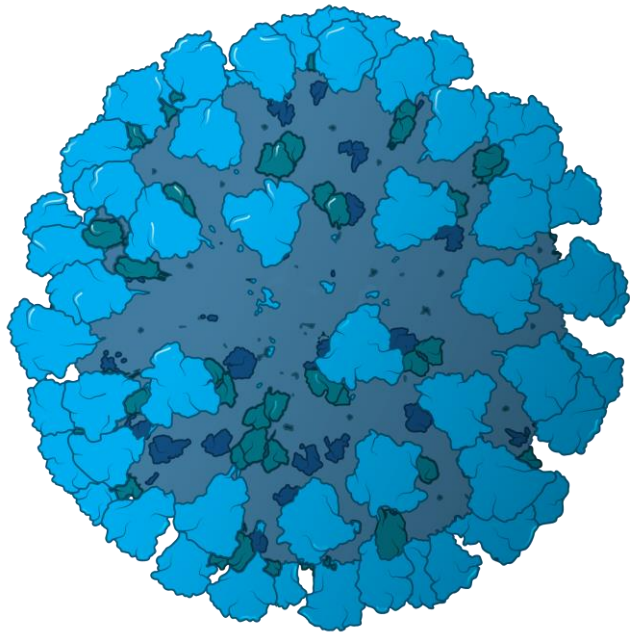
PCV: Needle-to-Needle



CMV



SARS-CoV-2 Antigen



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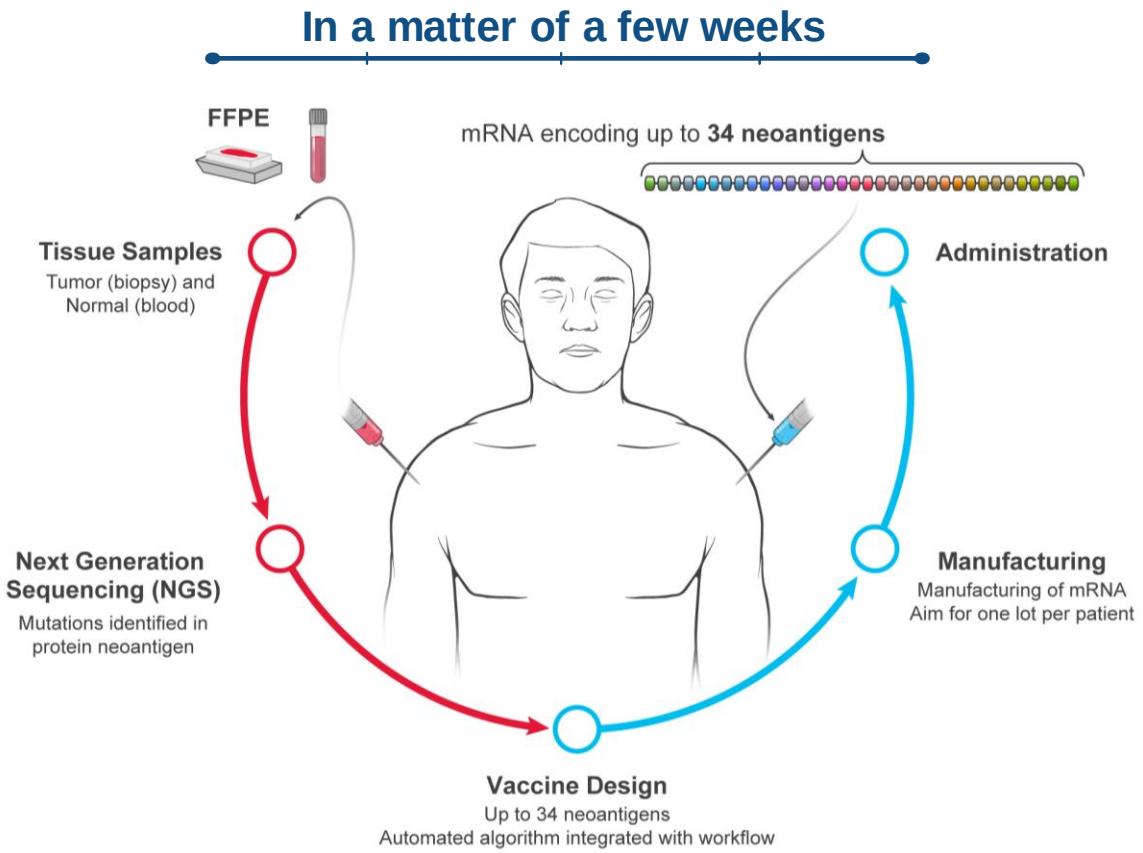
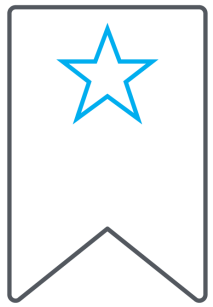
Case Study 1: PCV



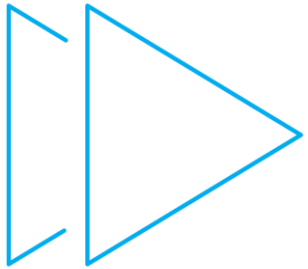
- Up to 200 patients for proof of concept (phase 2)
- Coincides with Keytruda dosing regiment
- Scale “out” (not up)

Learning curve



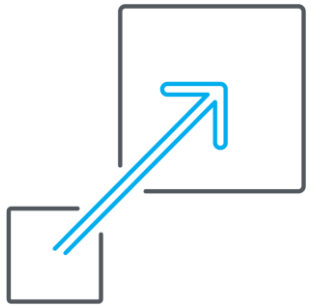
Quality

Success rate



Speed

Cycle time



Scale

Yield change

Cost

Capacity change

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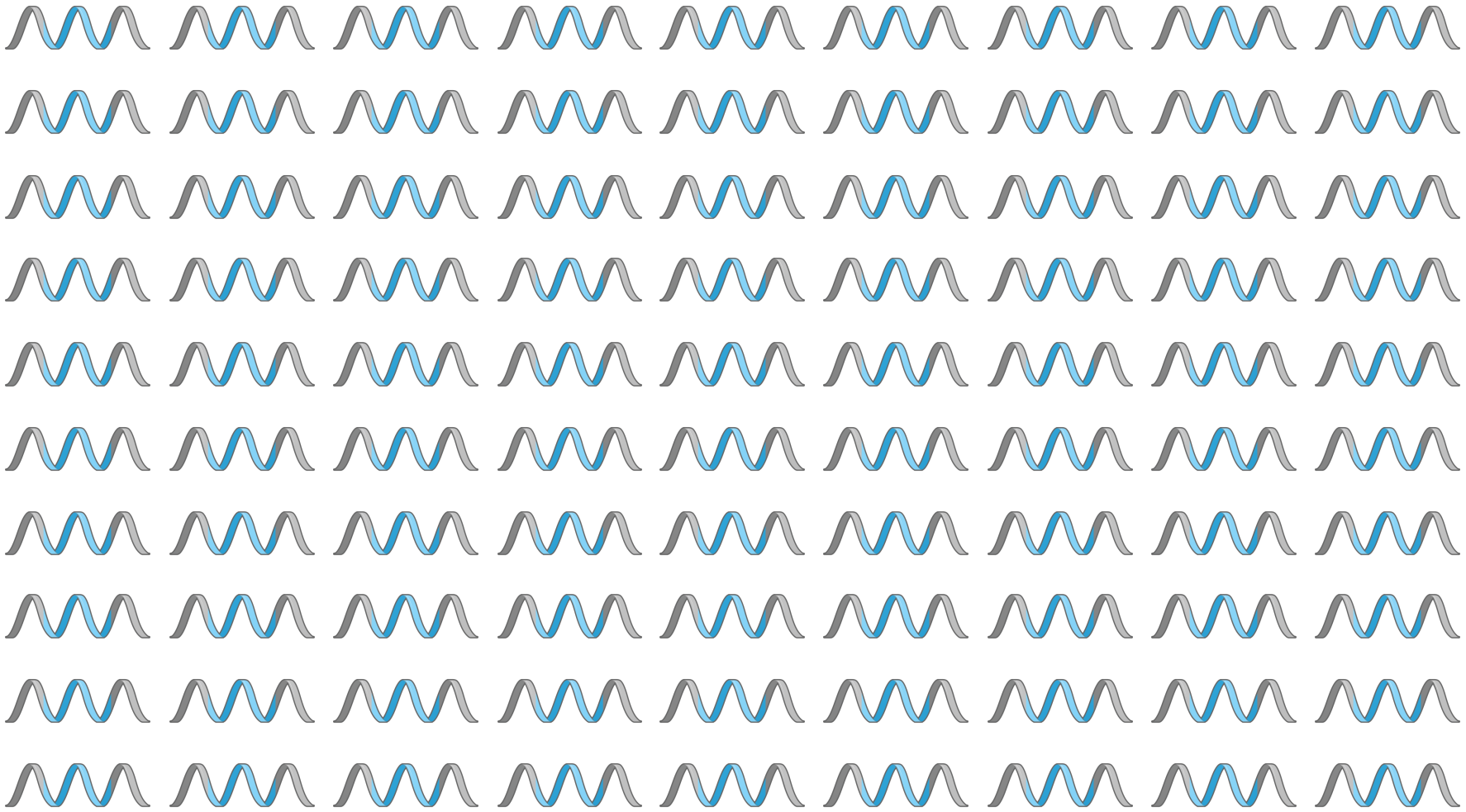
Learning

>90

UNIQUE PRODUCTS



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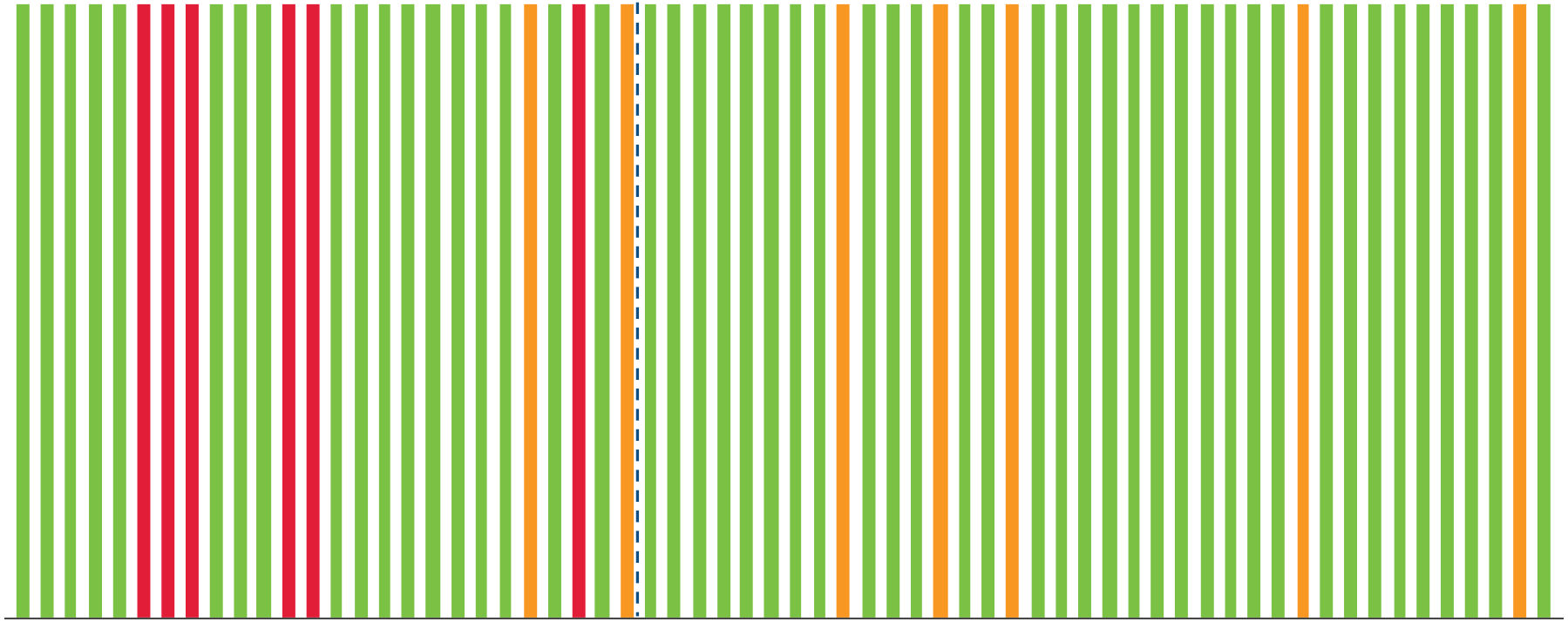
Increase learning…

Quality

Cost

Phase 1 Success rate:
69%

Phase 2 Success rate:
87%



Number of Patient Batches

Number of Patient Batches

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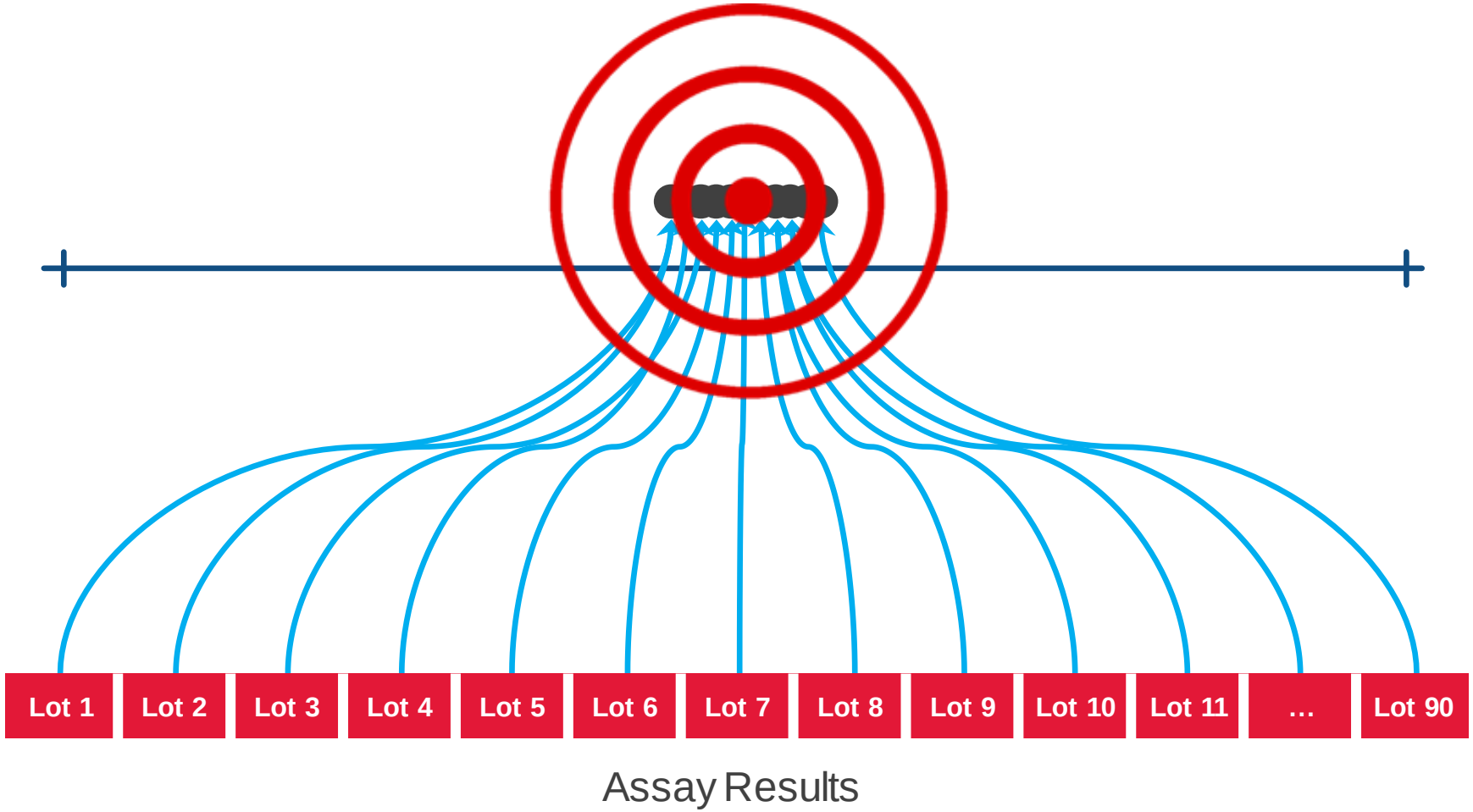
Multiple patient batches, same performance

Quality

Cost



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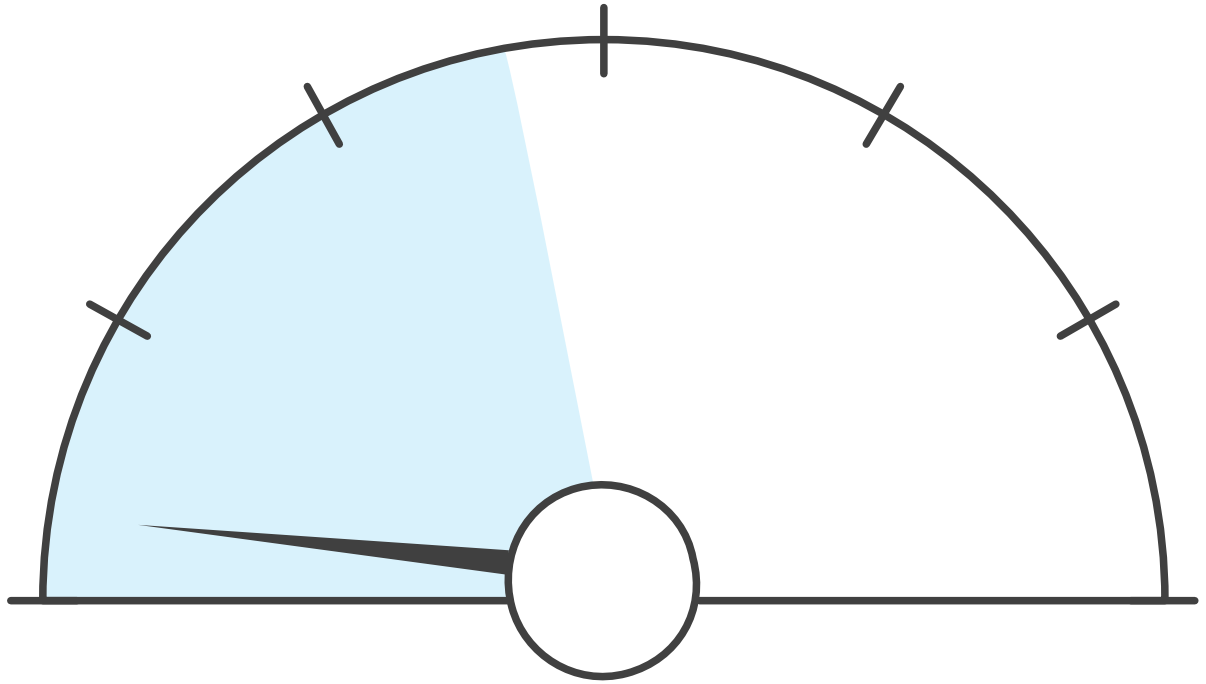
…Increase speed

Speed



40% faster since 2018

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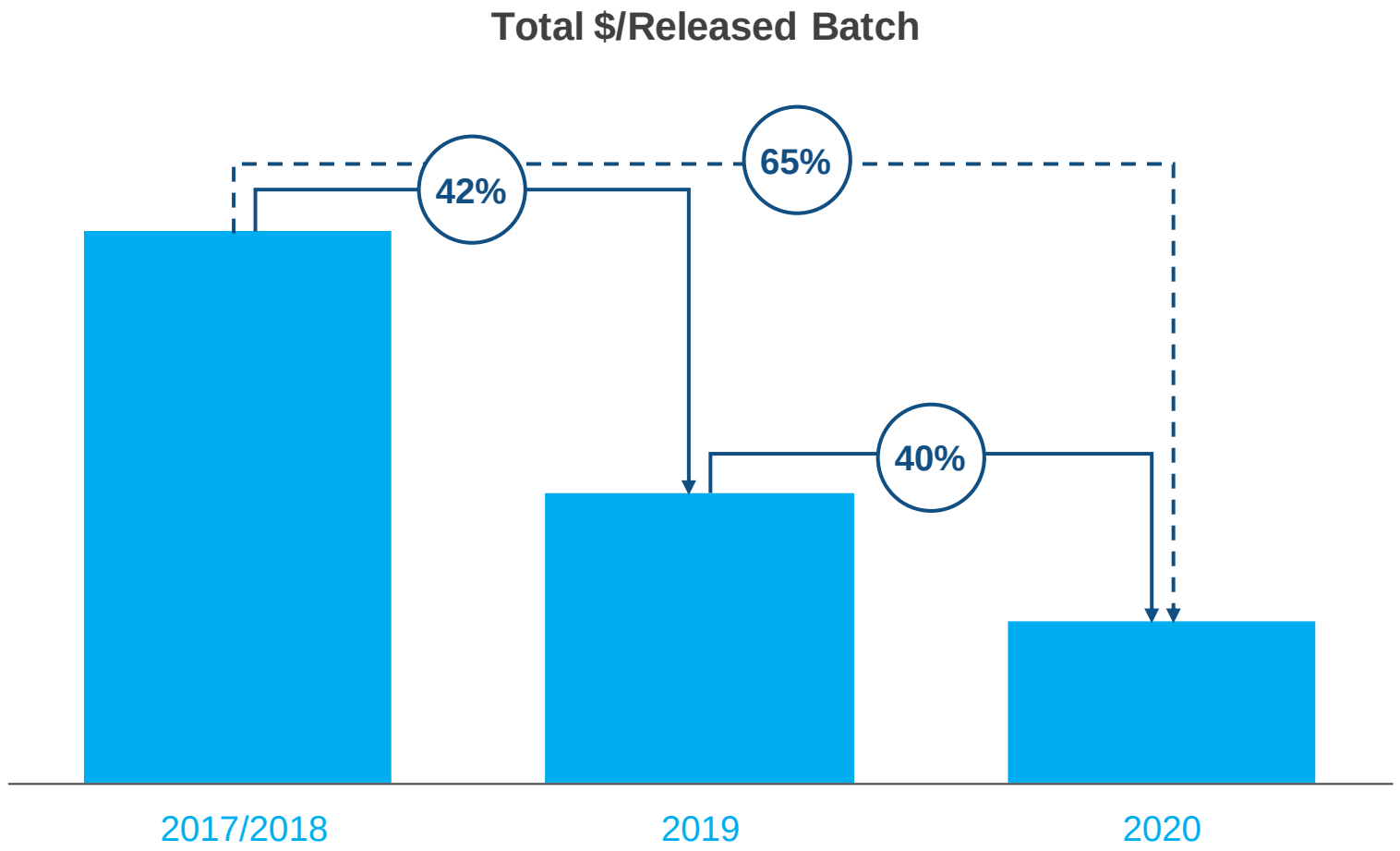
Cost improvement

Cost



	2017/2018	2019	2020
Patients served	34	54	>90

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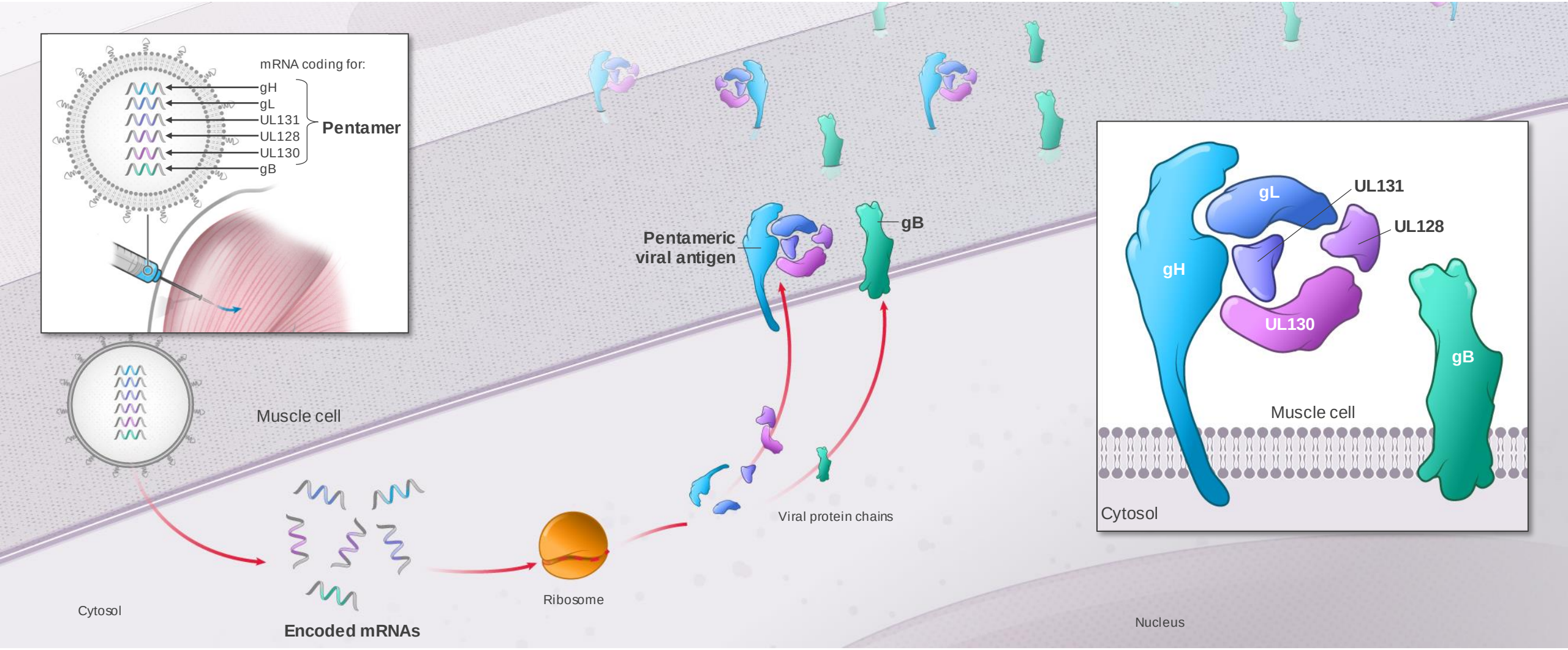
Case Study 2: CMV



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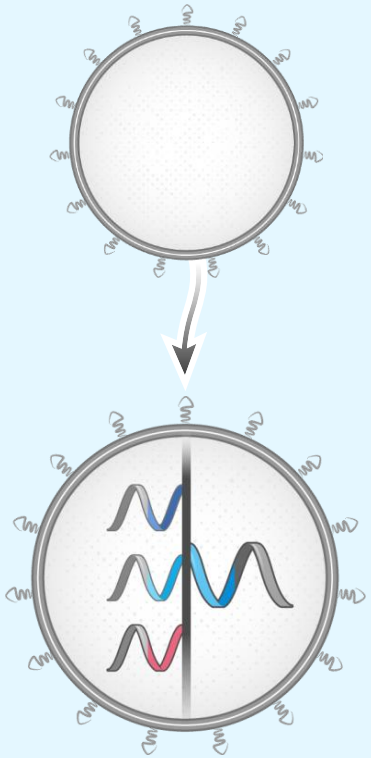
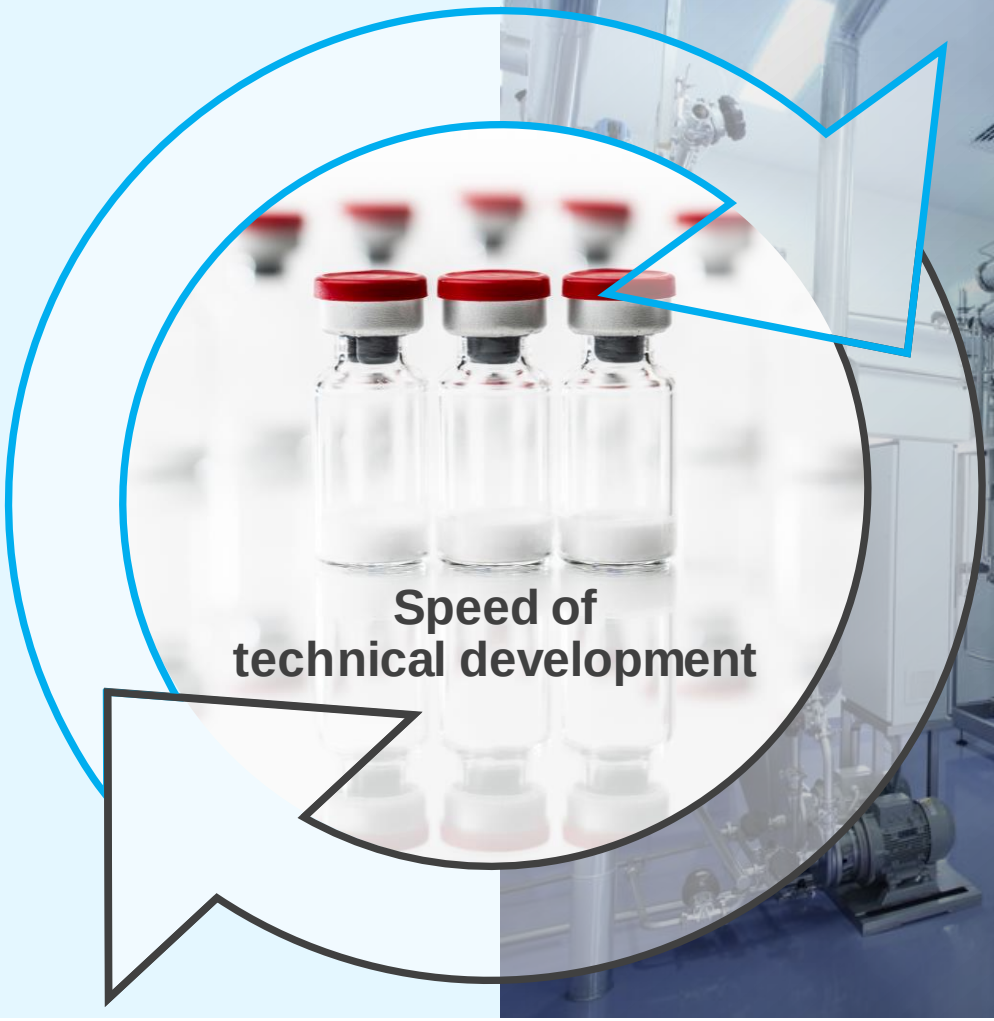
CASE STUDY 2: CMV

Quality

Create





Make

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From few to many

Speed

Scale

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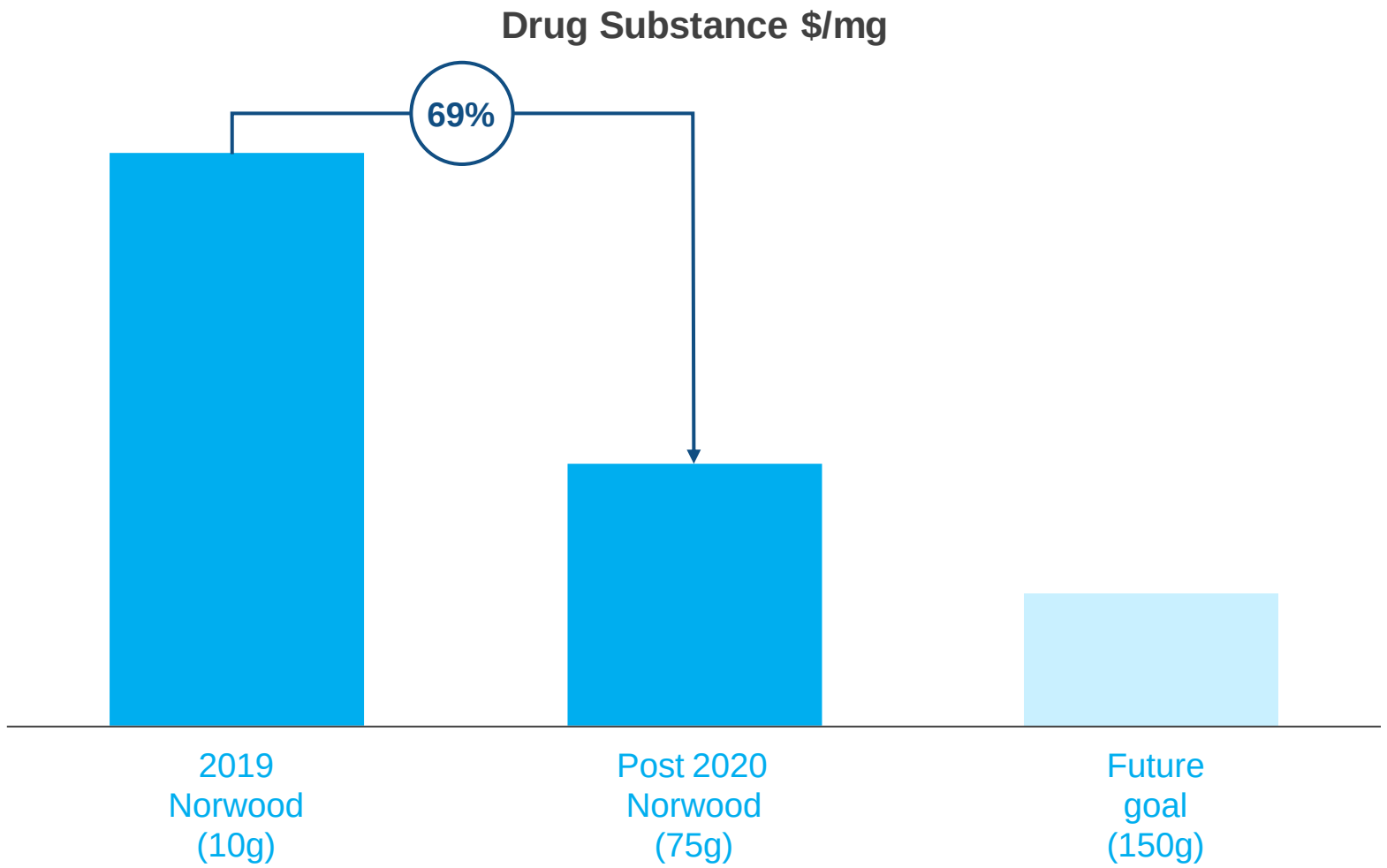
Manufacturing cost reduction

Cost



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CMV vials already produced for Phase 2 trial

- Same lyophilized image intended for Phase 3
- Norwood site can produce Phase 3 and support commercial launch with fill/finish done at CMO
- Over 10+ million doses/year could be made in Norwood

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CASE STUDY 3: SARS-CoV-2 Unplanned

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Convergence + Bold + Collaboration

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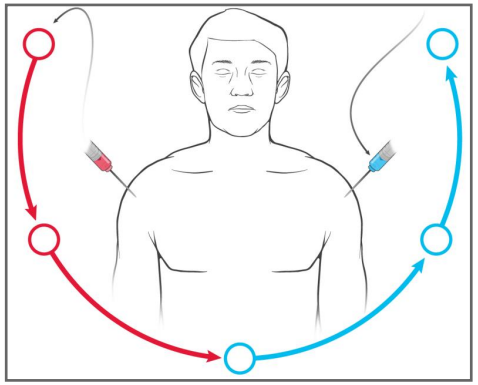
Firing up on all engines…

	PRECLINICAL	PERSONALIZED VACCINE UNIT	CLINICAL
Batches			
	23,500	1 batch/1 patient; 90 to date	1 batch/many patients
Scale			
	10mg	>100mg	5g-75g+

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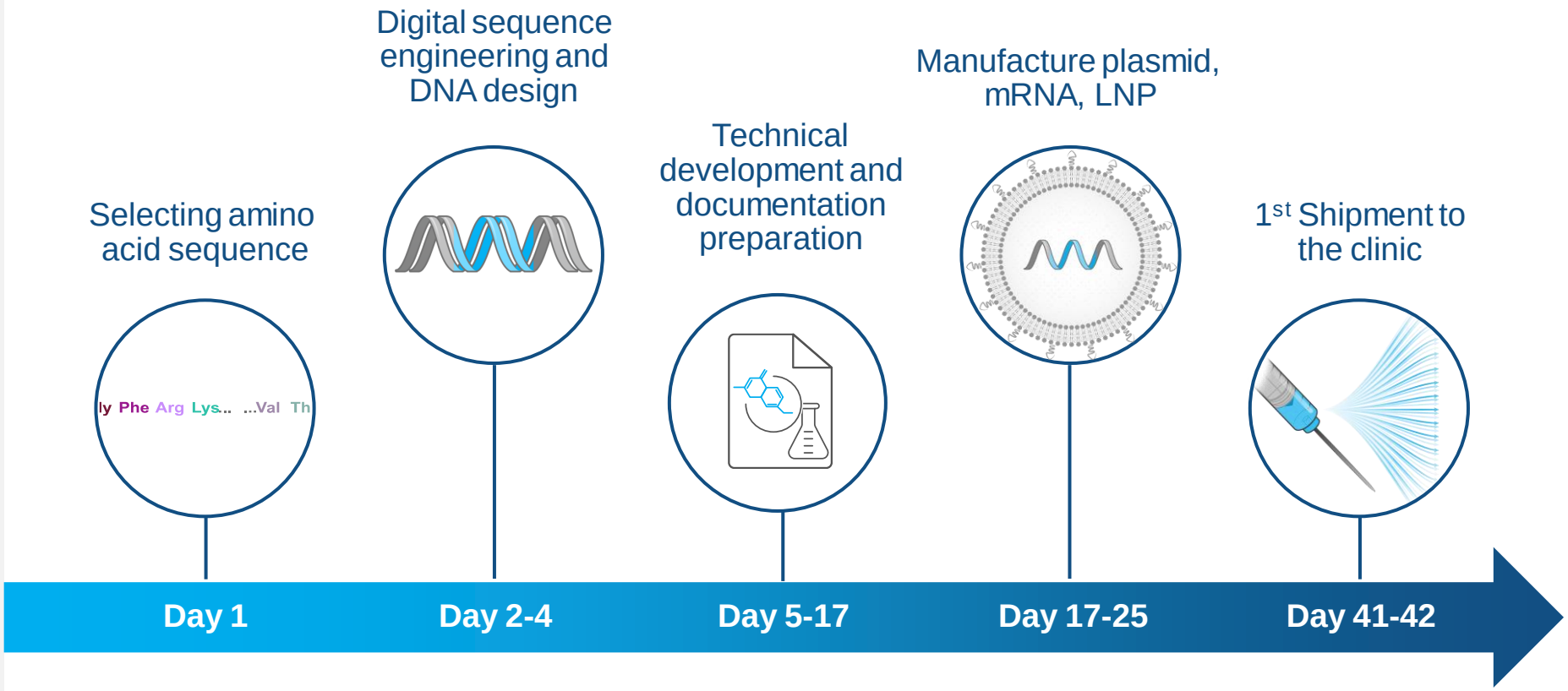
SARS-CoV-2

Speed

- Jan 13
- Feb 7
- Feb 23



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CASE STUDY 3: SARS-CoV-2

Image Source: Success Kid meme. Know Your Meme, Literally Media, 26 Aug. 2007, knowyourmeme.com/memes/success-kid-i-hate-sandcastles

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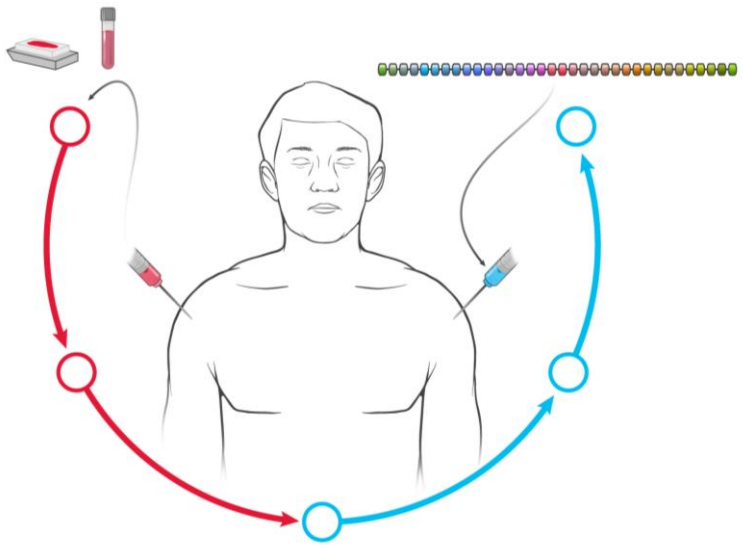
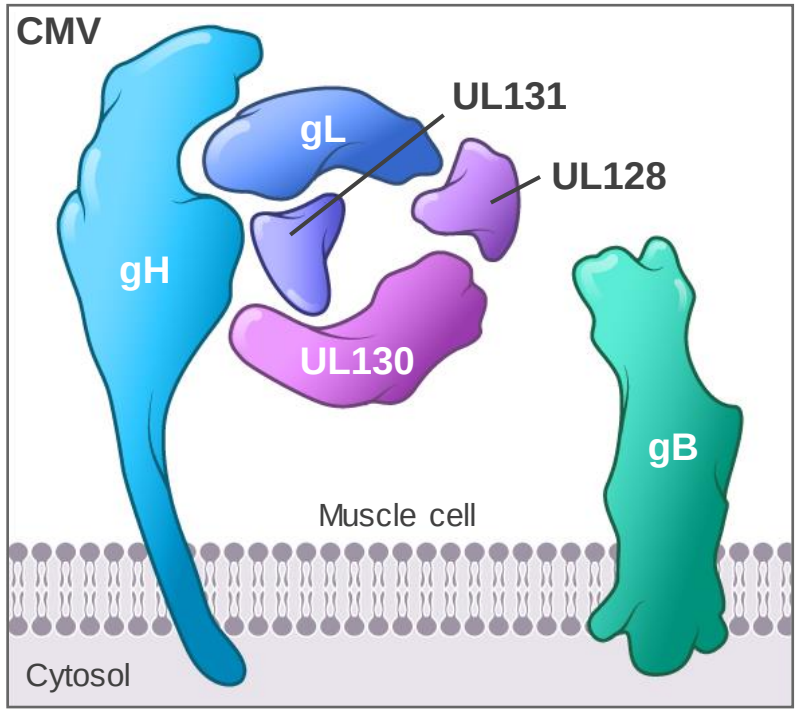
Case studies

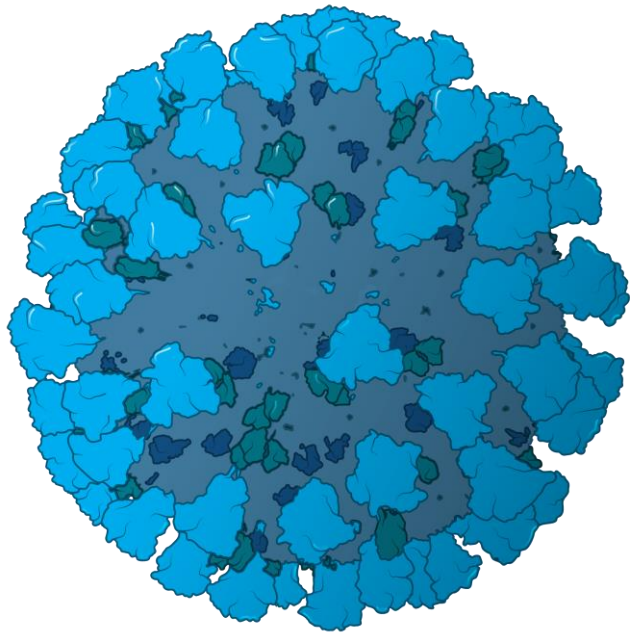
PCV: Needle-to-Needle



CMV



SARS-CoV-2 Antigen



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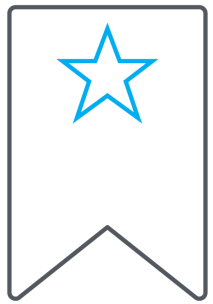
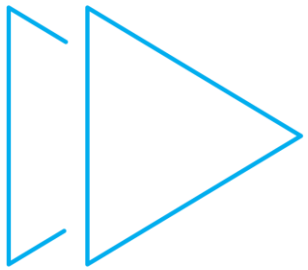
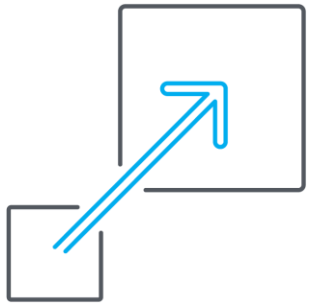
Paving the future…



Quality



Speed



Scale

Cost

…we can do this!

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Q&A

Manufacturing & Digital Day Agenda

Introduction	*Stéphane Bancel, CEO*	*1:00–1:20 PM*	*20 min*
Norwood Overview	*Juan Andres, Chief Technical Operations & Quality Officer*	*1:20–1:50 PM*	*30 min*
Q&A Session		*1:50–2:05 PM*	*15 min*
Competing in the Age of AI	*Karim R. Lakhani, Charles E. Wilson Professor of Business Administration* *Dorothy & Michael Hintze Fellow* *Harvard Business School, Laboratory for Innovation Science at Harvard*	*2:05–2:50 PM*	*45 min*
Moderna Digital Strategy	*Marcello Damiani, Chief Digital and Operational Excellence Officer*	*2:50-3:20 PM*	*30 min*
Advanced Analytics and AI @ Moderna	*Dave Johnson, PhD*	*3:20-3:50 PM*	*30 min*
Q&A Session		*3:50-4:05 PM*	*15 min*
Closing	*Stéphane Bancel, CEO*	*4:05-4:15 PM*	*10 min*

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Competing in the Age of AI

Marco Iansiti | miansiti@hbs.edu | @marcoiansiti
Karim R. Lakhani | k@hbs.edu | @klakhani

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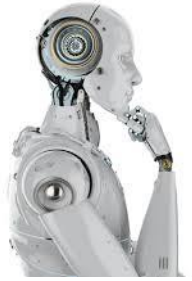
Definitions of AI



"Machines that can think and act in a way that matches or surpasses human intelligence" ("Strong AI")

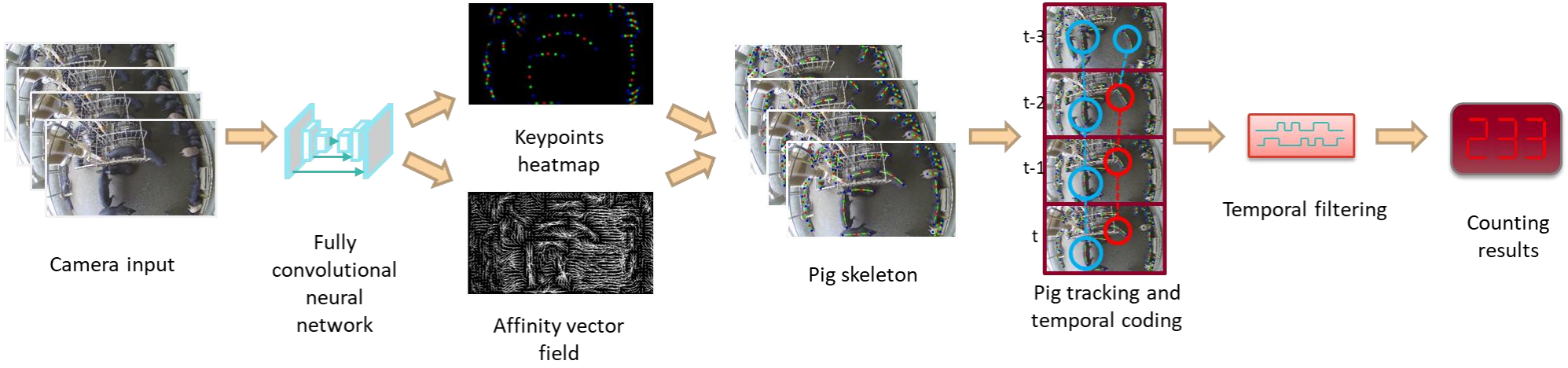
Any activity computers are able to perform that humans once performed" ("Weak AI")

Nils J. Nilsson, 2010; Stanford AI 100 report, 2016.

Example: Pig Counting

Difficulties in manual pig counting:

- ❑ Pigs have similar appearance and move around quickly
- ❑ Large overlapping areas between pigs due to high breeding density
- ❑ Potential disease infection from frequent interaction between pigs and humans



Example: Radiation therapy targeting

JAMA Oncology

Original Investigation

April 18, 2019

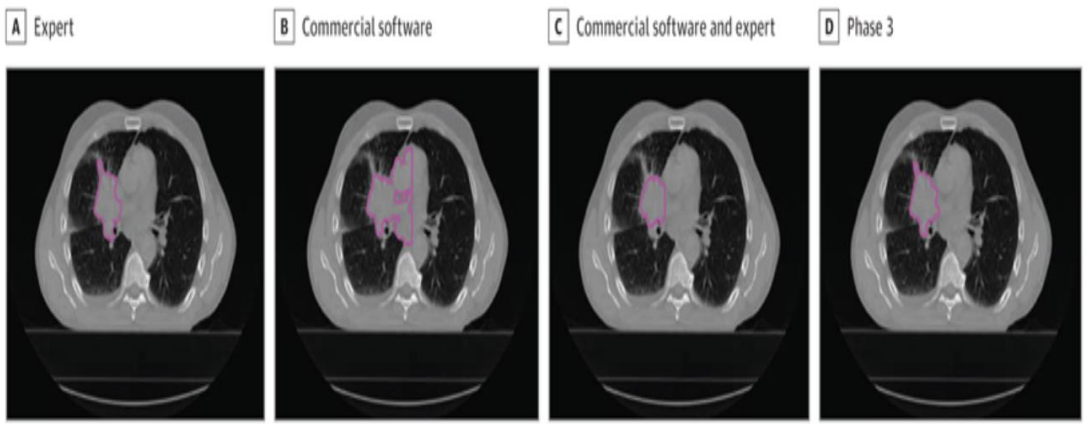
Use of Crowd Innovation to Develop an Artificial Intelligence–Based Solution for Radiation Therapy Targeting

Raymond H. Mak, MD[1]; Michael G. Endres, PhD[2,3]; Jin H. Paik, MA[2,4]; Rinat A. Sergeev, PhD[2,4]; Hugo Aerts, PhD[1,5]; Christopher L. Williams, PhD[1]; Karim R. Lakhani, PhD[2,4,6]; Eva C. Guinan, MD[1,2]

» Author Affiliations | Article Information

JAMA Oncol. 2019;5(5):654-661. doi:10.1001/jamaoncol.2019.0159

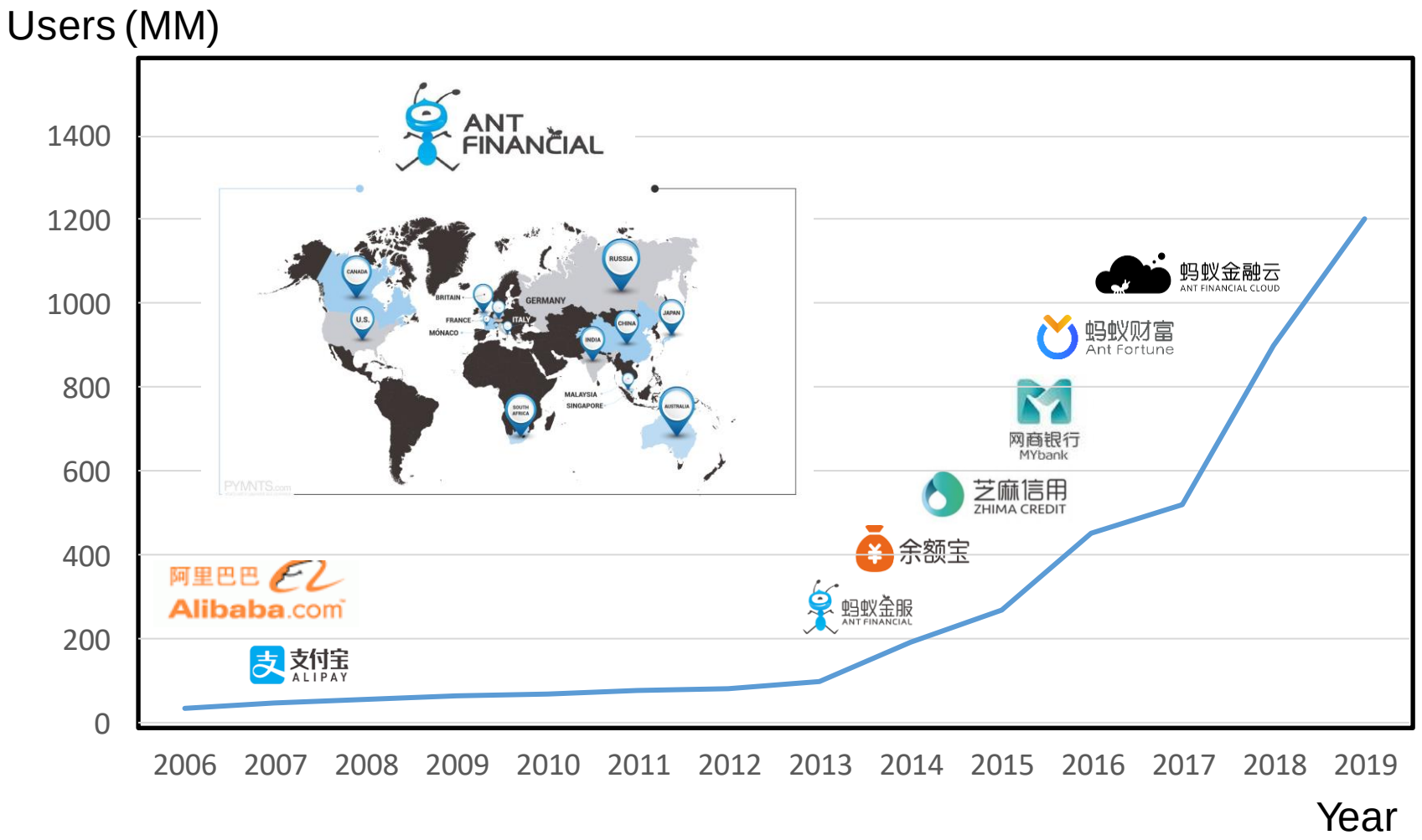
Machine Learning Website



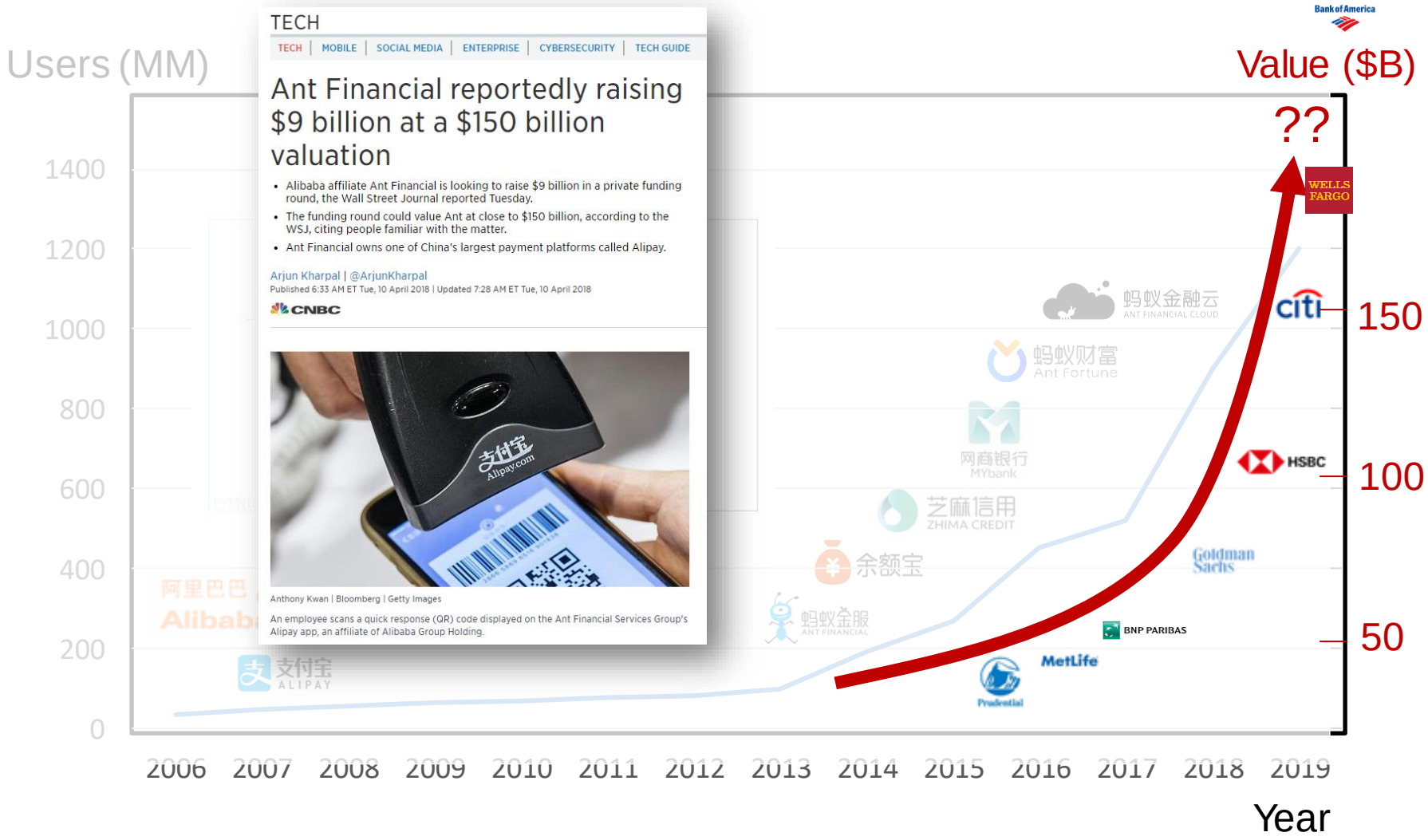
Lung Tumor Segmentations

Example of a human expert segmentation (A) compared with automated segmentation from commercially-available region growing–based segmentation technique before (B) and after (C) human adjustment of settings, and automated segmentations from the top artificial intelligence algorithm from phase 3 of the contest (D).

Broadly deployed "weak" AI is changing the nature of firms: The Ant Financial Story



Broadly deployed "weak" AI is changing the nature of firms: The Ant Financial Story



TECH

TECH | MOBILE | SOCIAL MEDIA | ENTERPRISE | CYBERSECURITY | TECH GUIDE

Ant Financial reportedly raising $9 billion at a $150 billion valuation

- Alibaba affiliate Ant Financial is looking to raise $9 billion in a private funding round, the Wall Street Journal reported Tuesday.
- The funding round could value Ant at close to $150 billion, according to the WSJ, citing people familiar with the matter.
- Ant Financial owns one of China's largest payment platforms called Alipay.

Arjun Kharpal | @ArjunKharpal

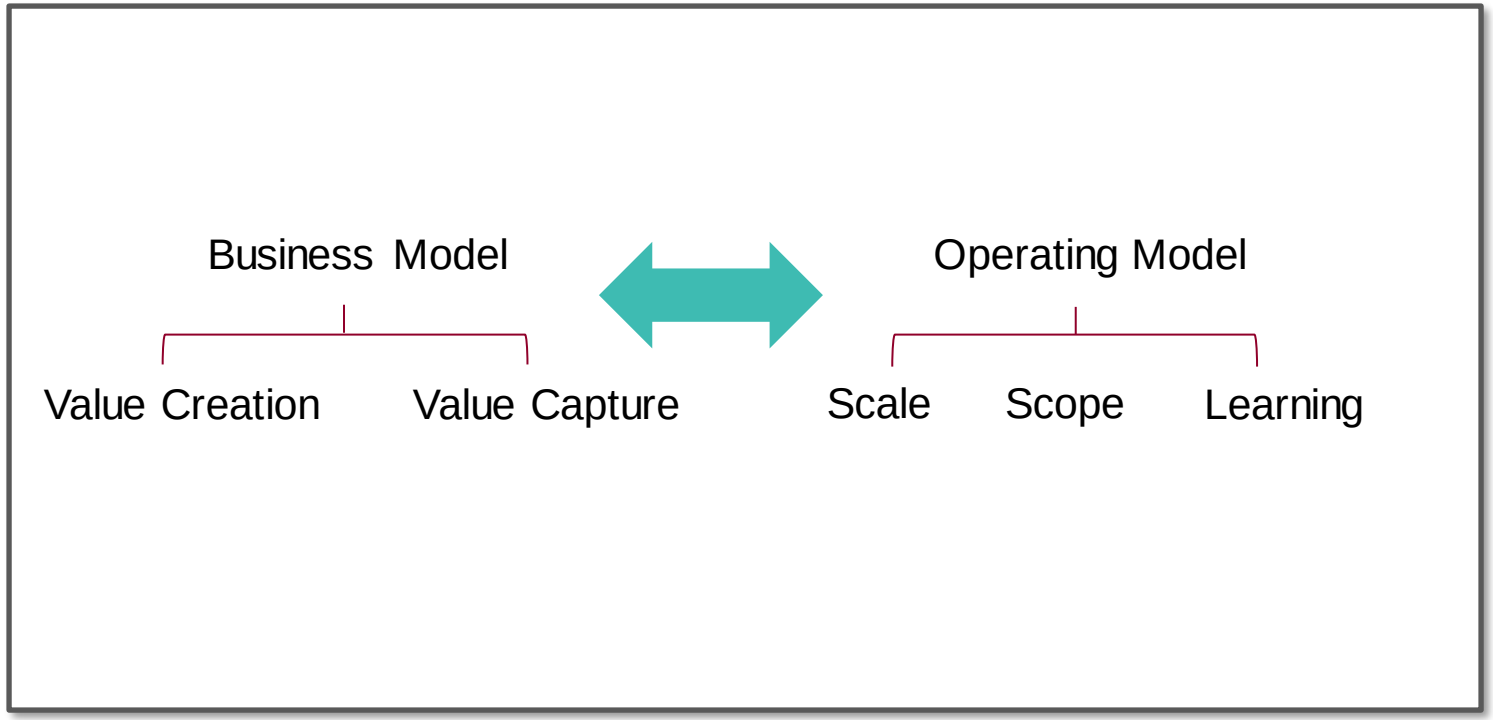
Published 6:33 AM ET Tue, 10 April 2018 | Updated 7:28 AM ET Tue, 10 April 2018

CNBC

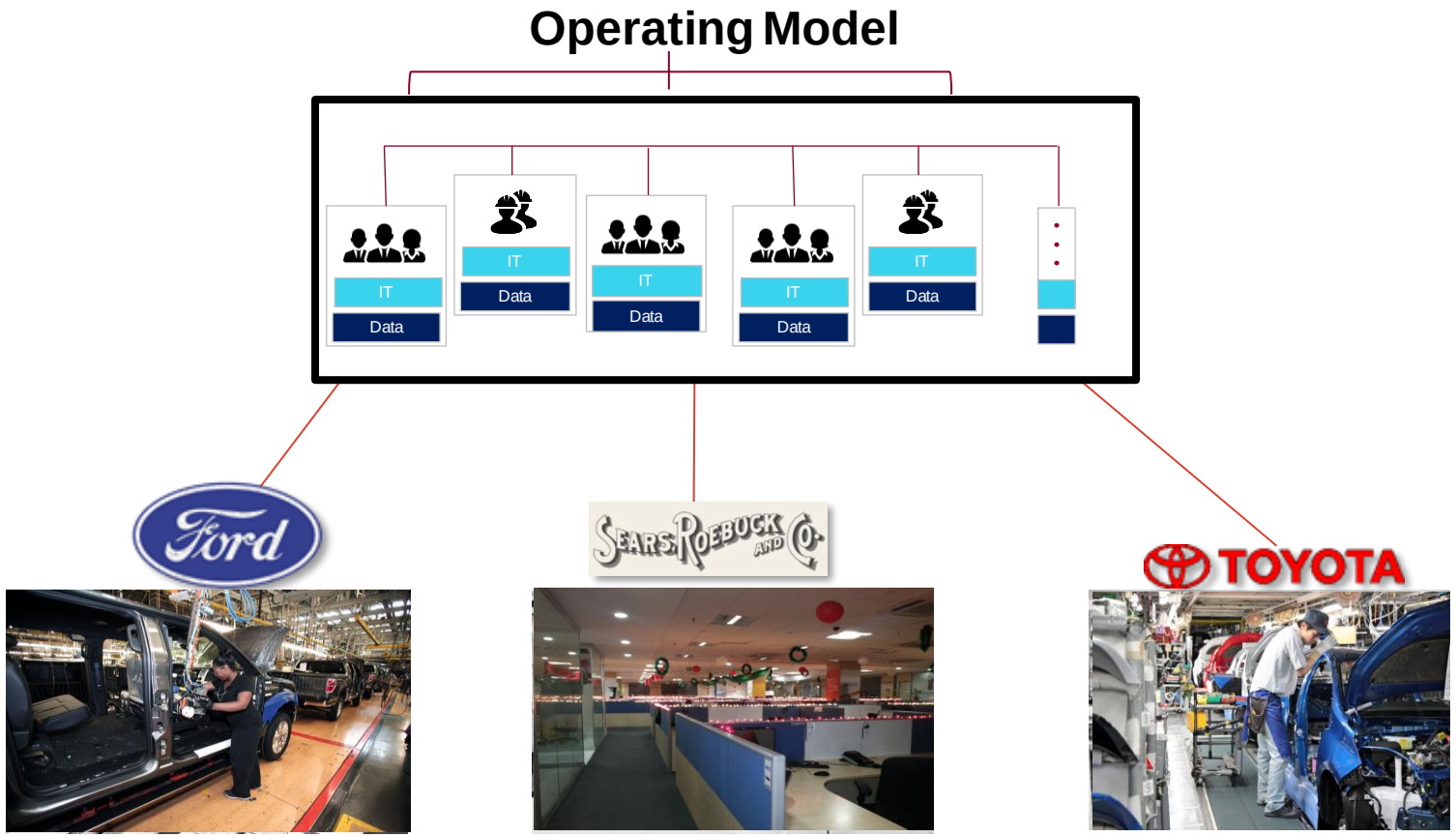
Anthony Kwan | Bloomberg | Getty Images

An employee scans a quick response (QR) code displayed on the Ant Financial Services Group's Alipay app, an affiliate of Alibaba Group Holding.

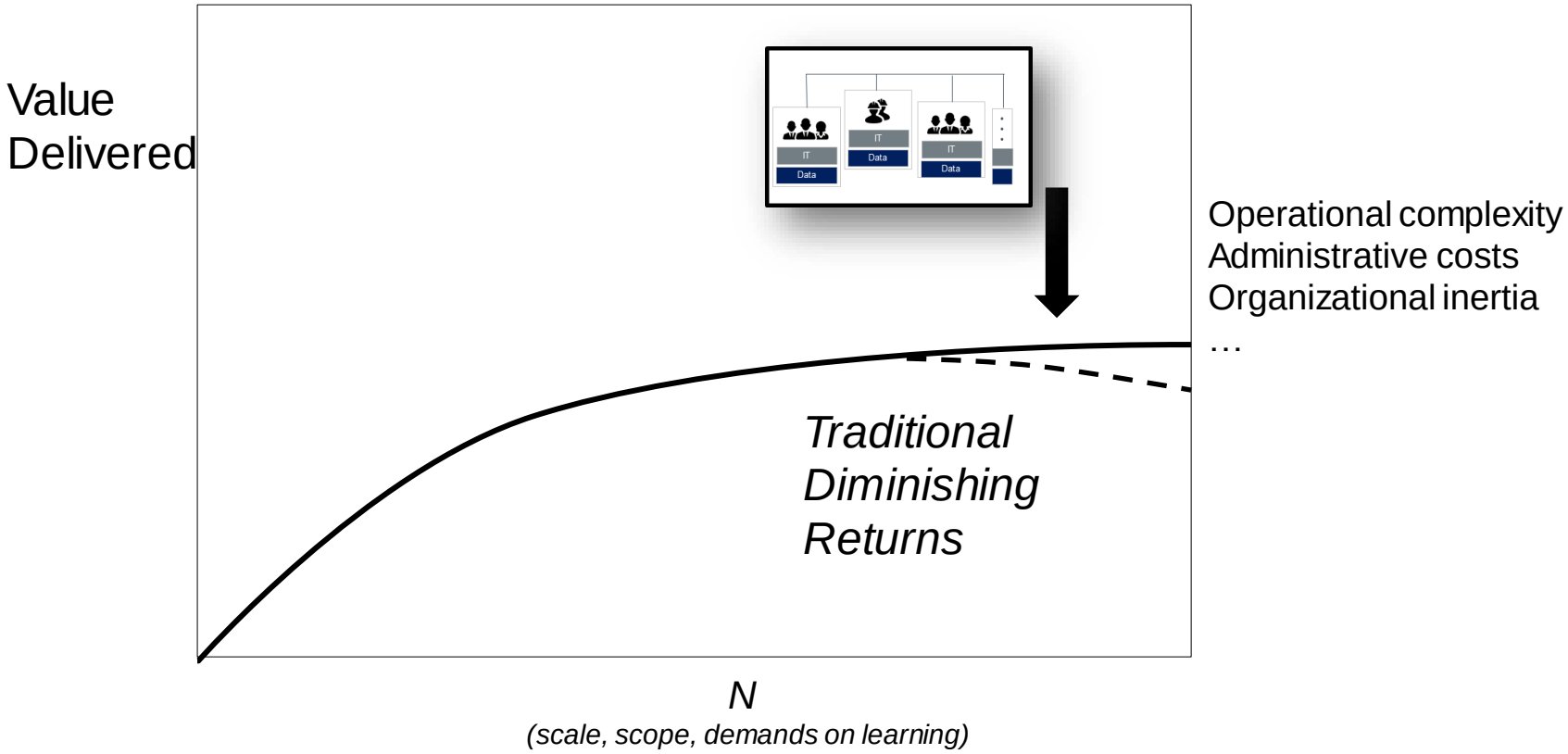
To understand companies like Ant Financial we need to reflect on how firms create, capture and deliver value



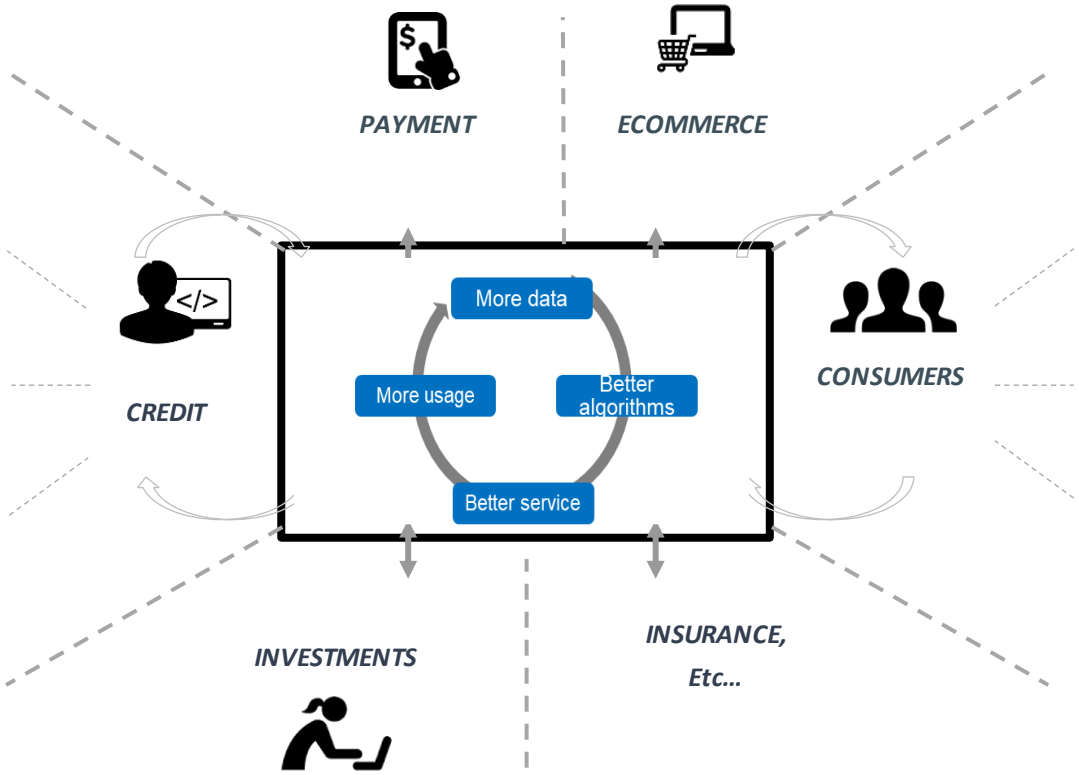
Traditional Operating Performance Drivers



Traditional operating models can constrain the value of the firm



Firms like Ant use AI to drive digital scale, scope, and learning

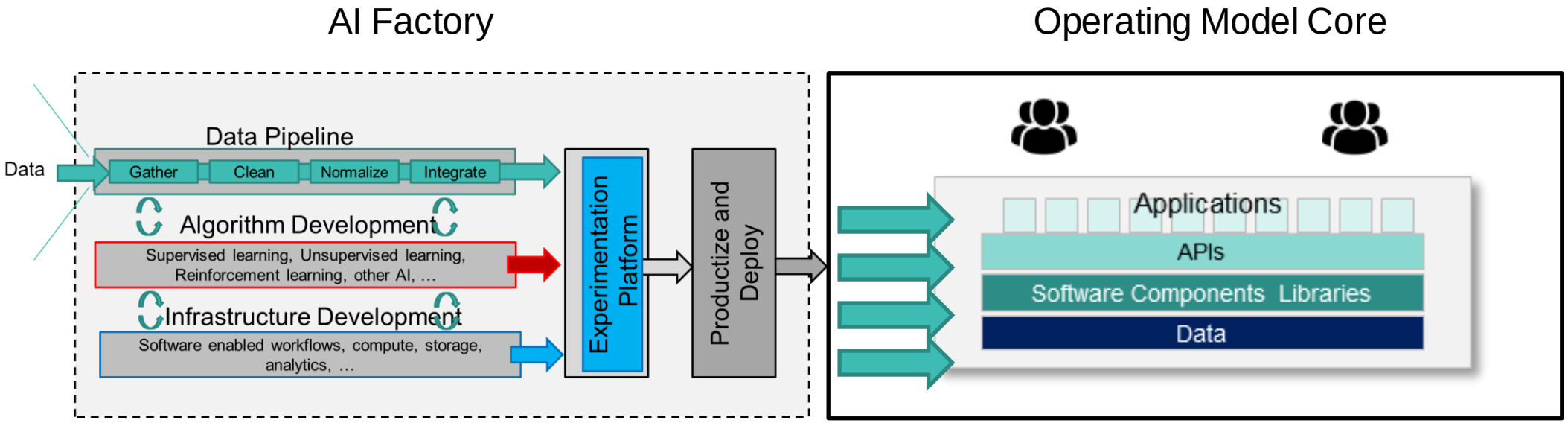


At Ant traditional human centered processes are digitized to connect with market opportunities at near zero marginal cost. Operational bottlenecks are digitized.

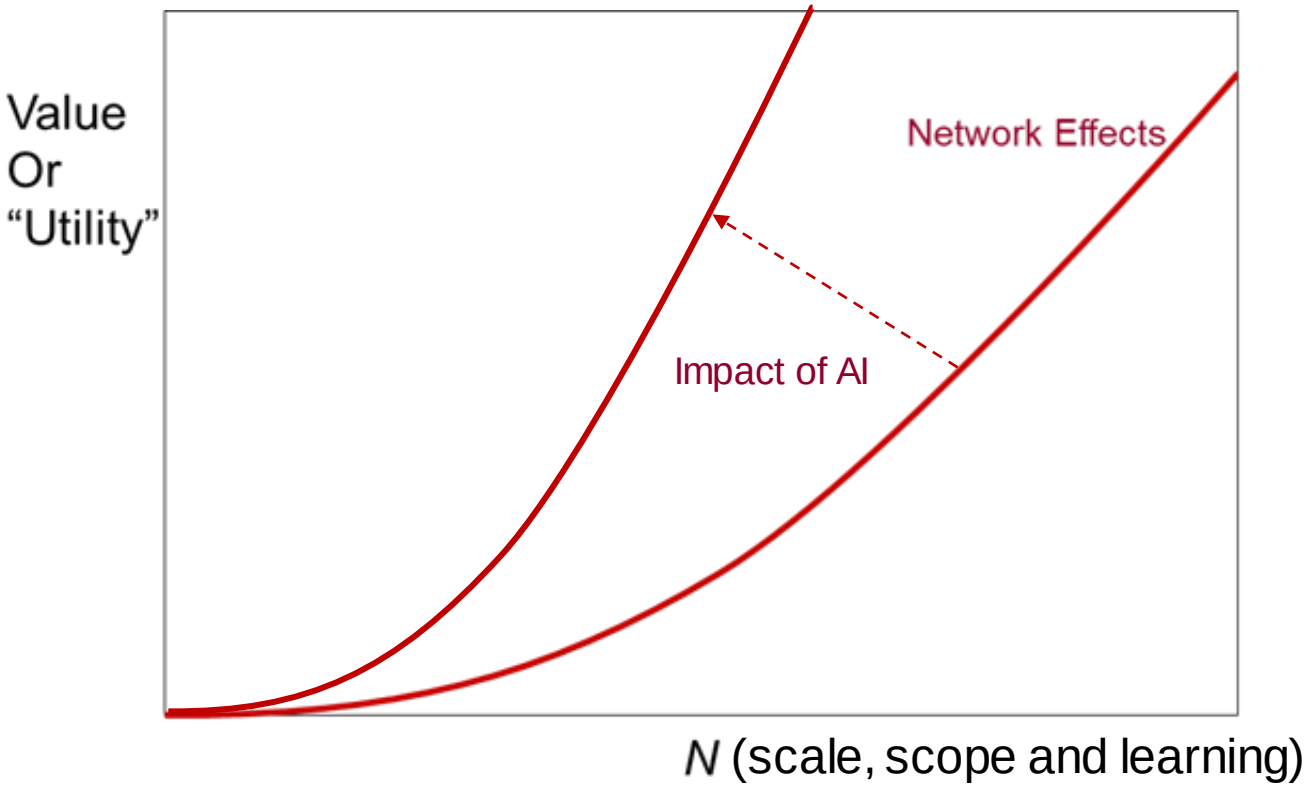
"AI is the new runtime that is going to shape all that we do"

- Satya Nadella

Ant's operating model is enabled by an "AI Factory"

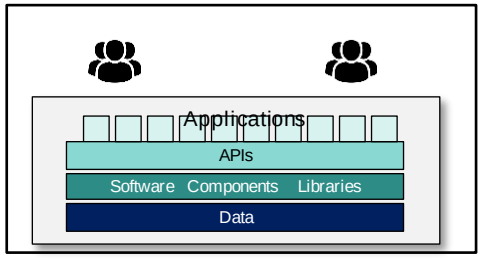


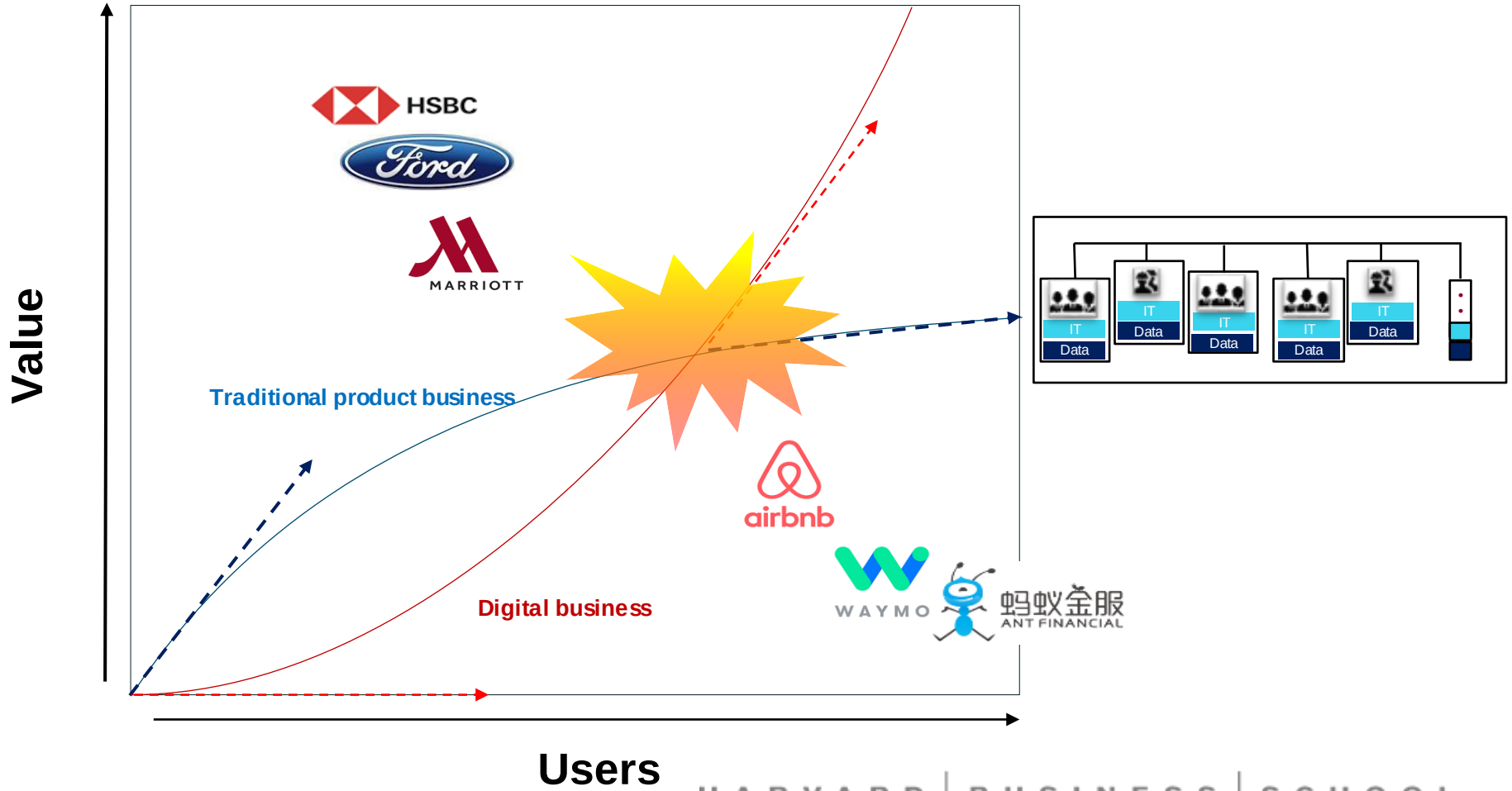
Learning effects and network effects can combine to drive value



From Disruption to "Collision"…

What happens when a firm that has competed in a traditional market starts to compete with a firm based on a digital operating model?

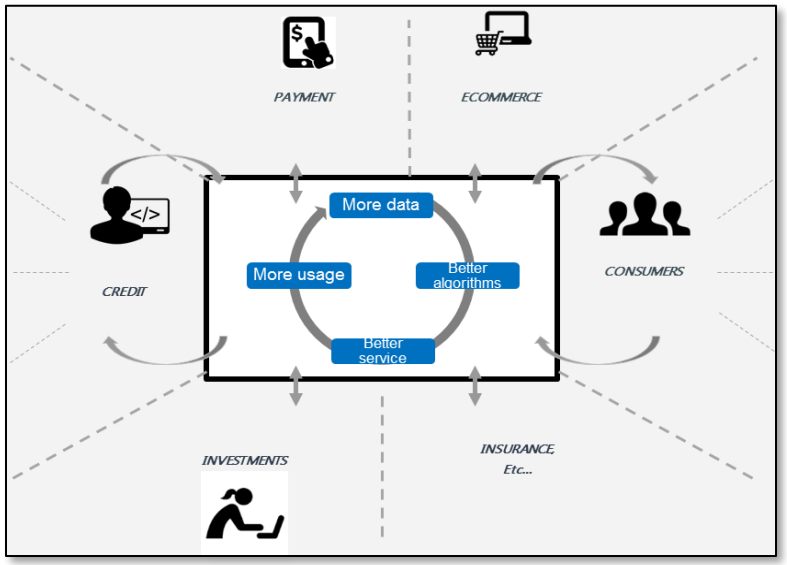


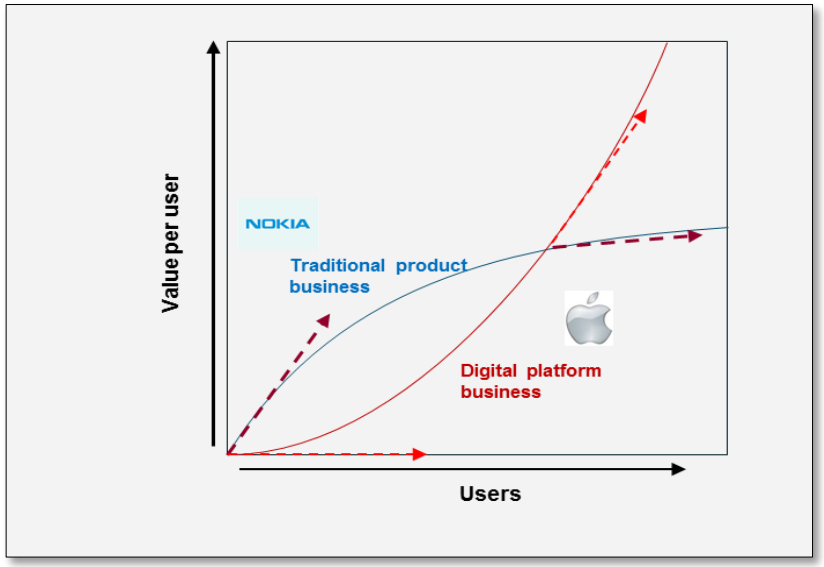


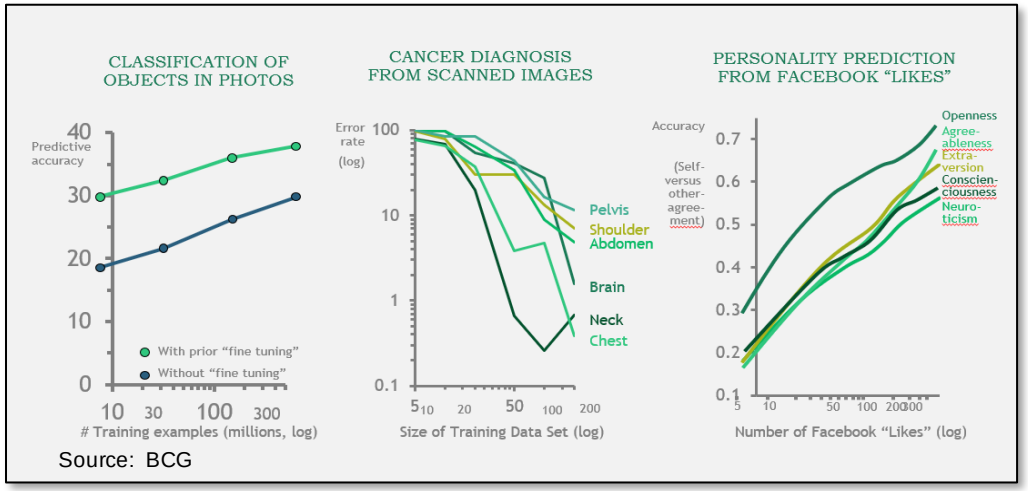
The New Meta

Universality

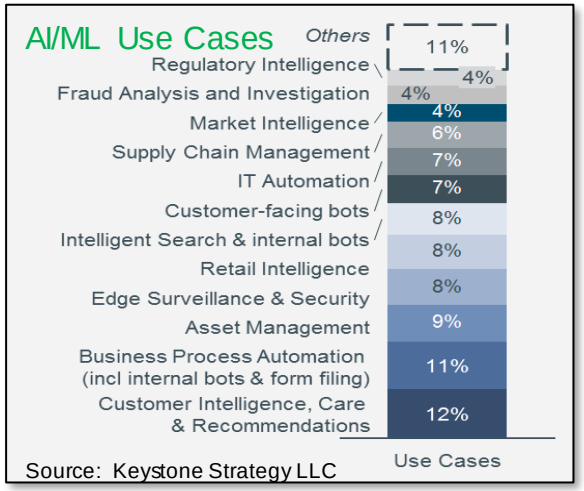
From media to financial services, our economy is increasingly dominated by digital market dynamics and digital capabilities







Source: BCG



Source: Keystone Strategy LLC

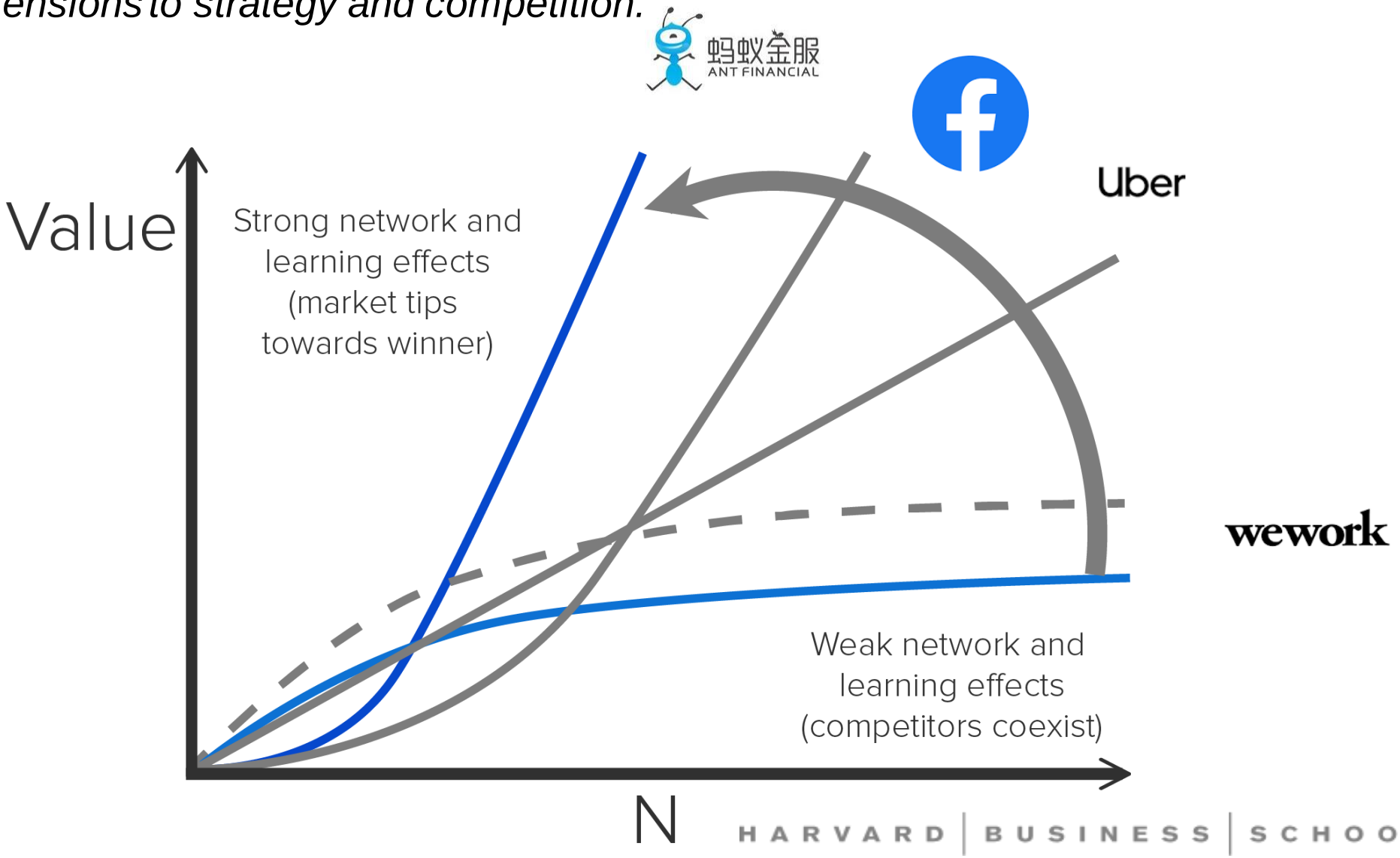
New Opportunities

AI can improve a virtually infinite variety of compelling use cases, cutting across every segment of our economy

By moving human labor and management off the critical path, AI can transform the enterprise by dramatically increasing operational scale, scope, and learning

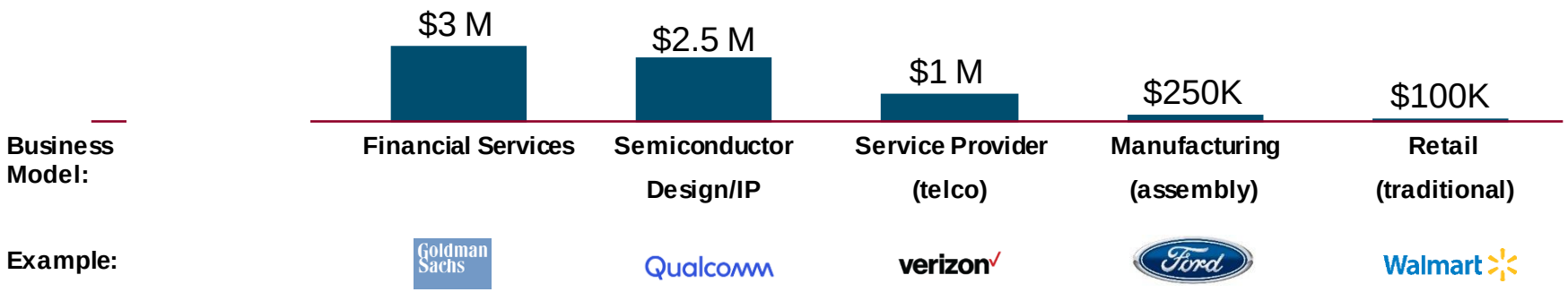
New Strategies….

Not all "digital" firms are the same!!! Digital networks and AI are adding new (frequently subtle) dimensions to strategy and competition.



…driving the emergence of a new kind of firm.

Market capitalization per employee



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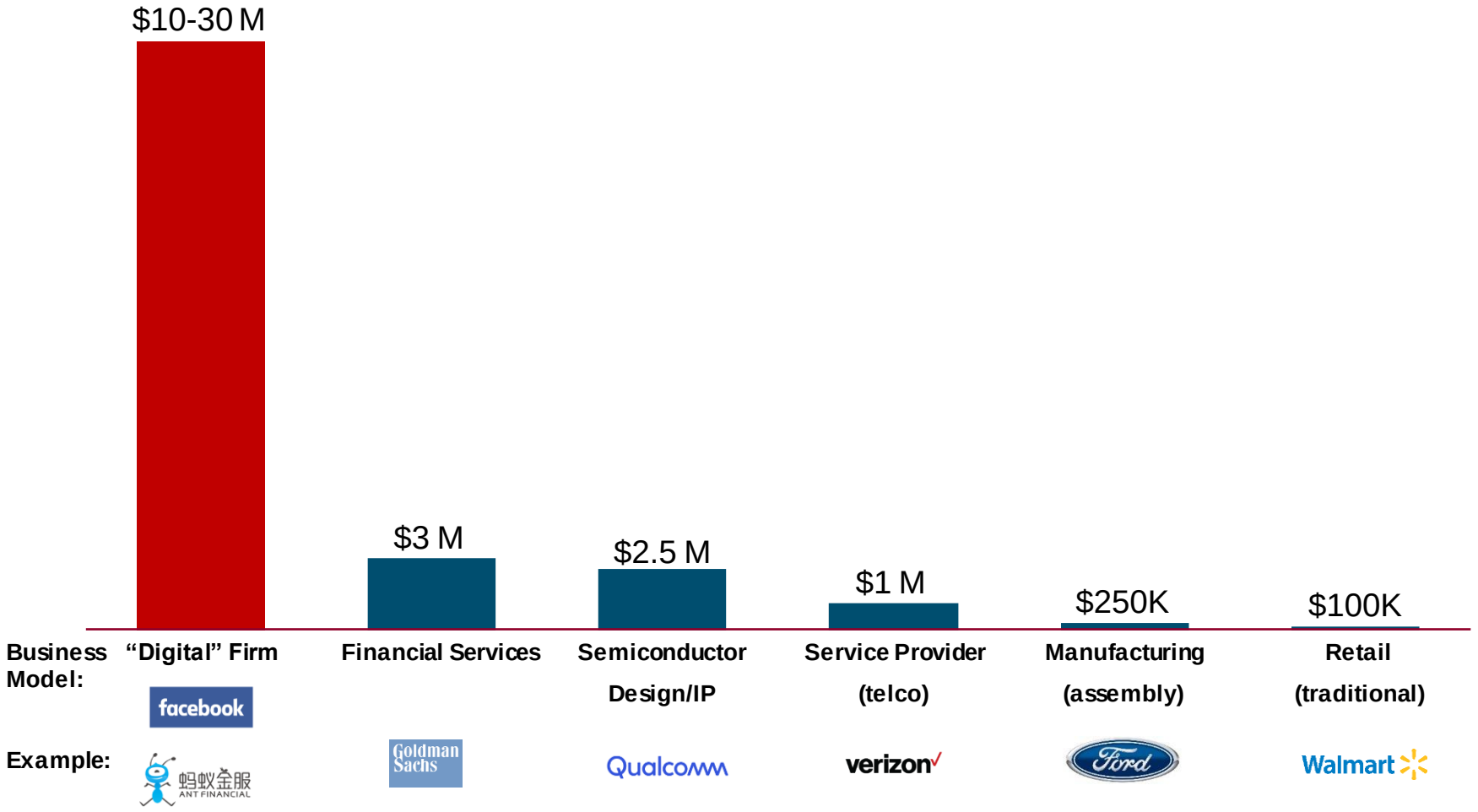

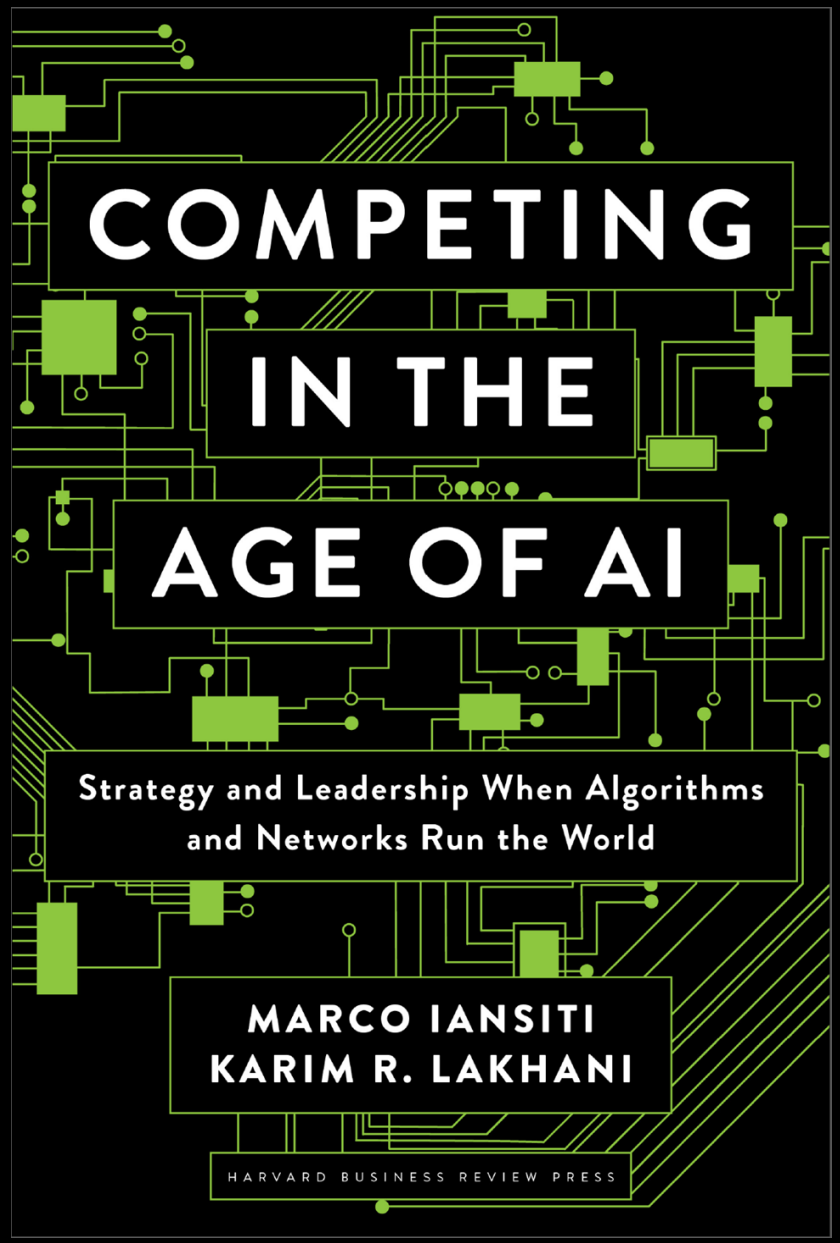
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Strategy and Leadership When Algorithms and Networks Run the World
MARCO IANSITI
KARIM R. LAKHANI
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Competing in the Age of AI

Marco Iansiti | miansiti@hbs.edu | @marcoiansiti
Karim R. Lakhani | k@hbs.edu | @klakhani

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Moderna's Digital Strategy

Marcello Damiani

March 4, 2020

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Marcello Damiani, Chief Digital and Operational Excellence Officer

As Chief Digital and Operational Excellence Officer, Marcello Damiani brings a wealth of experience from both Tech companies and Life Science companies and a true passion for making Digital a reality. He has 20 years experience working in the IT field, with the last 10 years being spent in leadership roles for multinational companies in Europe and in the U.S.

Prior to joining Moderna, Mr. Damiani was instrumental in conceiving and building creative IT solutions to help solve business challenges, first at Motorola and then at bioMérieux.

Data: The most valuable resource

Source: The world's most valuable resource is no longer oil, but data
www.economist.com/leaders/2017/05/06/the-worlds-most-valuable-resource-is-no-longer-oil-but-data

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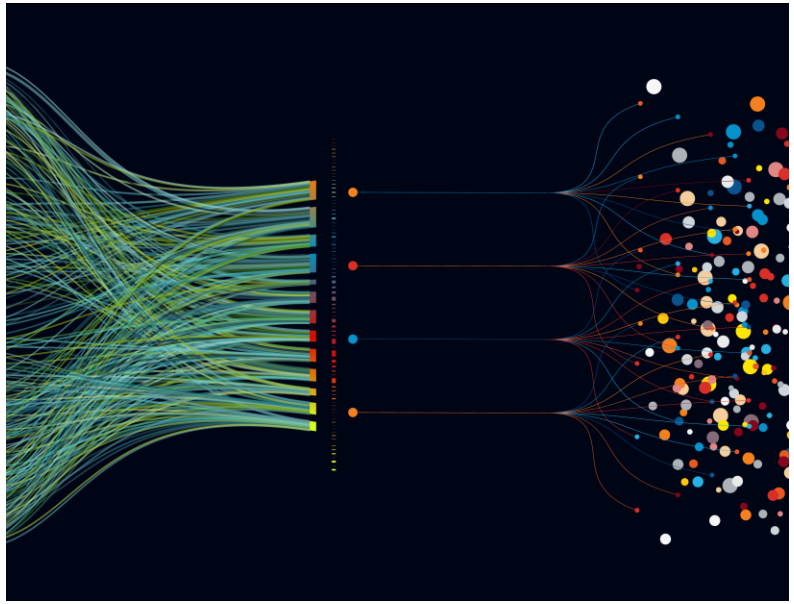
Digital a key enabler for advanced analytics & AI

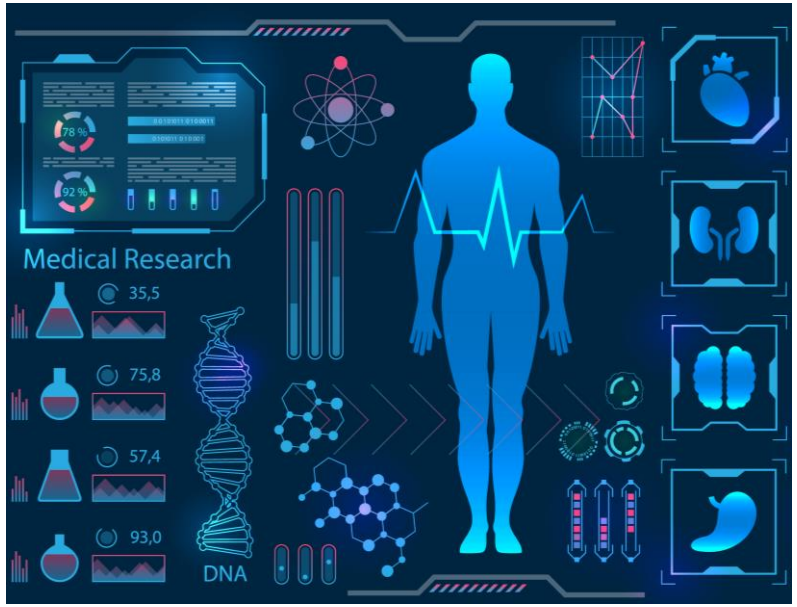


AI/Machine learning

Requires large, structured, well-annotated datasets

Unified data sources

Diverse internal and external data sources linked and made accessible



Digital transformation

Create a data-centric organization to build foundation for AI

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Moderna 10-year vision

We are a leading mRNA platform and continue to invest like it's the beginning of the journey

We and our partners are discovering and developing an unprecedented breadth of meaningful investigational vaccines and therapeutics

We integrate automation and digital technology into everything we do

We are one team achieving the extraordinary – by being agile, highly networked and deeply committed to our Mission

We believe corporate citizenship means we do the right thing in the right way

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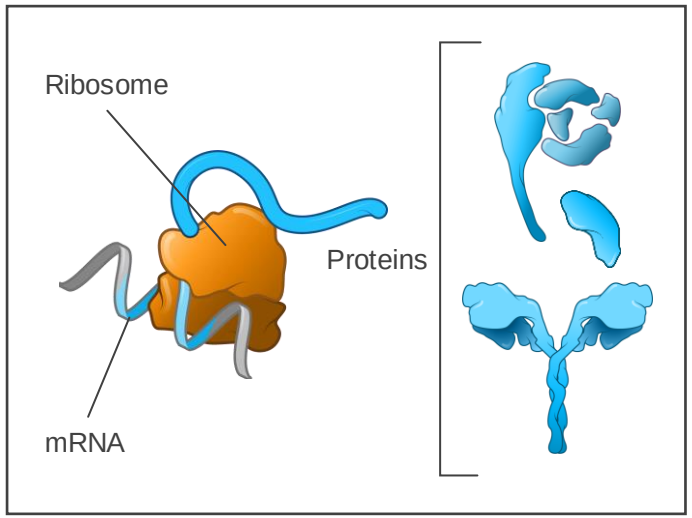
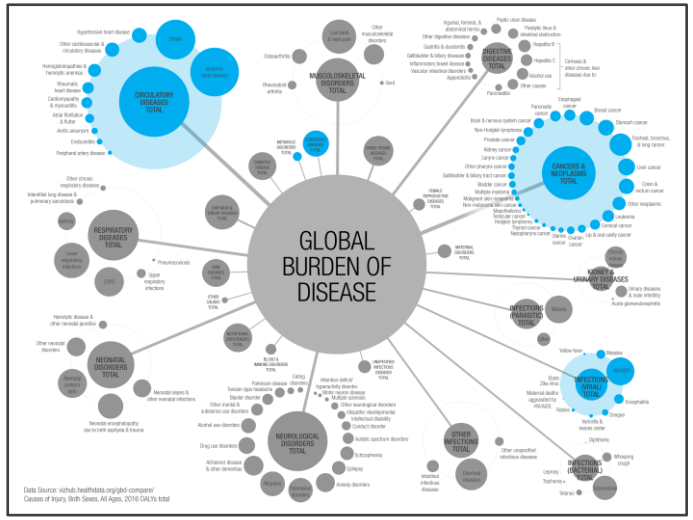
Why build a digital biotech?



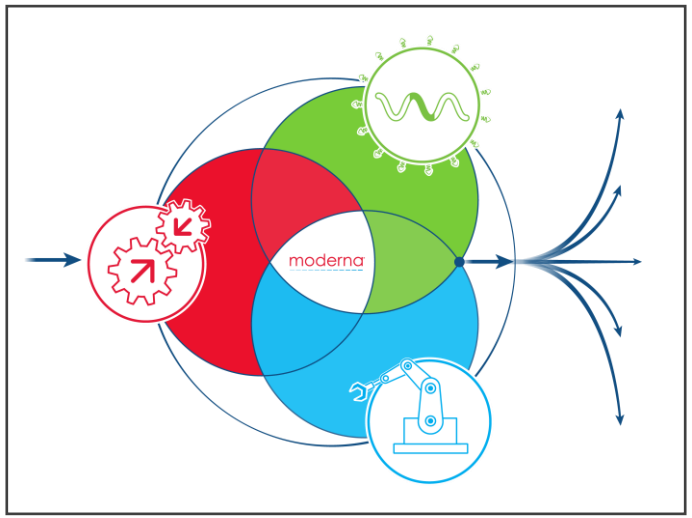
mRNA technology

- Instruct cells to produce protein
- Instructions are code
- The very essence of our medicines is digital in nature



Platform approach

- **Modalities: combine**
  - Chemistry
  - Bioinformatics
  - mRNA engineering
  - Process
  - Formulation
- Repeatable learning
- Multiple modalities



Business strategy

- Massively parallel R&D
- Ecosystem model
- Progress concurrent programs

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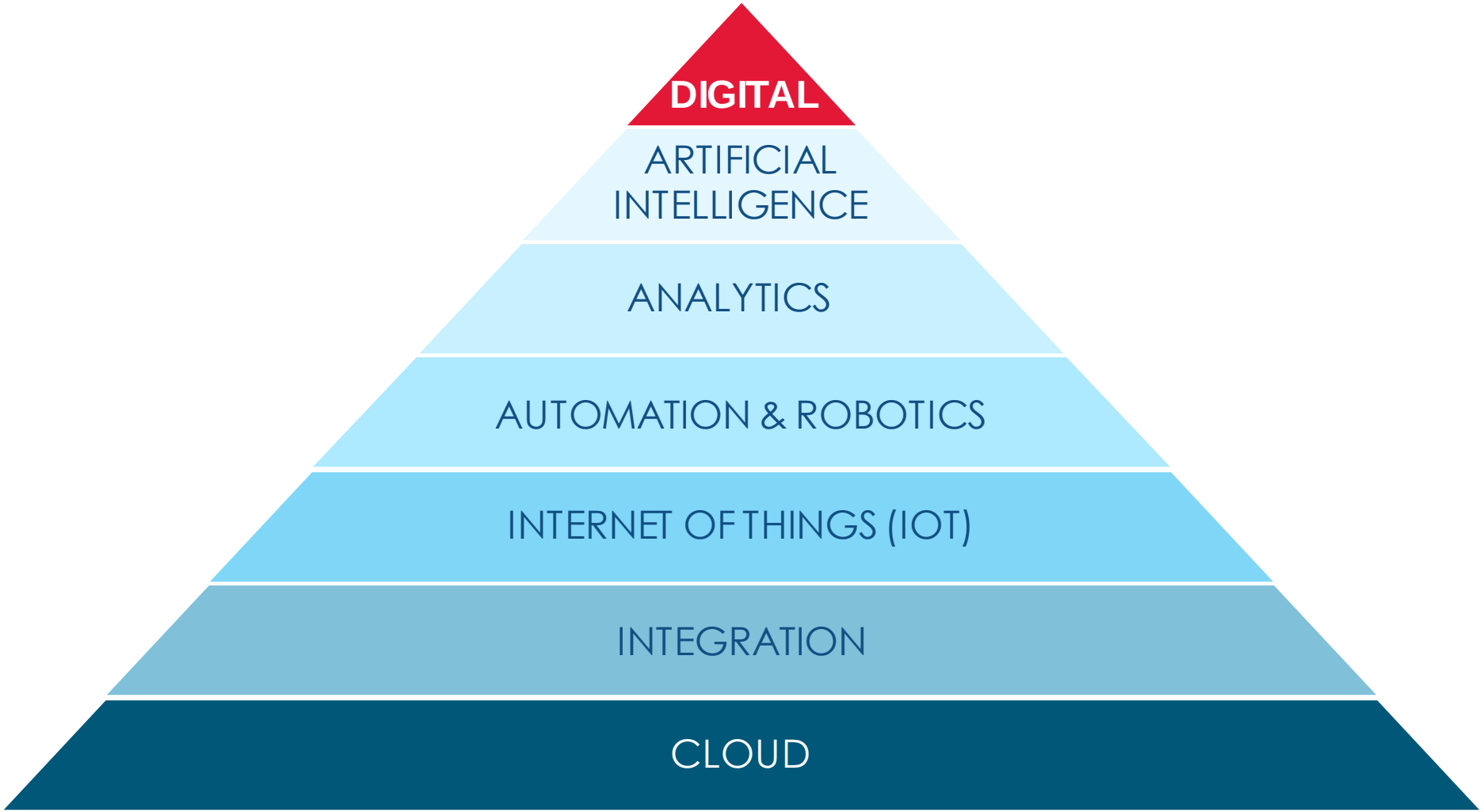
Moderna's digitization building blocks



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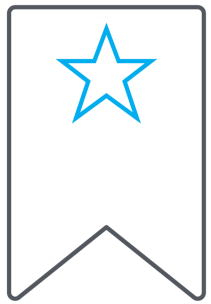
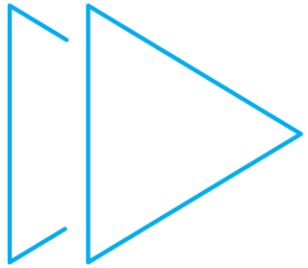
Building a *digital* biotech



Quality

Reduce errors

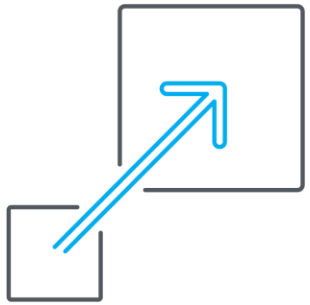
Increased probability of success



Speed

Accelerate learning

Increased agility to change



Scale

Support Increasing demand

Sustain and repeat processes

Cost

Reduce waste

Improve performance

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The digital ecosystem @ Moderna

People

Digital culture

User experience

User adoption

Processes

Value stream design

Lean/6σ principles

Compliance

Technology

Flexible

Future proof

Innovative

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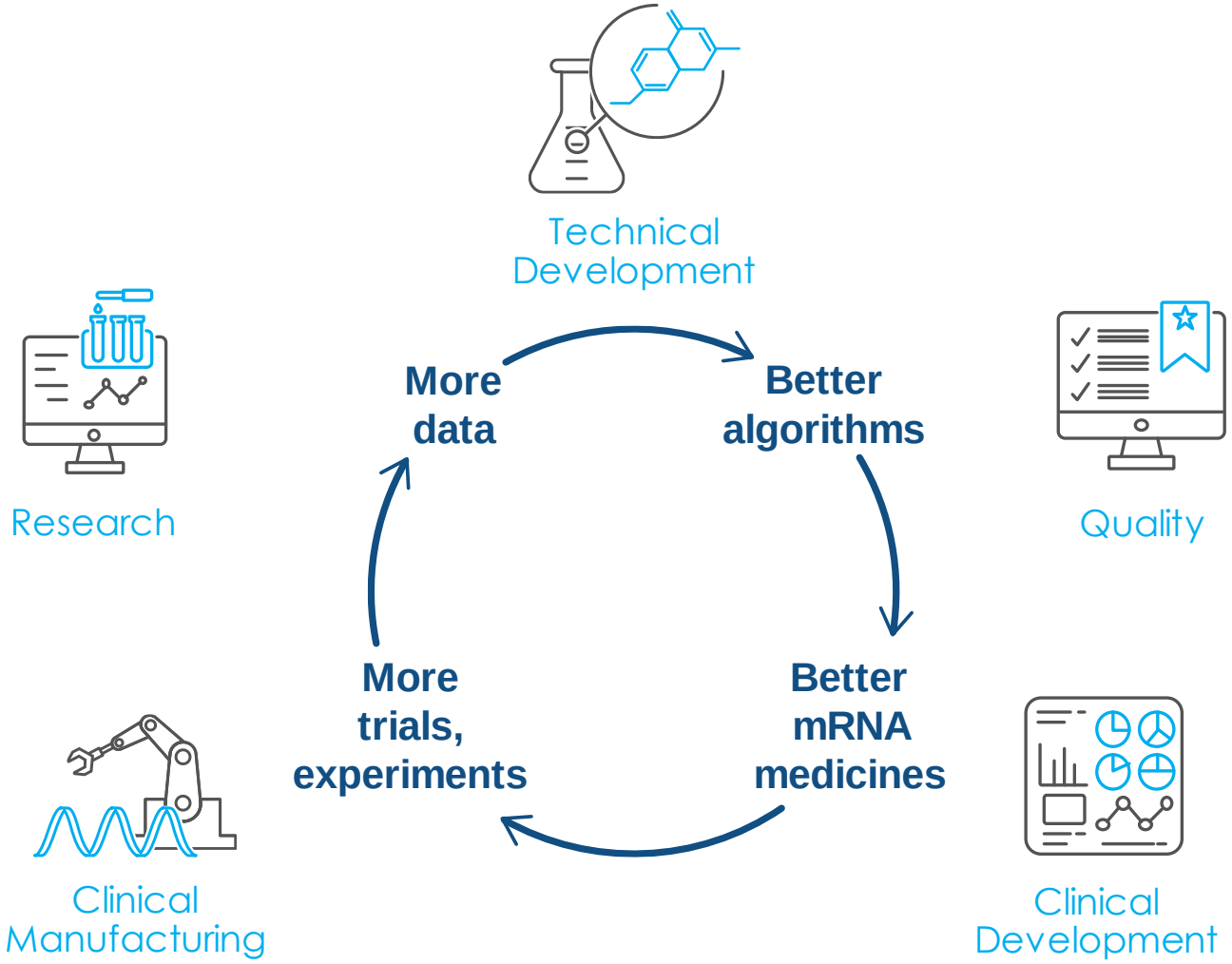
Digital integration @ Moderna



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Digital integration @ Moderna

Research

Advancing ideas to development candidates

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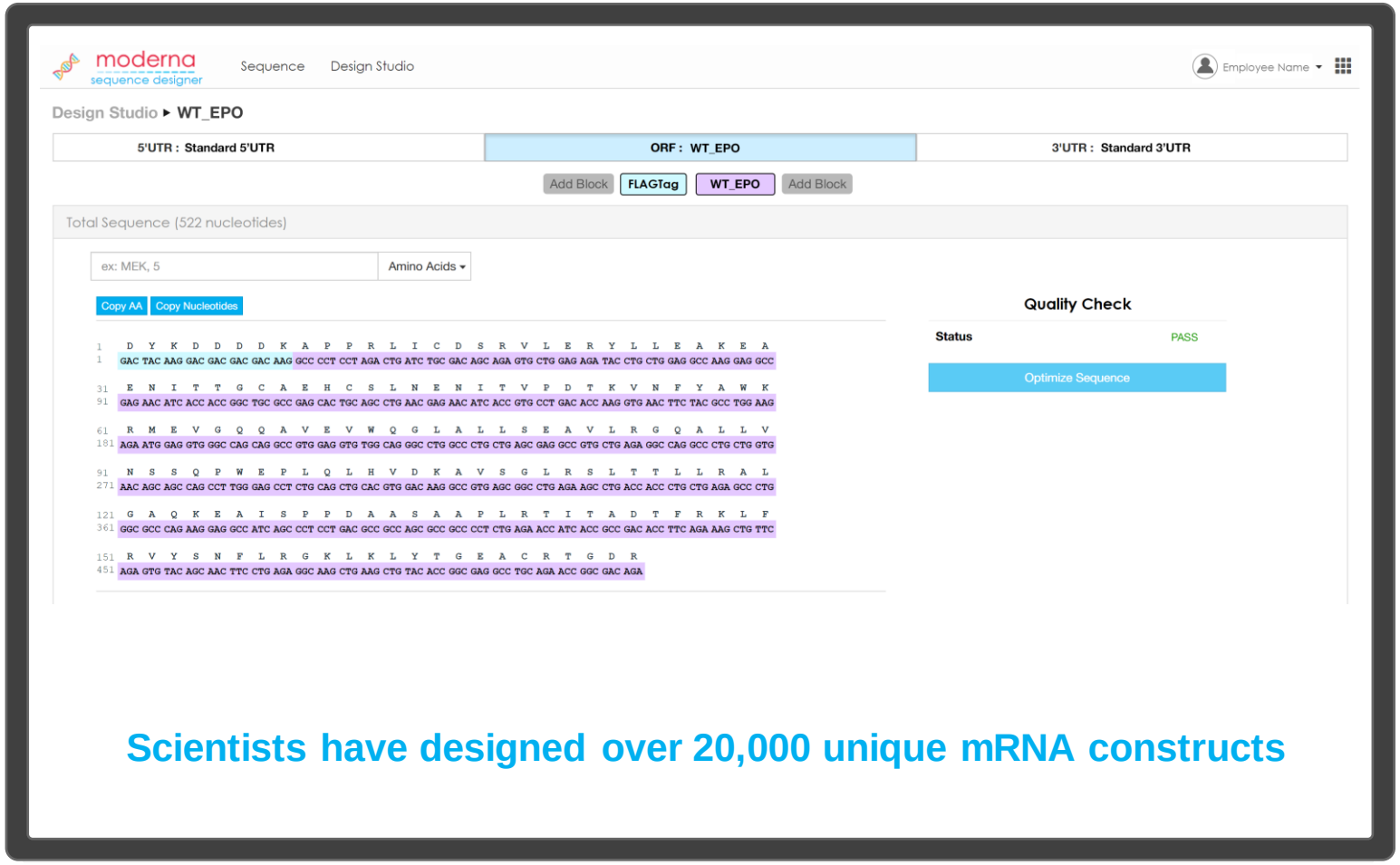
Research digitization

Design mRNA

- Intuitive design tools for building mRNA sequences
- Workflow tools for codon and nucleotide options
- AI-algorithms for back translation and sequence optimization to design the best mRNA



Scientists have designed over 20,000 unique mRNA constructs

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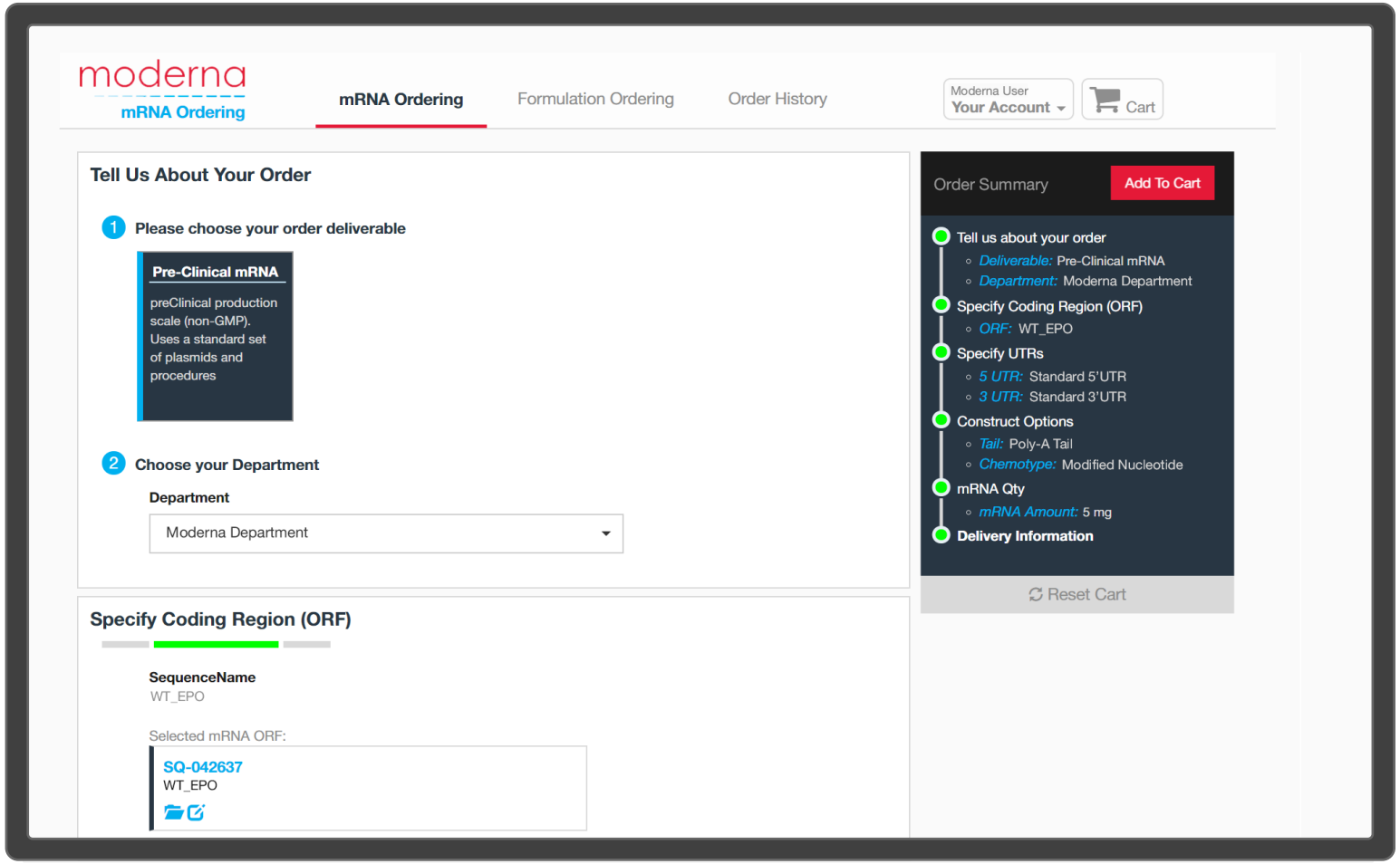
Research digitization

Order mRNA

- Intuitive, streamlined interface for rapid and accurate ordering
- Runs several automated quality checks and AI optimization algorithms
- Automated email notifications and shipment integrations to support coordination of studies
- Integrated with SAP for cost tracking and allocation



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Research digitization

Production and QC of Preclinical mRNA

- Integrated with over 30 robotics platforms
- Integrated with vendors for automated raw material purchases
- Massively parallel production for high throughput

Lot ID	Length	Targeted (mg)	Stage 1 Yield		Stage 2 Yield		Stage 3 Yield		Final Yield		QC'ed Yield (mg)	Requested (mg)	Yield Fraction
1726174.1	1505	20	28.9mg (+8.9mg / +44%) SS DA2885	69%	26.0mg (-2.9mg / -10%) SS DA2885	78%	10.9mg (-15.1mg / -58%) RP	84%	6.4mg (-4.5mg / -42%) C&S	100%	6.93	4	1.7x
1725794.1	2072	25	23.4mg (-1.6mg / -7%) MS LS2804	79%	14.9mg (-8.5mg / -36%) MS	75%	8.5mg (-6.4mg / -43%) RP	65%	4.4mg (-4.1mg / -48%) C&S	85%	5.23	4	1.3x
1725791.1	1890	50	32.4mg (-17.6mg / -35%) MS LS2834	60%	22.6mg (-9.8mg / -30%) MS	55%	9.1mg (-13.5mg / -60%) RP	27%	8.9mg (-0.2mg / -3%) C&S	45%	9.43	10	0.9x
1725567.3	913	25	50.6mg (+25.6mg / +102%) MS LS2896	97%	40.4mg (-10.2mg / -20%) MS	99%	30.7mg (-9.7mg / -24%) RP	100%	18.2mg (-12.5mg / -41%) C&S	100%	20.9	5	4.2x
1725423.1	1120	250	345.8mg (+95.8mg / +38%) MS LS2728	90%	185.2mg (-160.7mg / -47%) MS	80%	88.0mg (-97.1mg / -53%) RP	60%	54.4mg (-33.7mg / -38%) C&S	84%	55.39	50	1.1x
1724969.1	1814	10	7.0mg (-3.0mg / -30%) SS DA2737	31%	6.9mg (0.0mg / -1%) SS DA2737	31%	2.9mg (-4.0mg / -58%) UPLC	6%	1.6mg (-1.3mg / -45%) C&S	24%	1.86	2	0.9x
1724858.1	613	25	23.0mg (-2.0mg / -8%)	83%	21.2mg (-1.8mg / -8%)	87%	14.2mg (-7.0mg / -33%)	88%	9.2mg (-5.0mg / -35%)	100%	9.4	5	1.9x

Scaled capacity from 40/month to up to 1000/month

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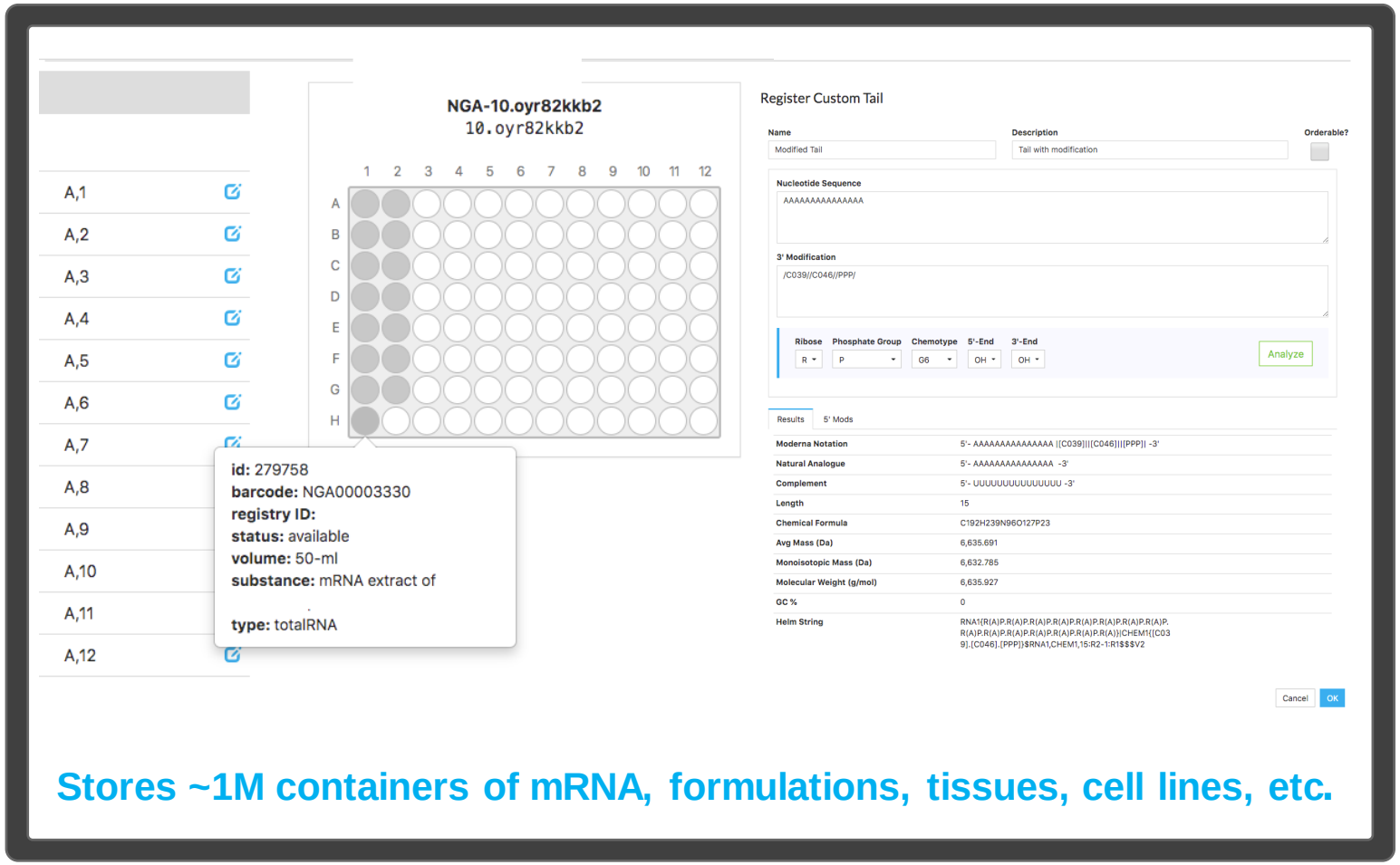
Research digitization

Inventory and Registry of mRNA

- Full chain-of-custody and audit trails for materials to ensure quality of data using samples
- Registration of every unique entity from its first conception
- Downstream applications point to unique registry IDs to tie together all data and processes



Stores ~1M containers of mRNA, formulations, tissues, cell lines, etc.

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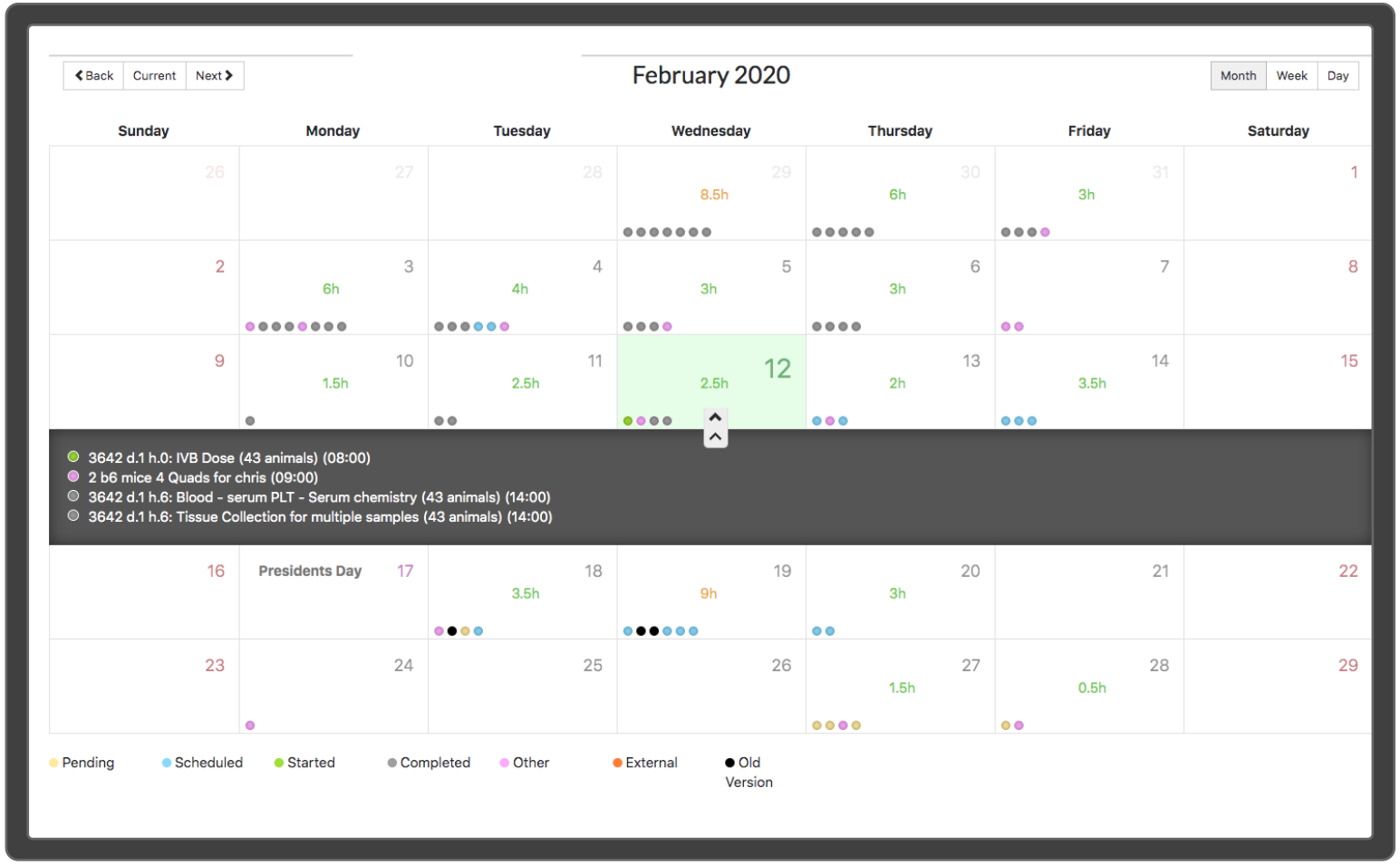
Research digitization

Study Design and Management

- Complex study design tools for capturing detailed metadata of all studies needed for better analysis
- Integration with mRNA ordering tools for tracking and planning to ensure studies start on time
- Sample collections integrated with shipping tools to ensure timely and accurate delivery
- Planning tools for optimal study scheduling



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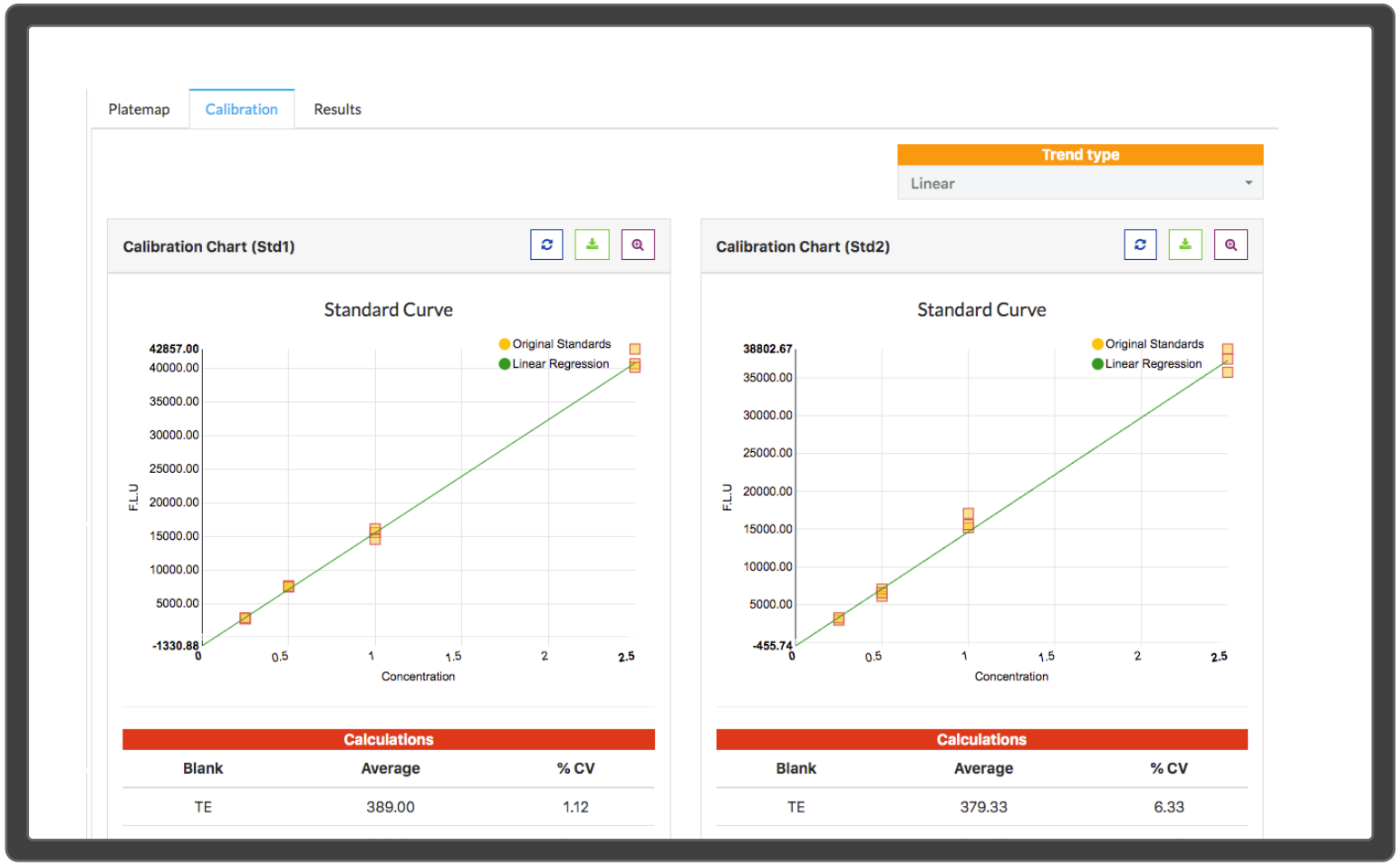
Research digitization

Automated Data Analysis

- Over 2 dozen automated data analysis and visualization tools
- Automates tedious and error-prone calculations
- Standardizes analyses so data is comparable and composable



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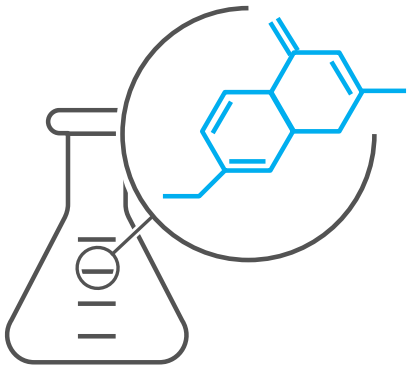
Digital integration @ Moderna



Technical Development

Transforming development candidates into medicines

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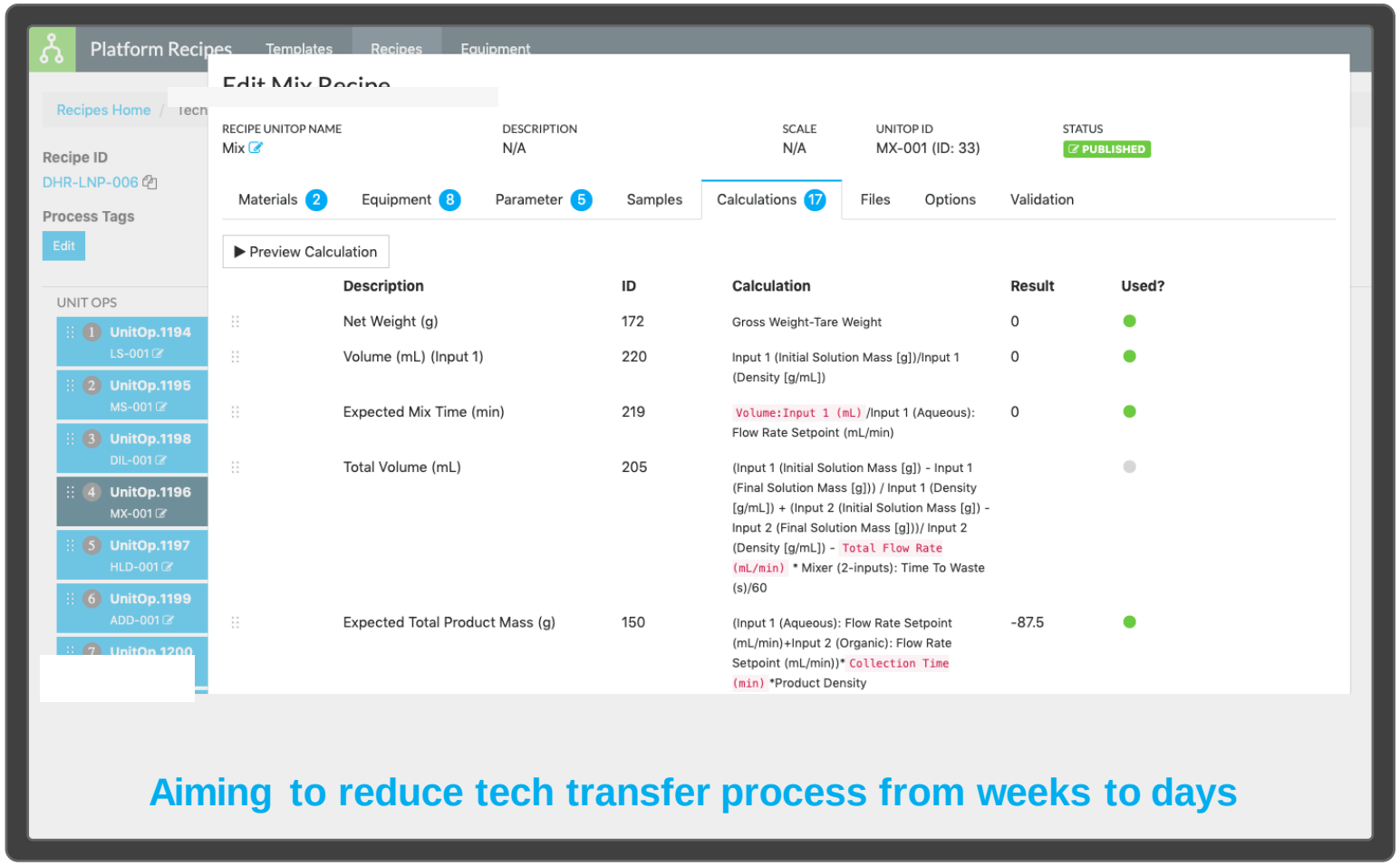
Tech dev digitization

Recipe Editor / Process Templating

- New product recipes can be built and deployed in just a few hours
- Support Moderna's core platform process development efforts, panning Cell Stocks, DNA, mRNA, and Formulations
- Auto-generate Tech Transfer Documents, as well as Electronic Batch Record design specs



Aiming to reduce tech transfer process from weeks to days

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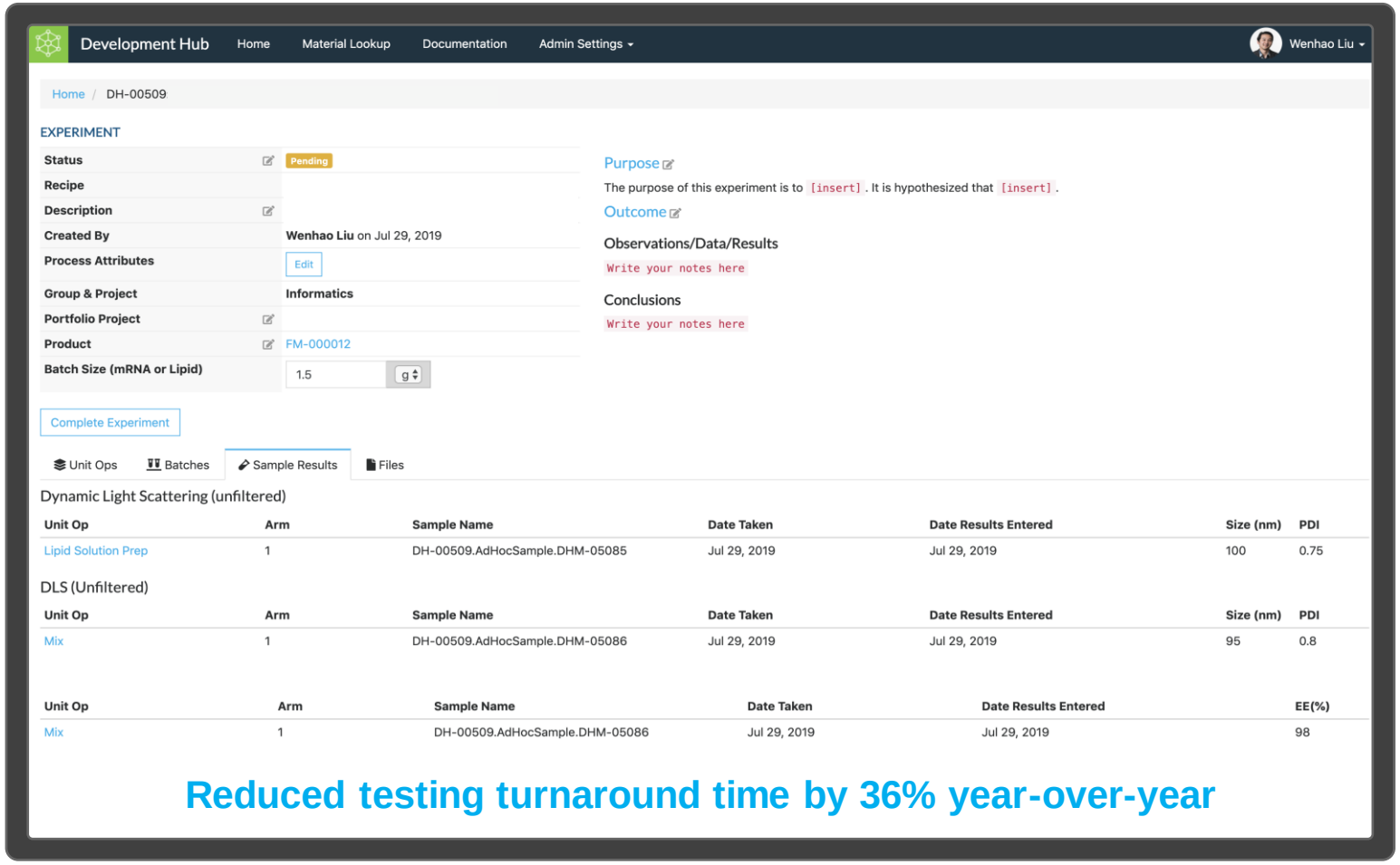
Tech dev digitization

Development Hub / Experiment Execution

- Structured capture of process parameters, materials and analytical results
- Integrated sample submissions and results, for high-throughput assay processing
- Integrated powerful data analytics, perform statistical analysis of process and analytical results



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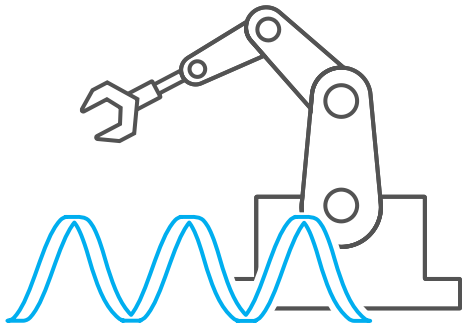
Digital integration @ Moderna



Clinical Manufacturing

Manufacturing investigational medicines

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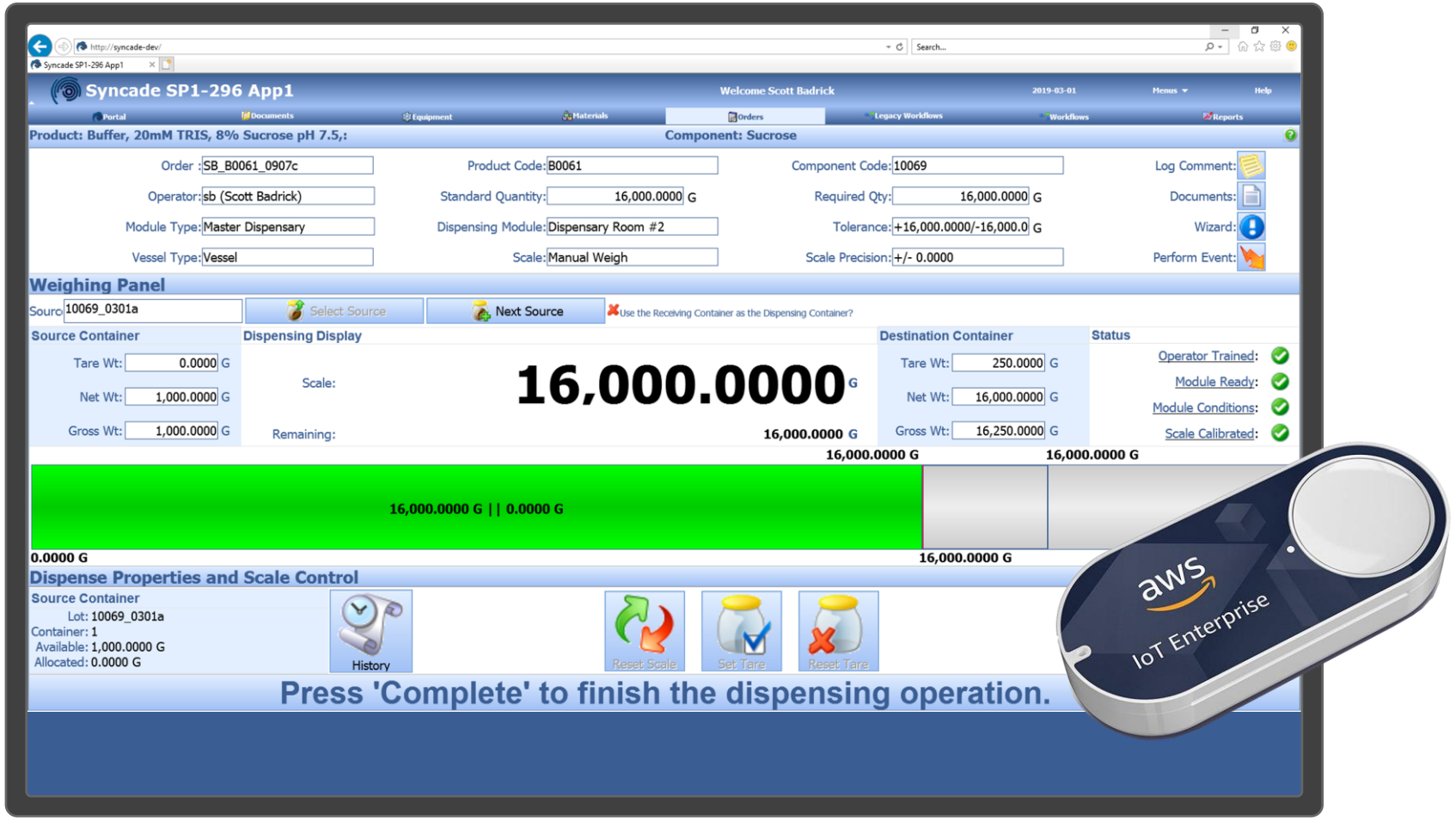
Manufacturing digitization

Materials

- The operators are digitally instructed to which raw materials to use through a real-time integration with SAP
- Materials are barcoded, scanned, mixed and charged to ensure accurate inventory controls
- The transformation of products is digitally tracked from raw materials to finished goods
- Buffers can be distributed to processing skids from the central buffer room
- All consumable materials are replenished using AWS IoT buttons with a single click



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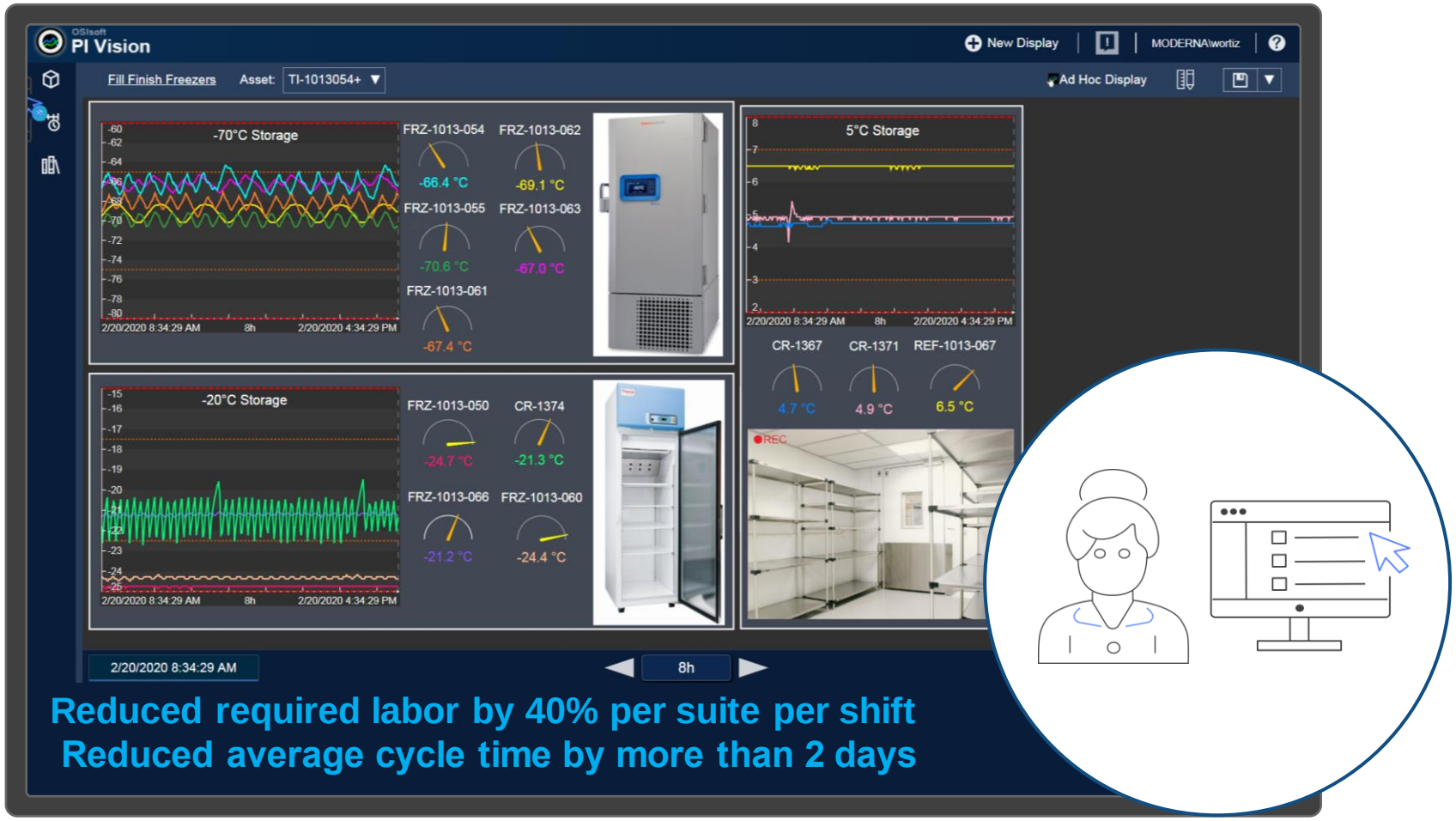
Manufacturing digitization

Equipment

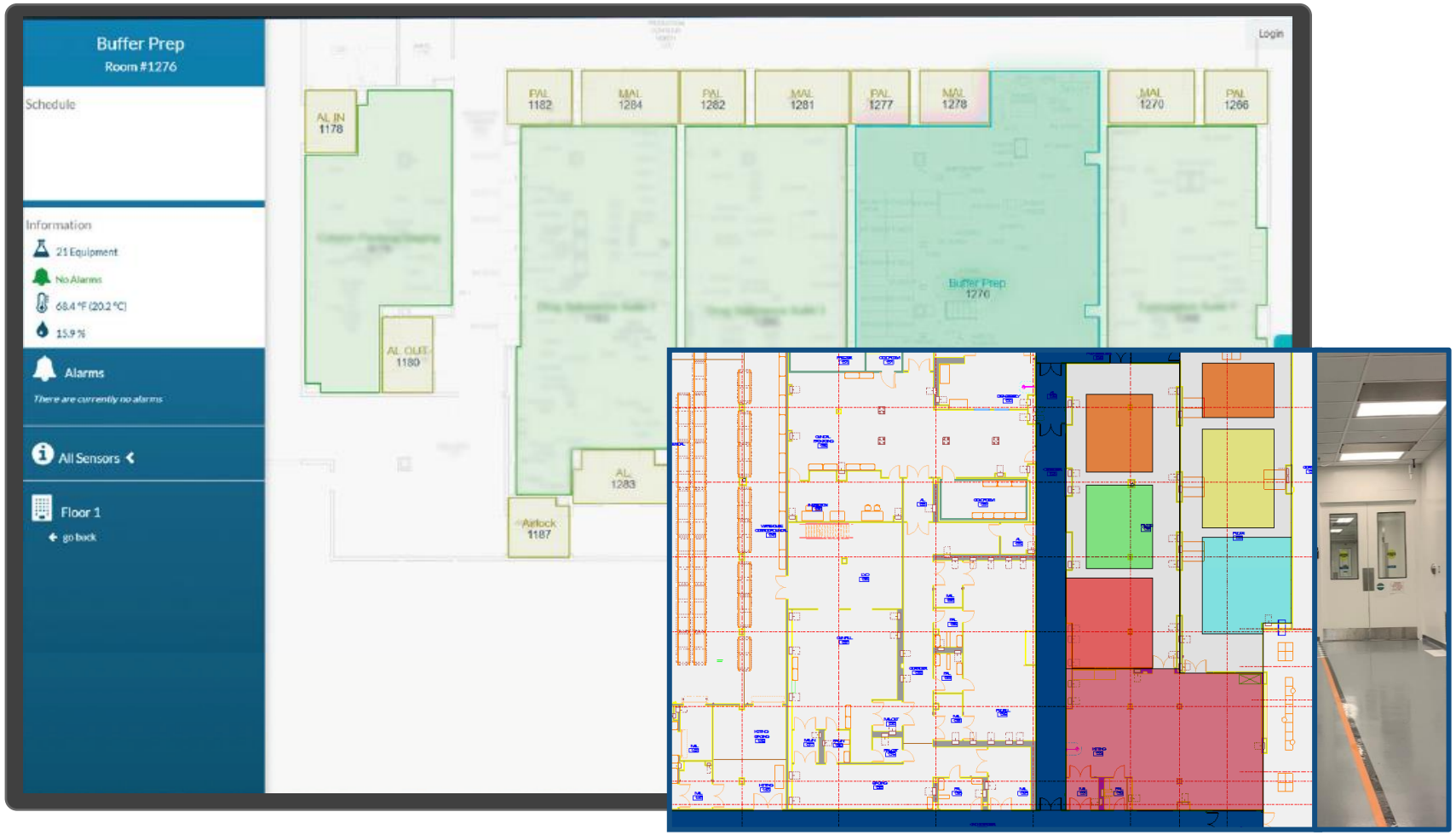
- Operators are digitally instructed to which equipment to use
- Readiness of the equipment is digitally verified
- Operations are controlled digitally on the equipment
- Data is collected and analyzed in-real time on the equipment



Manufacturing digitization

Analytics Driving Operations

- Ability to analyze personnel and materials flows to drive continuous improvement
- Visual boards to drive materials, sample and flows
- Digital fences to monitor and segregate trains
- Real time *visibility and response to alarm conditions*



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Digital integration @ Moderna

Quality

Testing and releasing medicines for intended use

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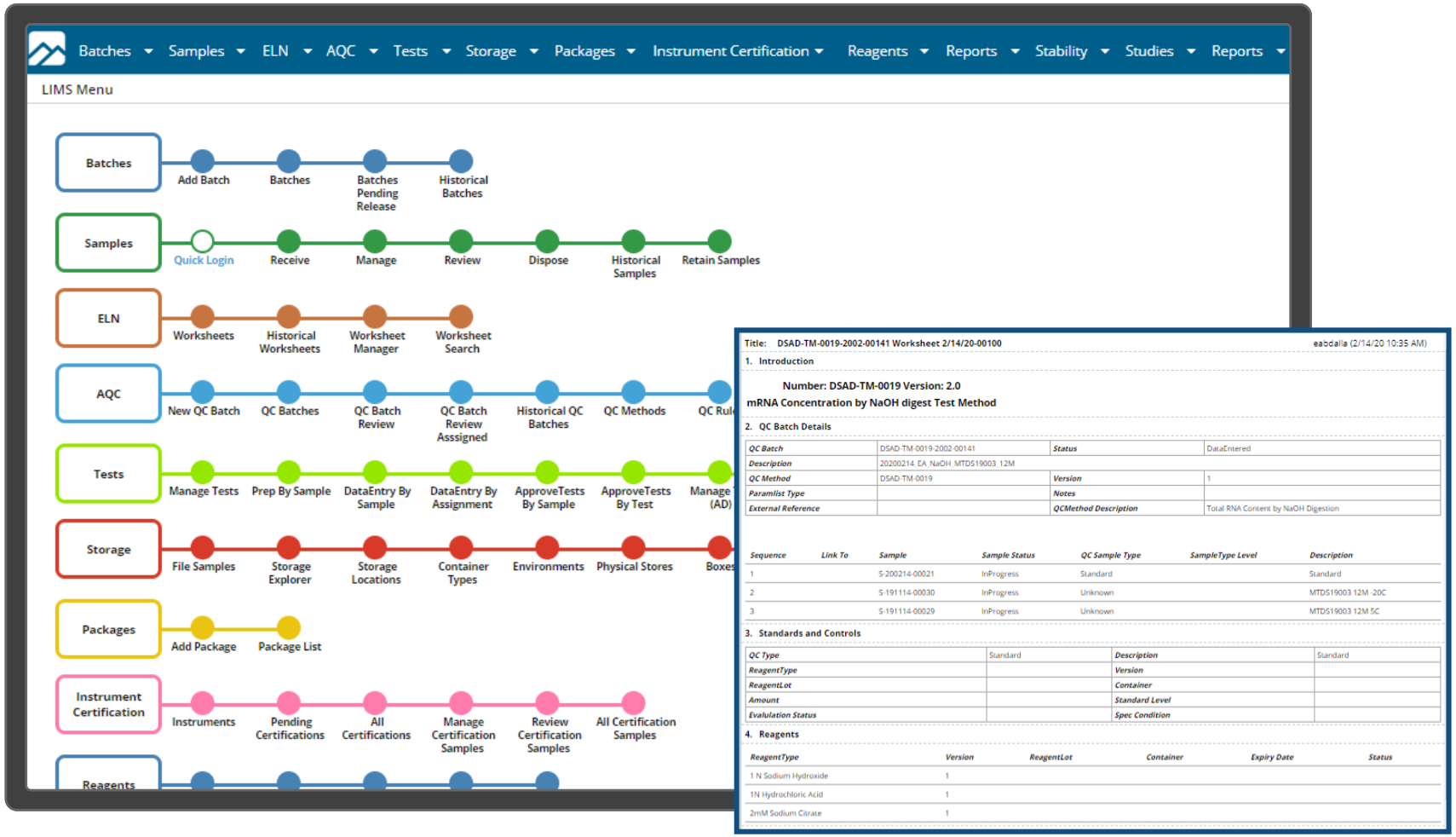
Quality digitization

Product & Raw Material Testing

- Operators are digitally instructed to what samples to take
- Real-time integration with the LIMS sample plans
- Sample labels are printed and applied on the shop-floor
- All information required for testing is passed digitally to the LIMS system to enable QC testing
- When QC test are approved, the results required for batch records calculations are passed back automatically



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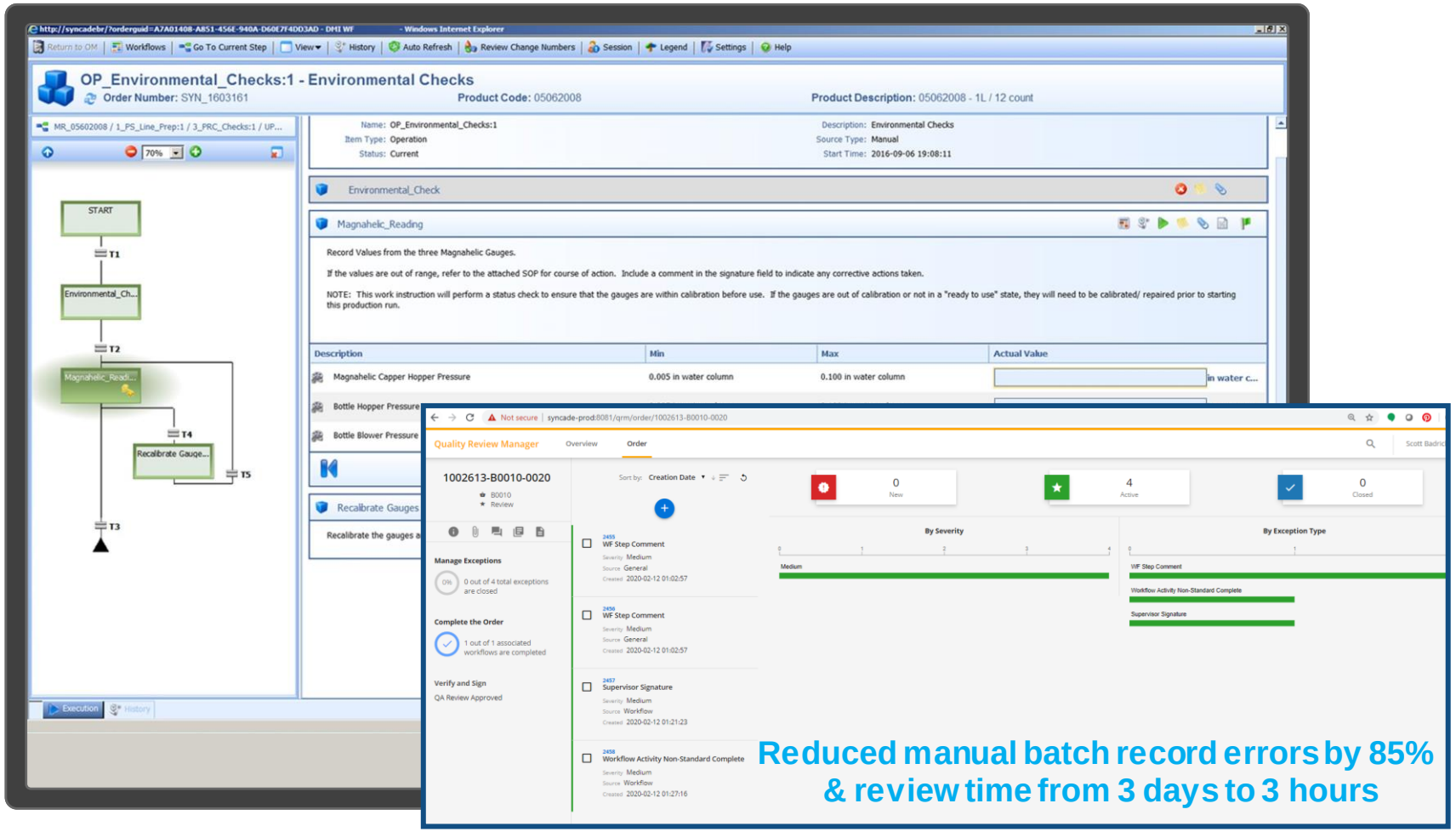
Quality digitization

Release

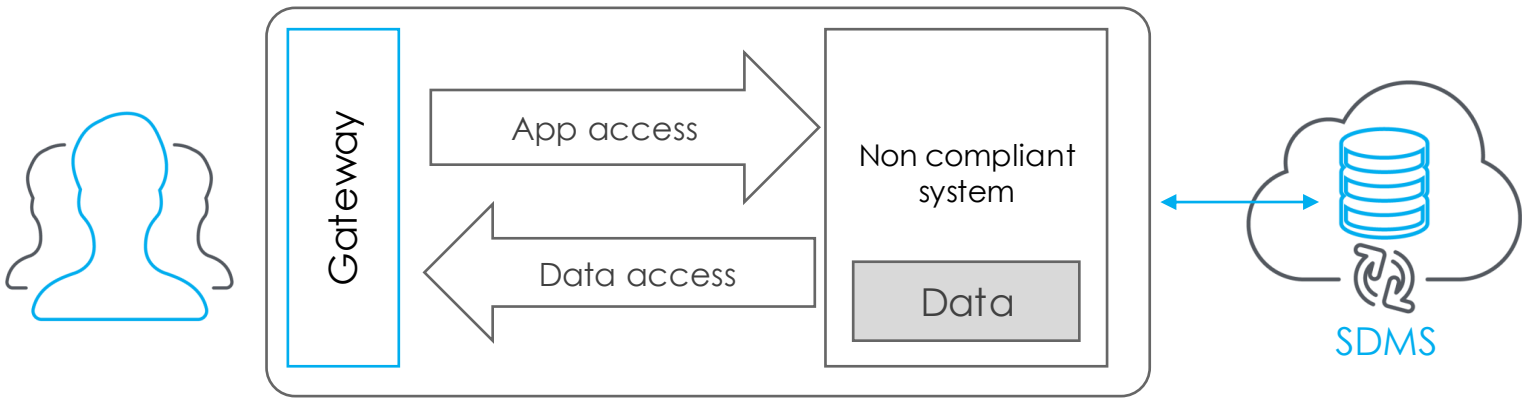
- QC test results are passed electronically with release conditions
- Batch record exceptions are captured digitally and can be reviewed in real-time
- Certificate of Analysis (COA) generated electronically



Quality digitization

Laboratory Data Integrity

- QC labs have an integrated data integrity solution
- Captures equipment data in real-time with audit trails
- Store in the cloud with security controls



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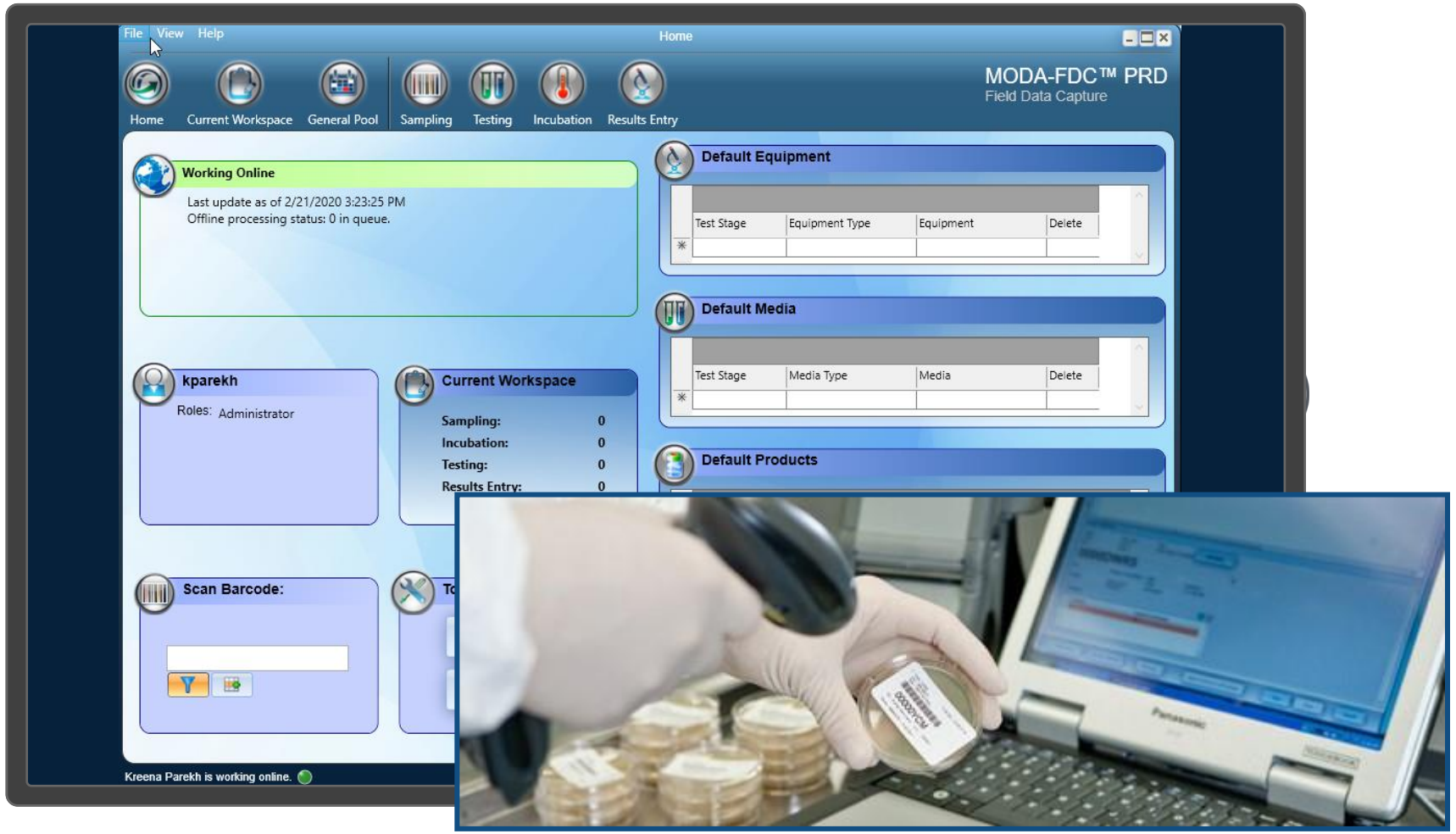
Quality digitization

Environmental Monitoring

- Self-contained testing carts allow flexibility
- Integrated instrumentation ensures data integrity
- Microorganism library allows us to quickly investigate excursions



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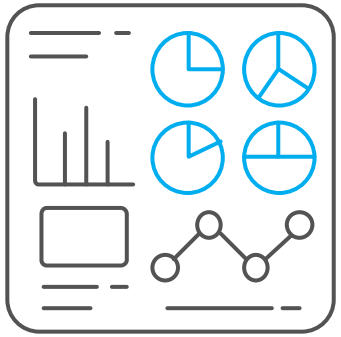
Digital integration @ Moderna



Clinical Development

Advancing new medicines to patients

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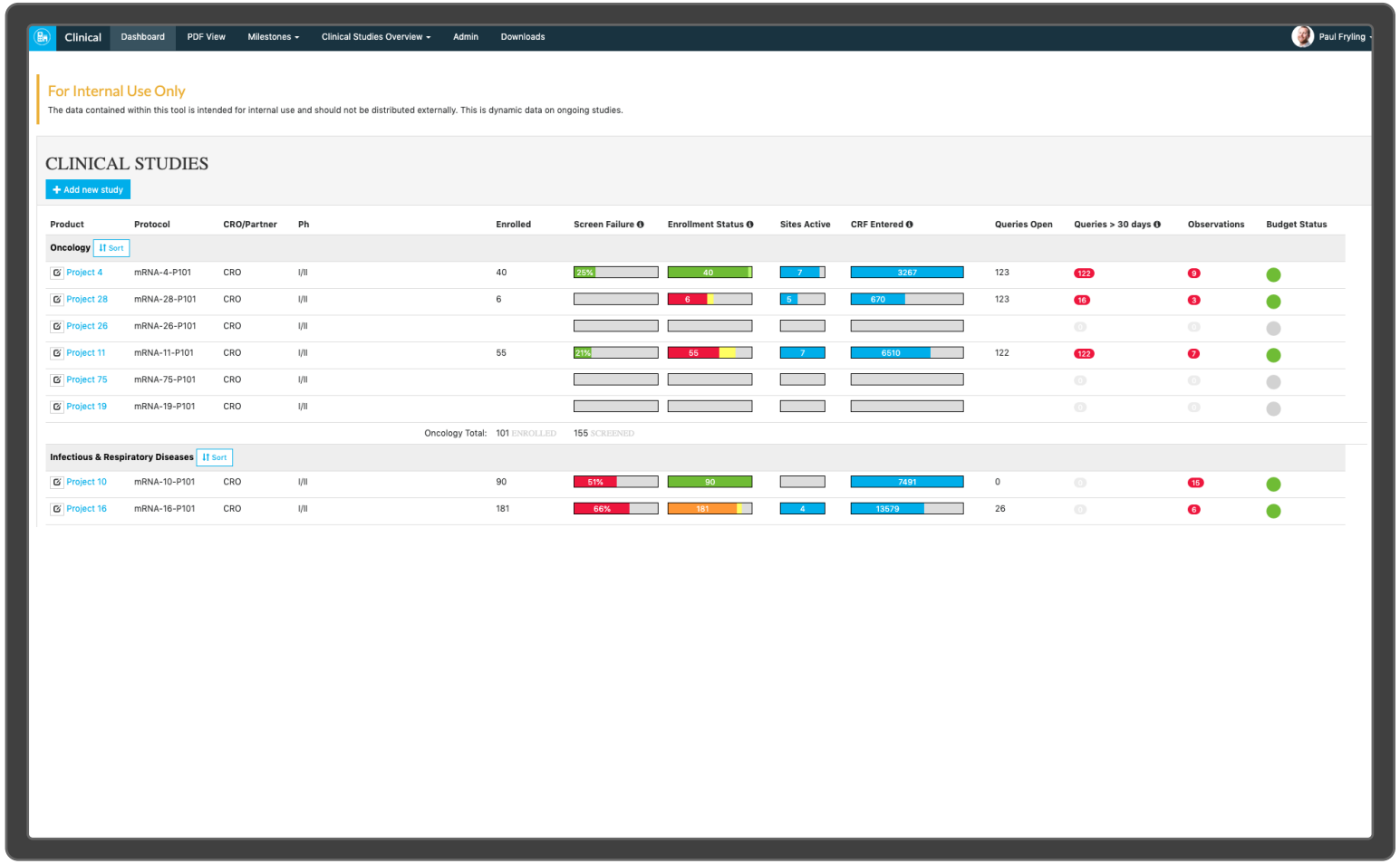
Clinical development digitization

Clinical Trial Dashboard

- Roles and responsibilities of the clinical trial team
- High level summary of key operational milestones
- Summary text informs team of important updates



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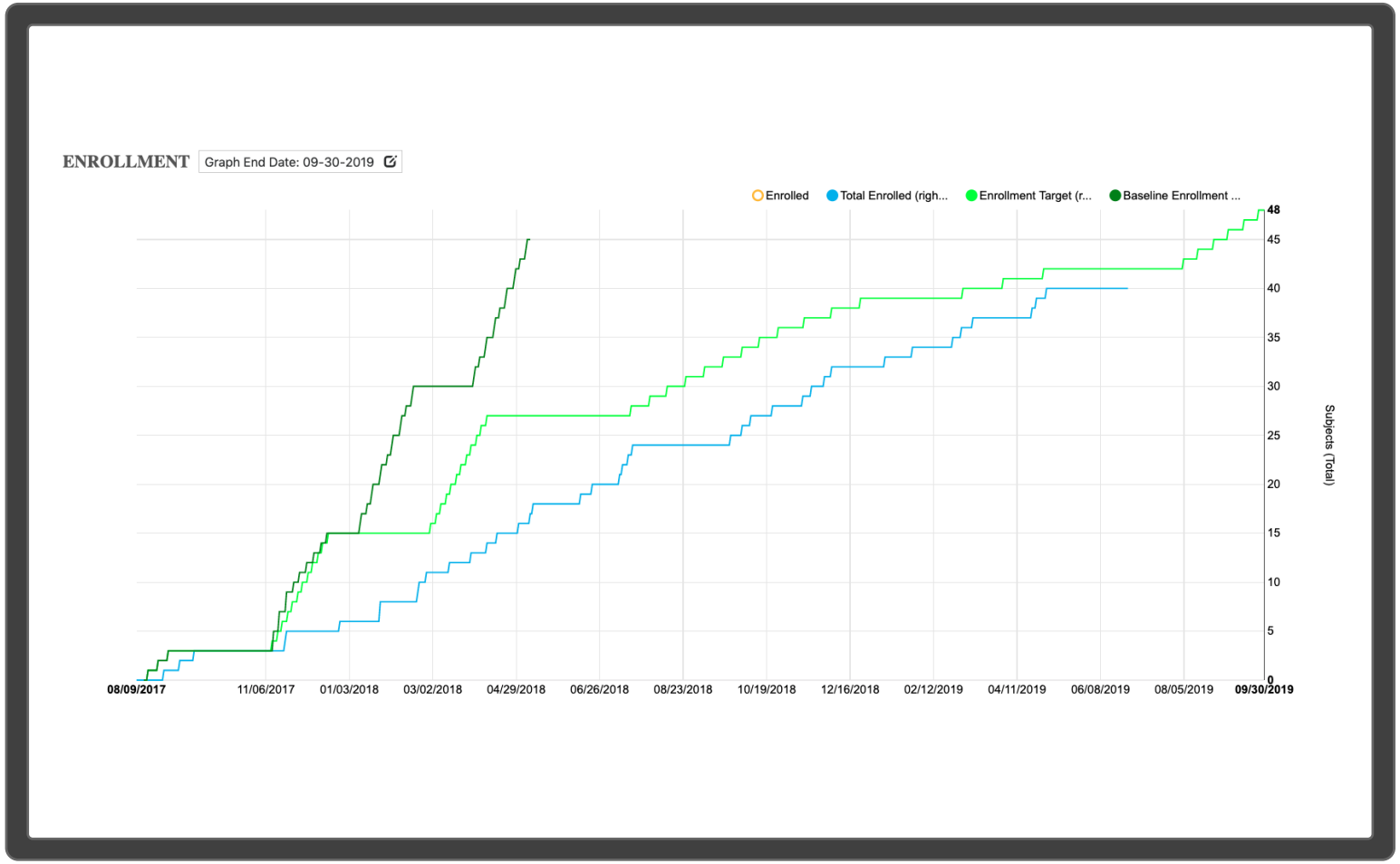
Clinical development digitization

Enrollment Forecasting

- Track actual subject enrollment relative to the plan
- Real-time detection of enrollment issues
- Enrollment trending across the portfolio of actual, target and baseline forecast



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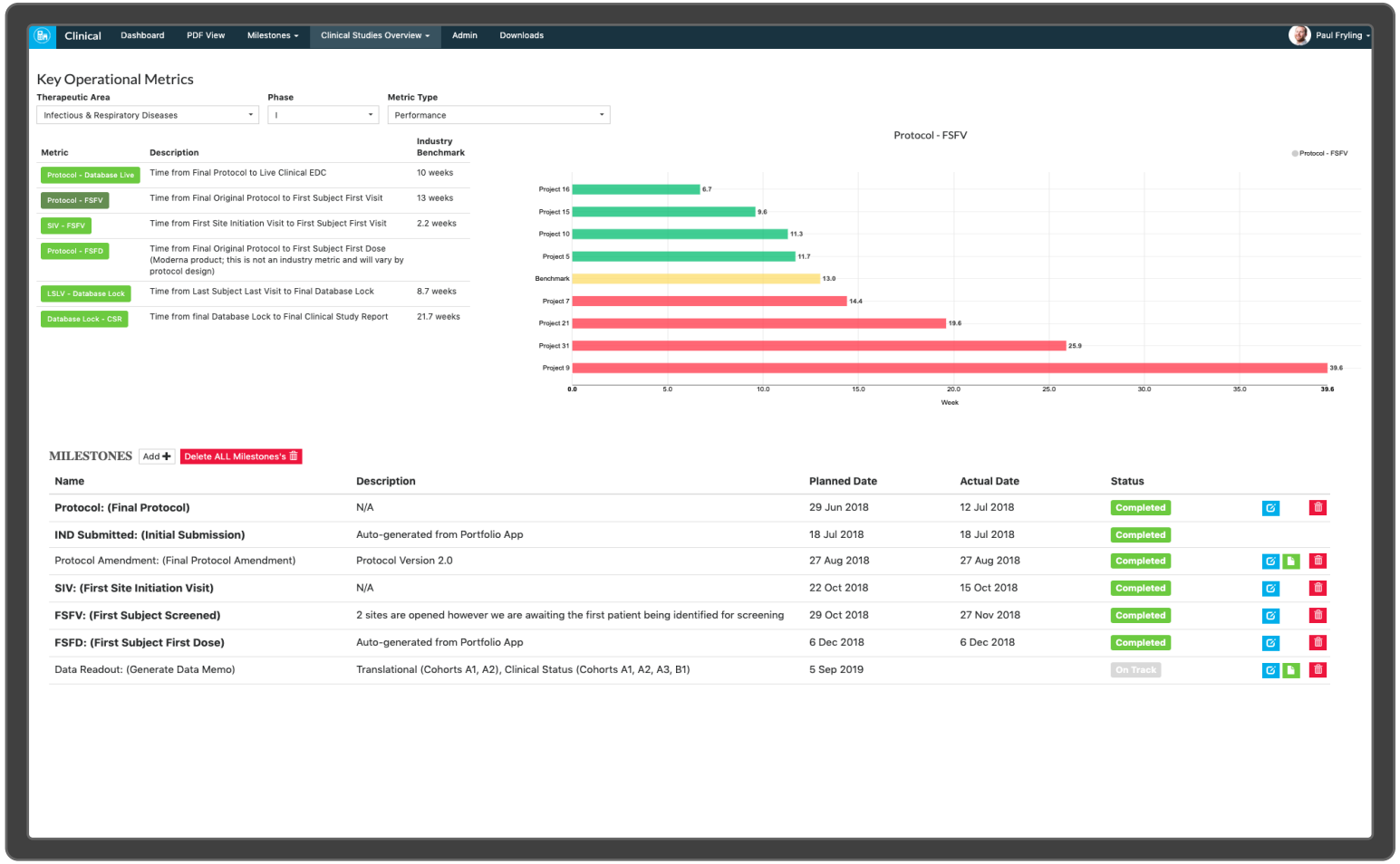
Clinical development digitization

Milestone Tracking (Target vs. Actuals)

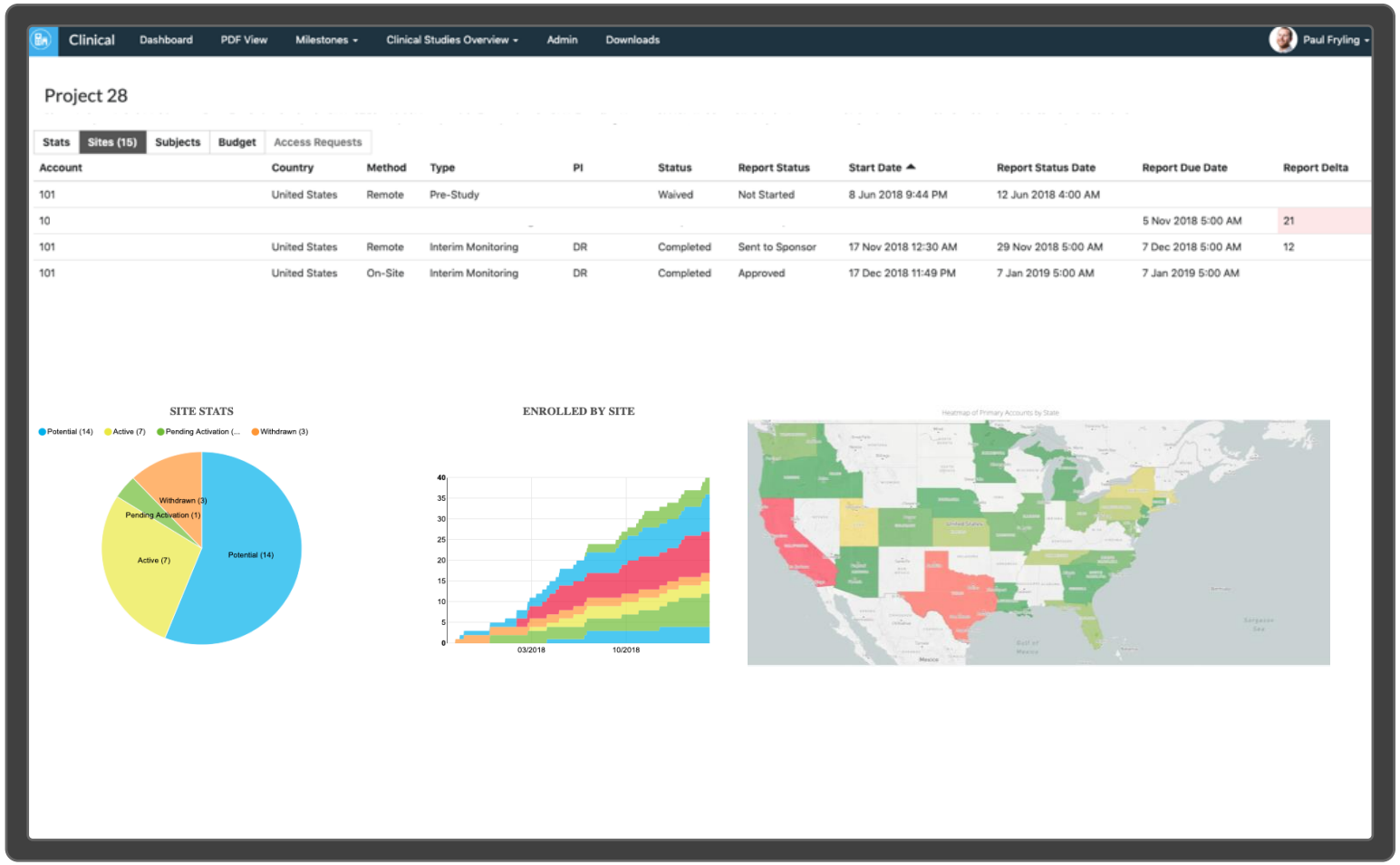
- Plan and monitor key milestones across all Moderna studies
- Easily compare key metrics against Industry Benchmark
- Publish all type of metrics categories (performance, quality and risk)



Clinical development digitization

Site Visit Monitoring

- Visibility of site monitoring, training and trip reports
- Automatically flag of reports that fall outside contracted windows
- Heatmap of clinical sites in USA



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Thank you!

Advanced Analytics and AI @ Moderna

Dave Johnson, PhD

March 4, 2020

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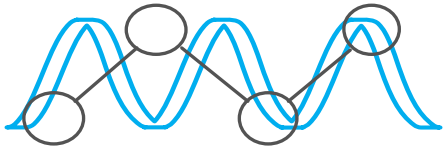
Dave Johnson, PhD

Dave Johnson is Head of Informatics, Data Science, and AI at Moderna, where he delivers innovative Digital and AI solutions to support Research and Clinical Development. Mr. Johnson holds a PhD in Information Physics and has over 15 years of experience in software engineering and data science. He has spent the last 10 years working exclusively for Life Science companies.

Advanced analytics and AI enables various parts of our platform



Algorithms In Production

- Long Sequence Deconstruction
- mRNA Sequence Optimization

Used in SARS-CoV-2 Vaccine

- PCV Supply Chain Simulation
- Vaccine design pipeline for the Personalized Cancer Vaccine
- Optimal Container Selection
- Preclinical Insufficient Yield Prediction
- Sanger Contamination Detector
- Sanger polyA Quality Control
- ….

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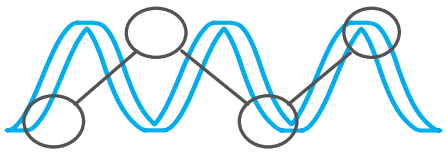
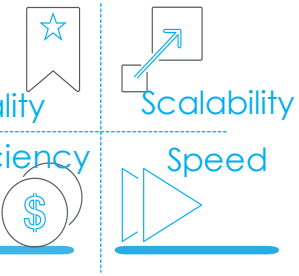
Advanced analytics and AI enables various parts of our platform





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Used in Personalized Cancer Vaccine

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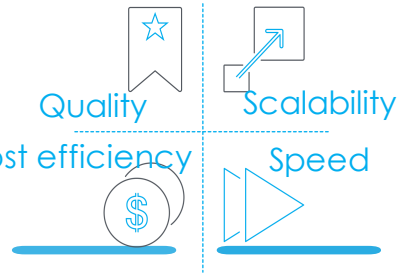
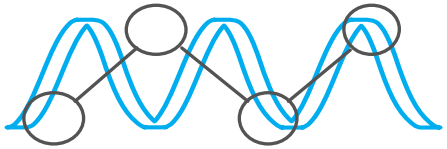
Advanced analytics and AI enables various parts of our platform





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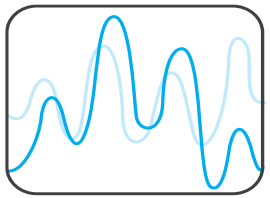

Algorithms In Development / Testing

- Improved mRNA sequence optimization
- Protein engineering and design
- Improved Neoantigen-MHC affinity prediction
- Sanger QC Analysis 2.0
- Inverse folding for RNA
- Improved Primer Picker
- Gene Block Deconstruction
- CryoEM Image Processing
- ….

Numerous Computational Techniques

- Rule based optimization
- Neural networks
- Bayesian inference
- Machine learning
- Simulated annealing
- Monte Carlo simulation

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AI use cases

Sanger Sequencing Analysis

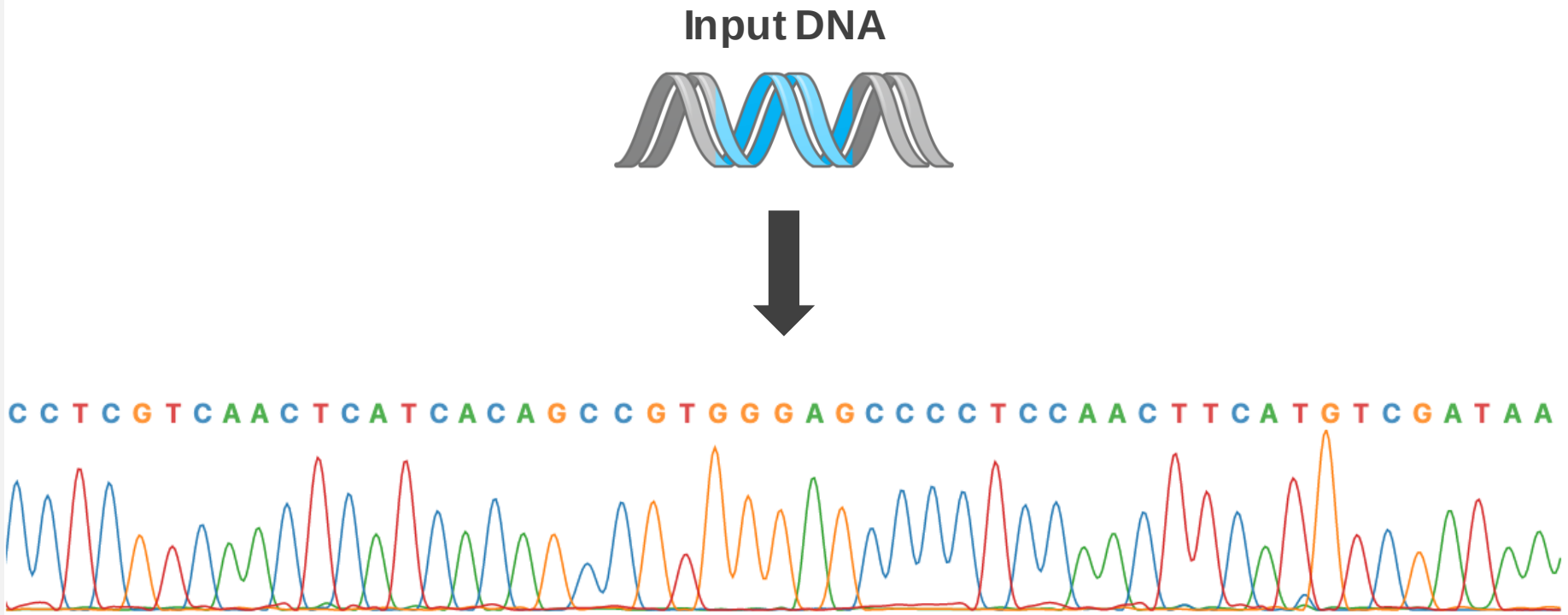
- Automated analysis pipeline
- Poly-A tail neural network QC
- Bayesian inference algorithm

CryoEM Image Analysis

- Neural network image segmentation
- Detection/classification of particle types
- Nanometer scale LNP morphology

Sanger sequencing

- Used to QC our DNA templates and final research grade mRNA
- A single nucleotide change can result in a nonfunctioning protein



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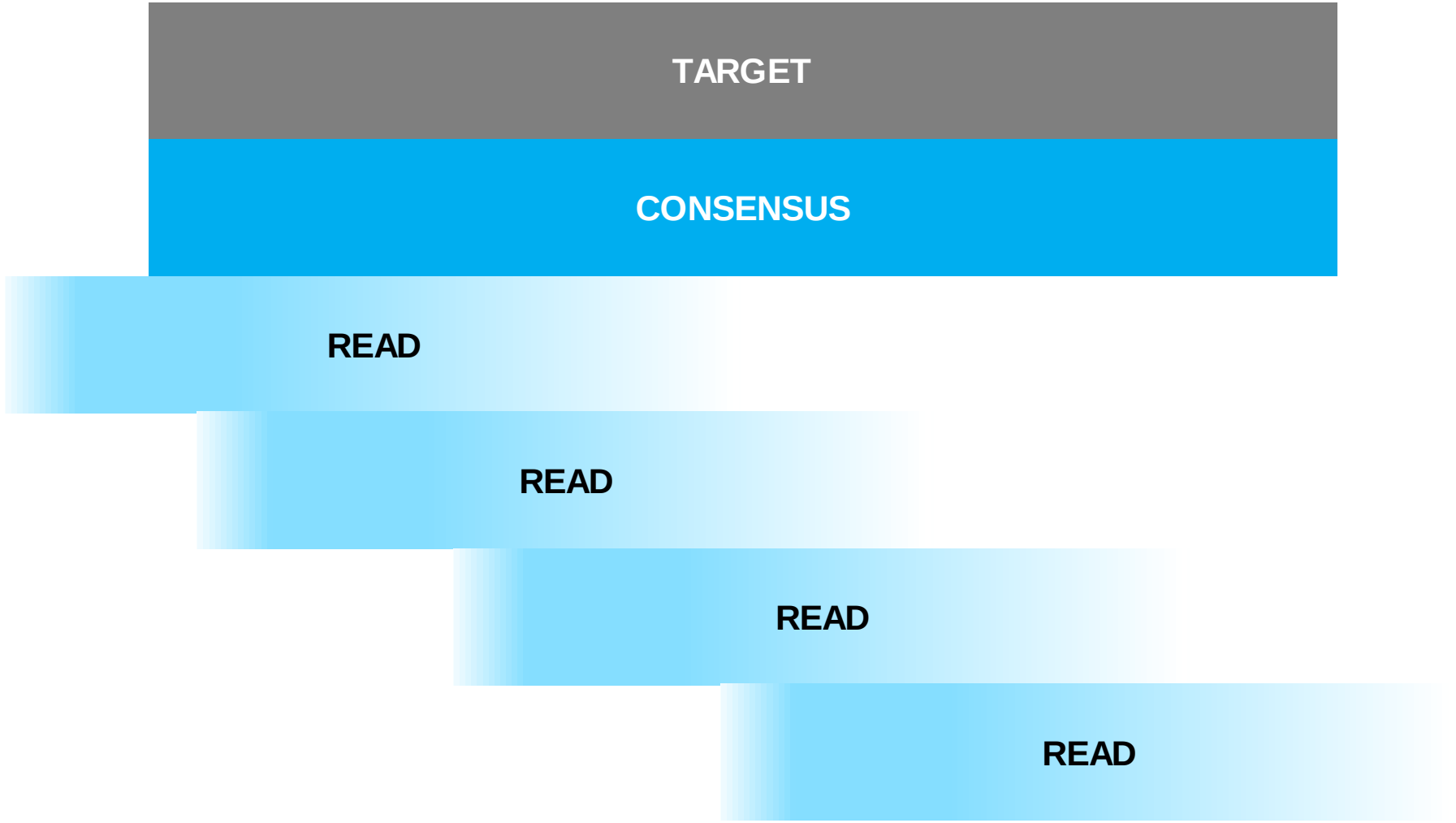
Sanger data analysis

- Analysis requires a complex pipeline of algorithms that does:
  1. Peak detection
  2. Base calling
  3. Contig building
  4. Consensus calling
  5. Discrepancy identification
- We licensed an off-the-shelf pipeline of algorithms
- Standard analysis tool for 20 years
- Used by thousands of labs



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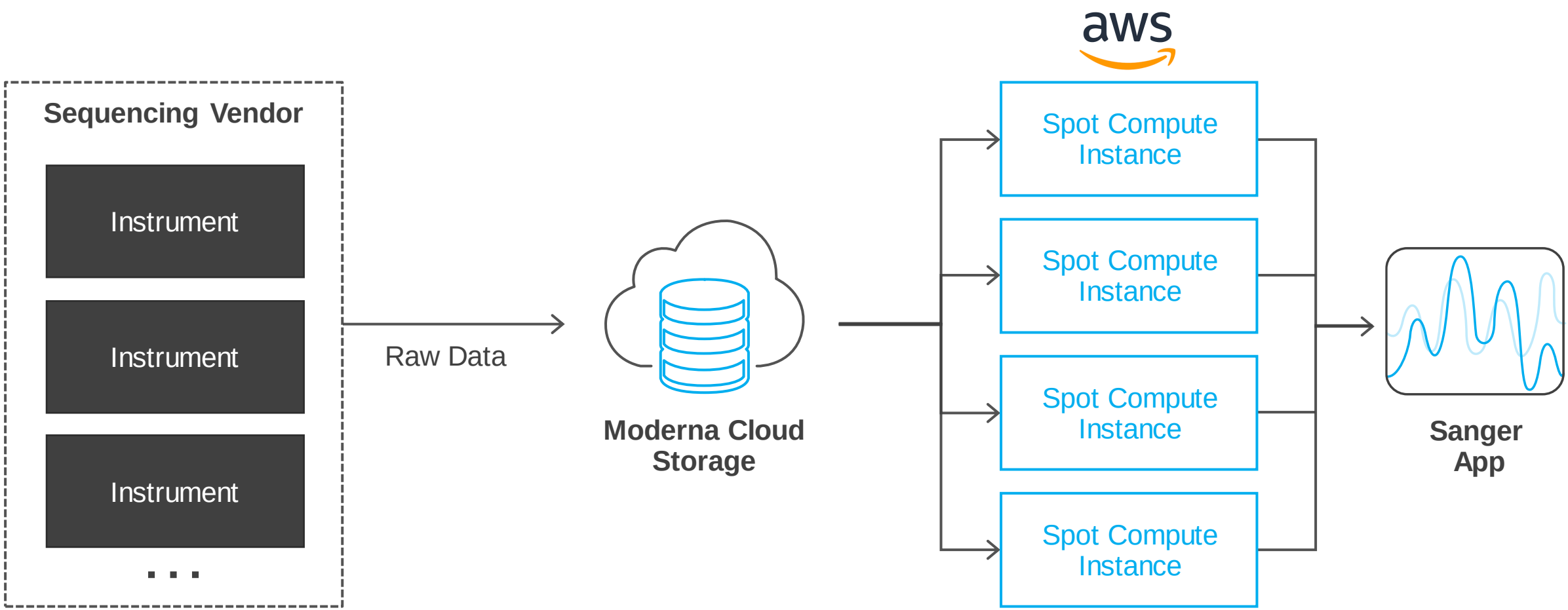
Automated Sanger analysis



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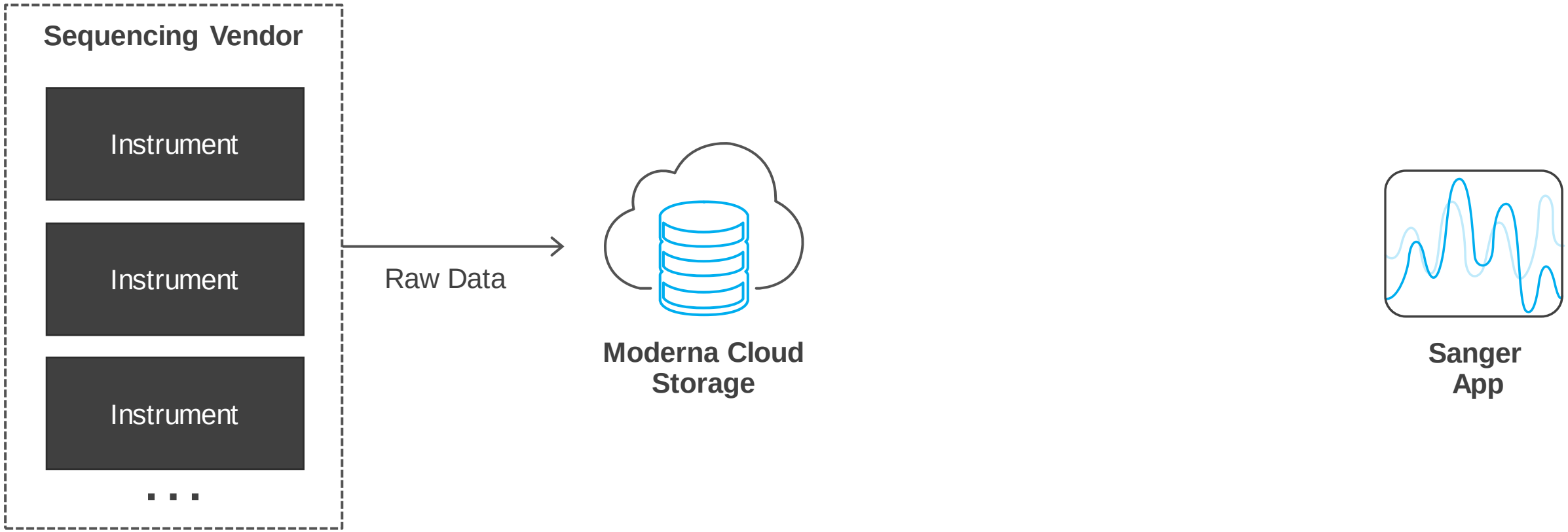
Automated Sanger analysis



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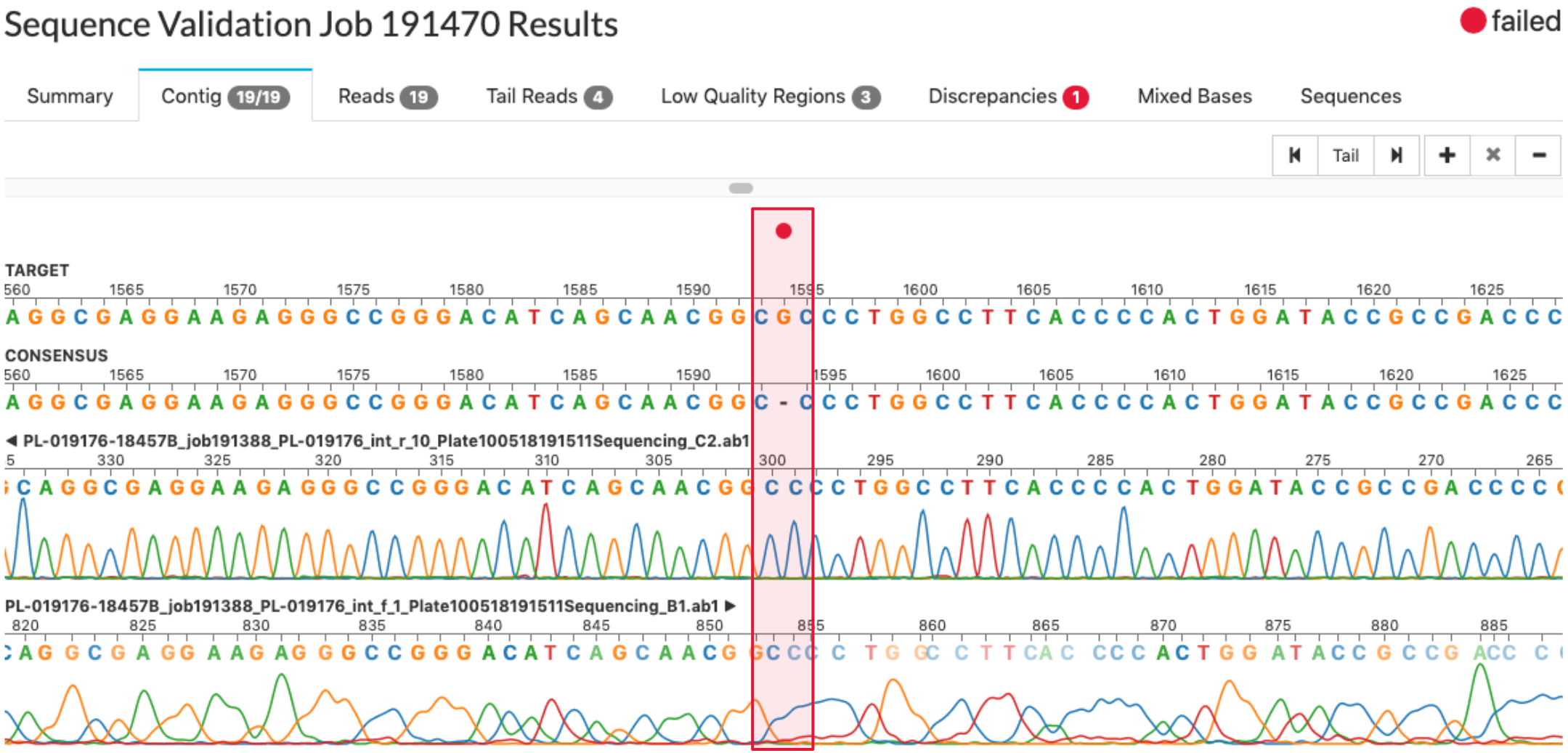
Visualization tool



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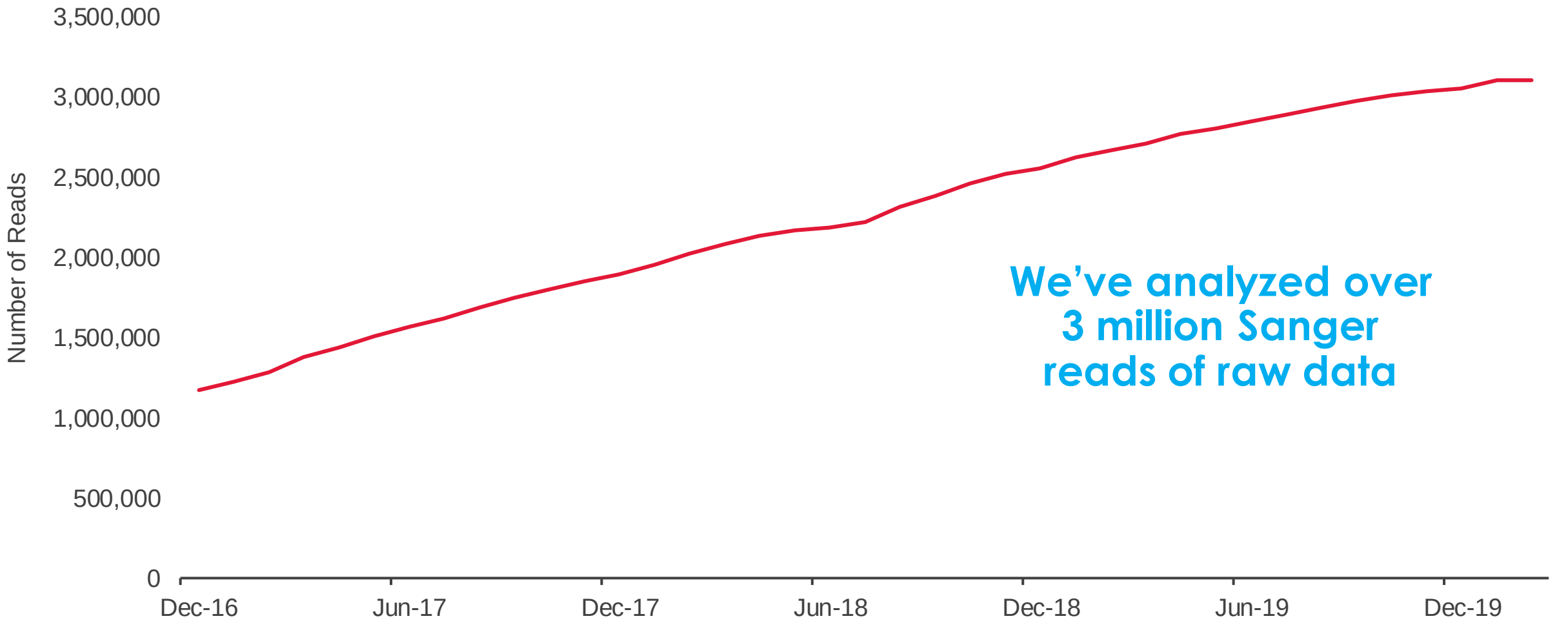
Analyses and data growth



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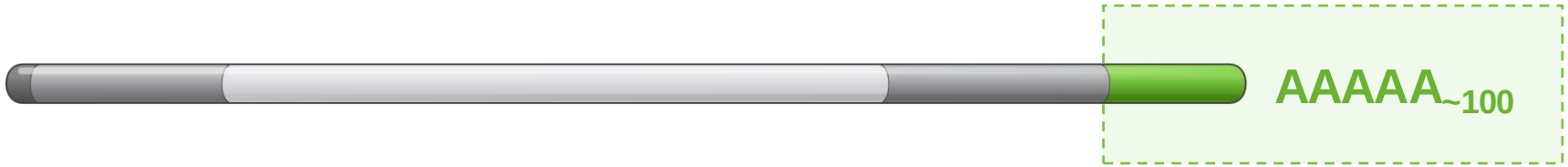
Poly-A tails

- Our mRNA typically ends with a poly-A 100 tail
- We build the poly-A 100 tail into our DNA templates



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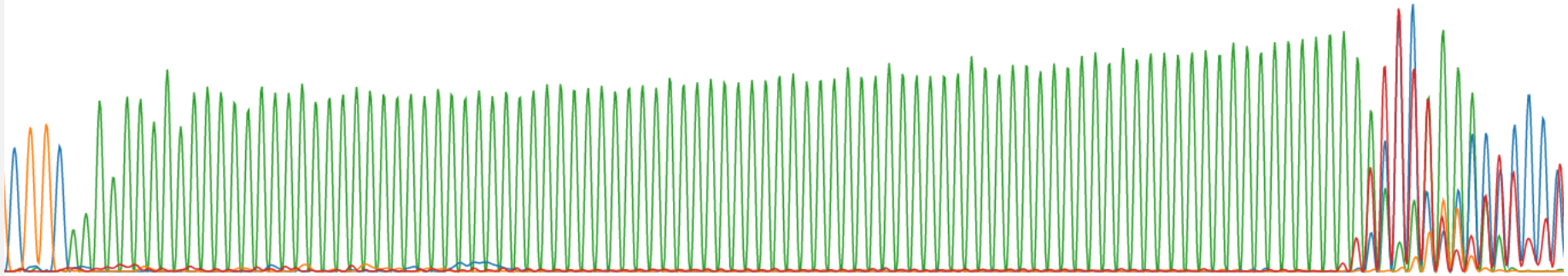
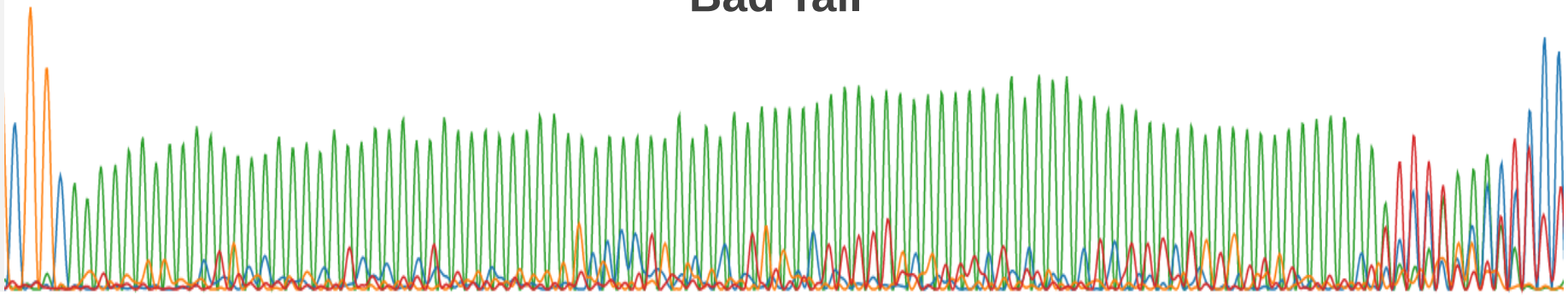
Sanger analysis of poly-A tails

- The off-the-shelf algorithm cannot distinguish these
- Need to be reviewed manually by trained operators

Good Tail



Bad Tail



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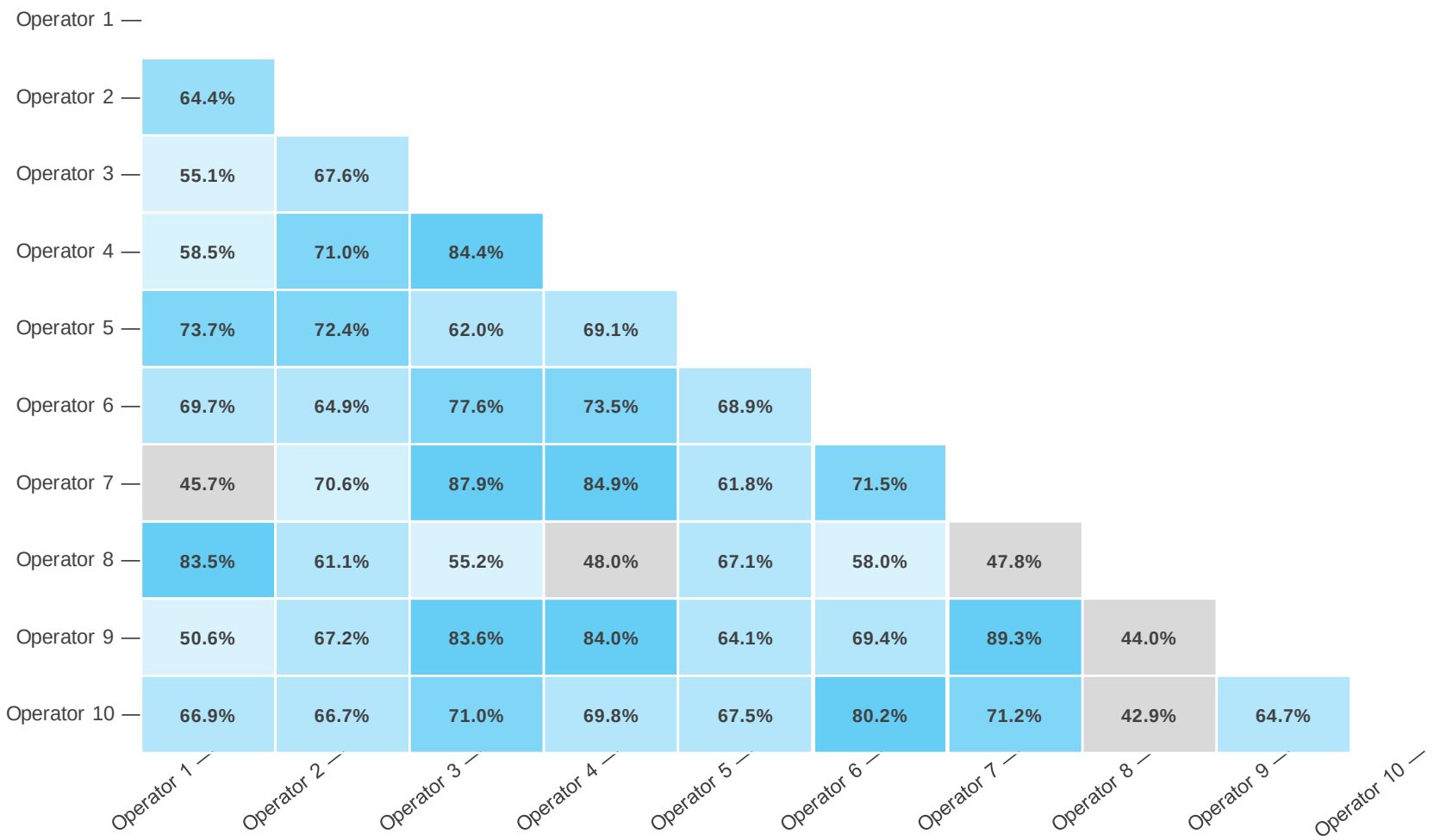
Human calling is expensive and inconsistent

- 10 operators manually created over 20k labels of pass/fail tail chromatograms



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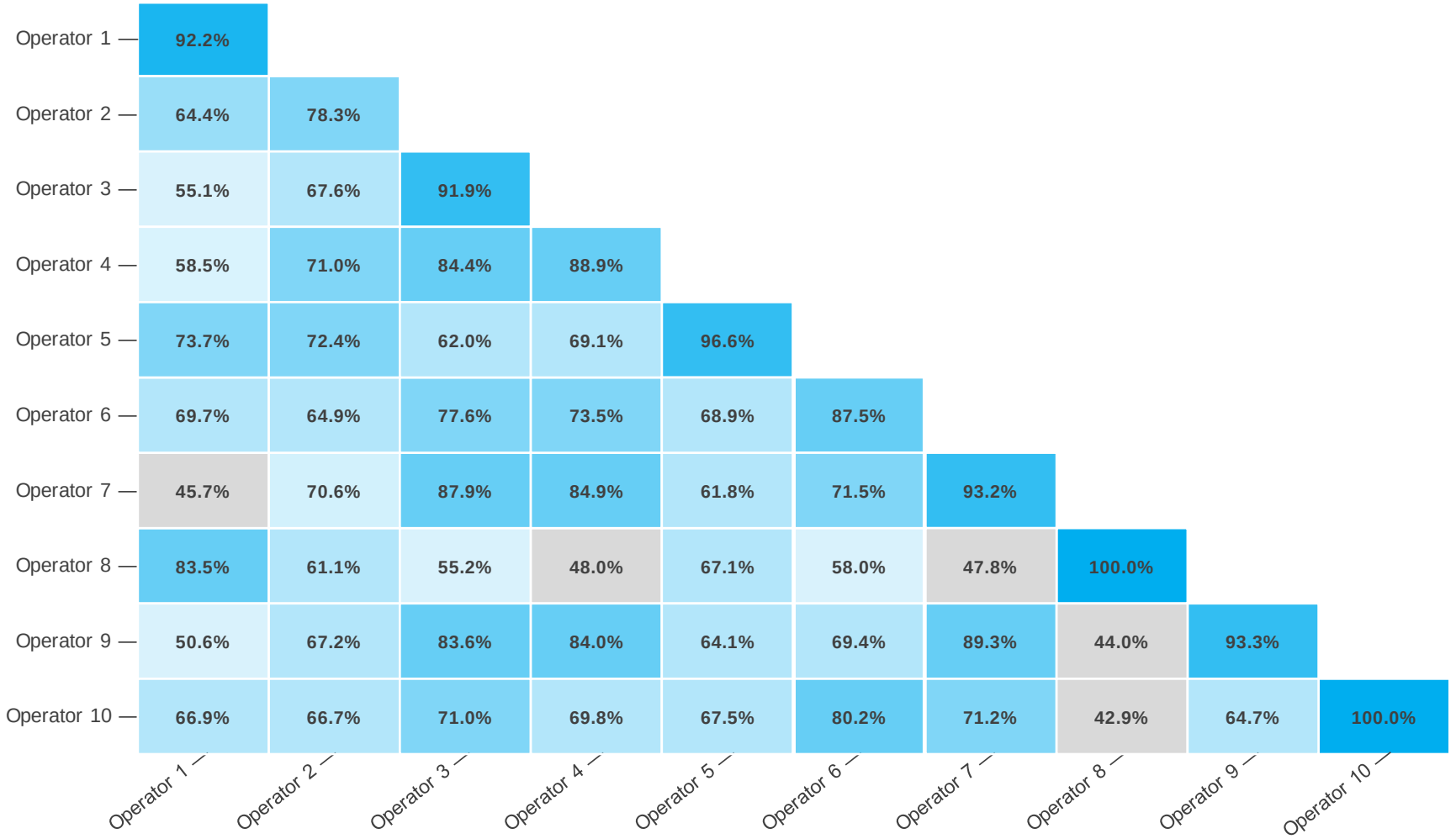

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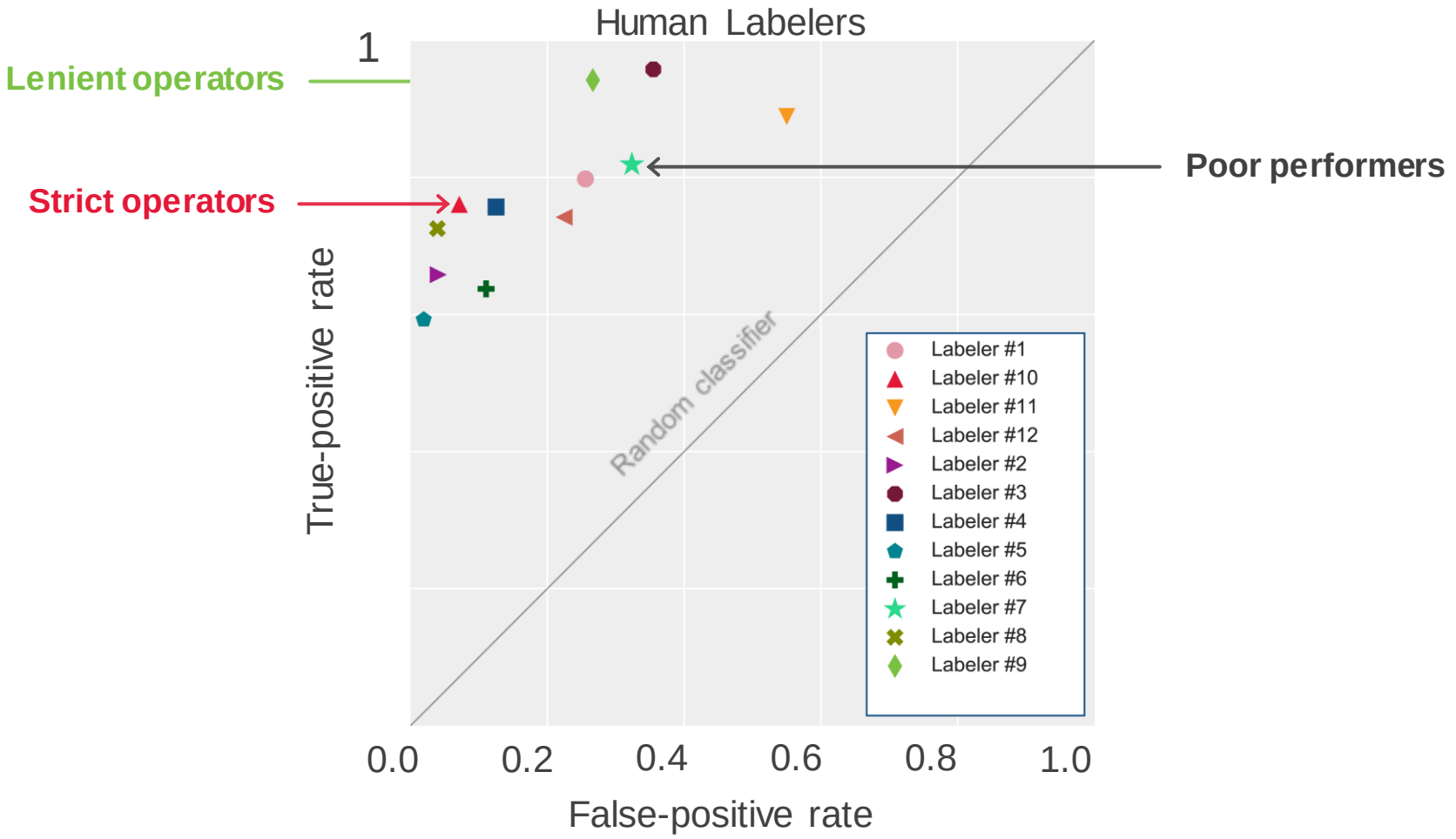
Poly-A CNN model



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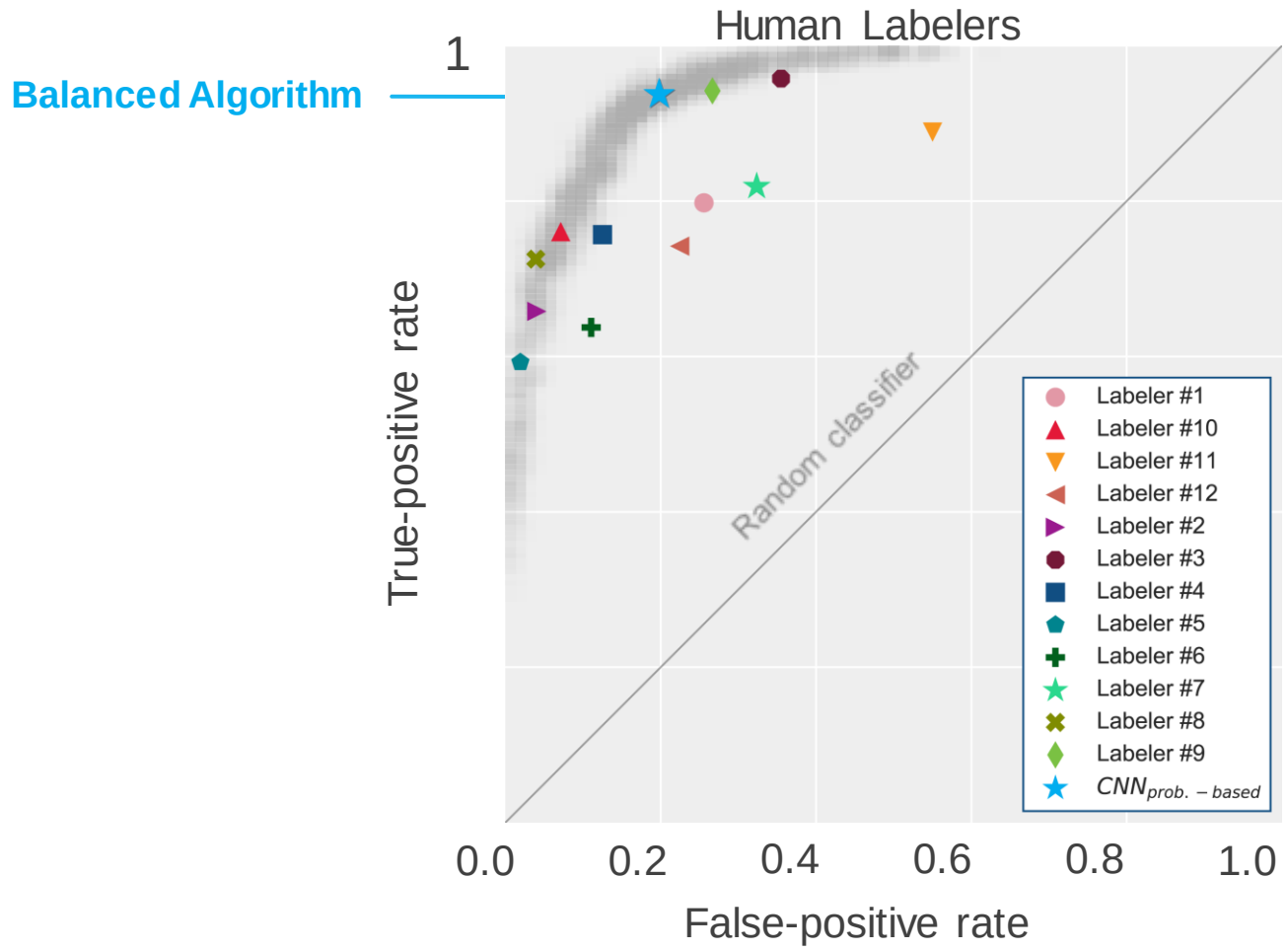
Poly-A CNN model

- We built a convolutional neural network (CNN) to predict call of entire team
- Running in production for over 1 year, saving countless hours of manual review



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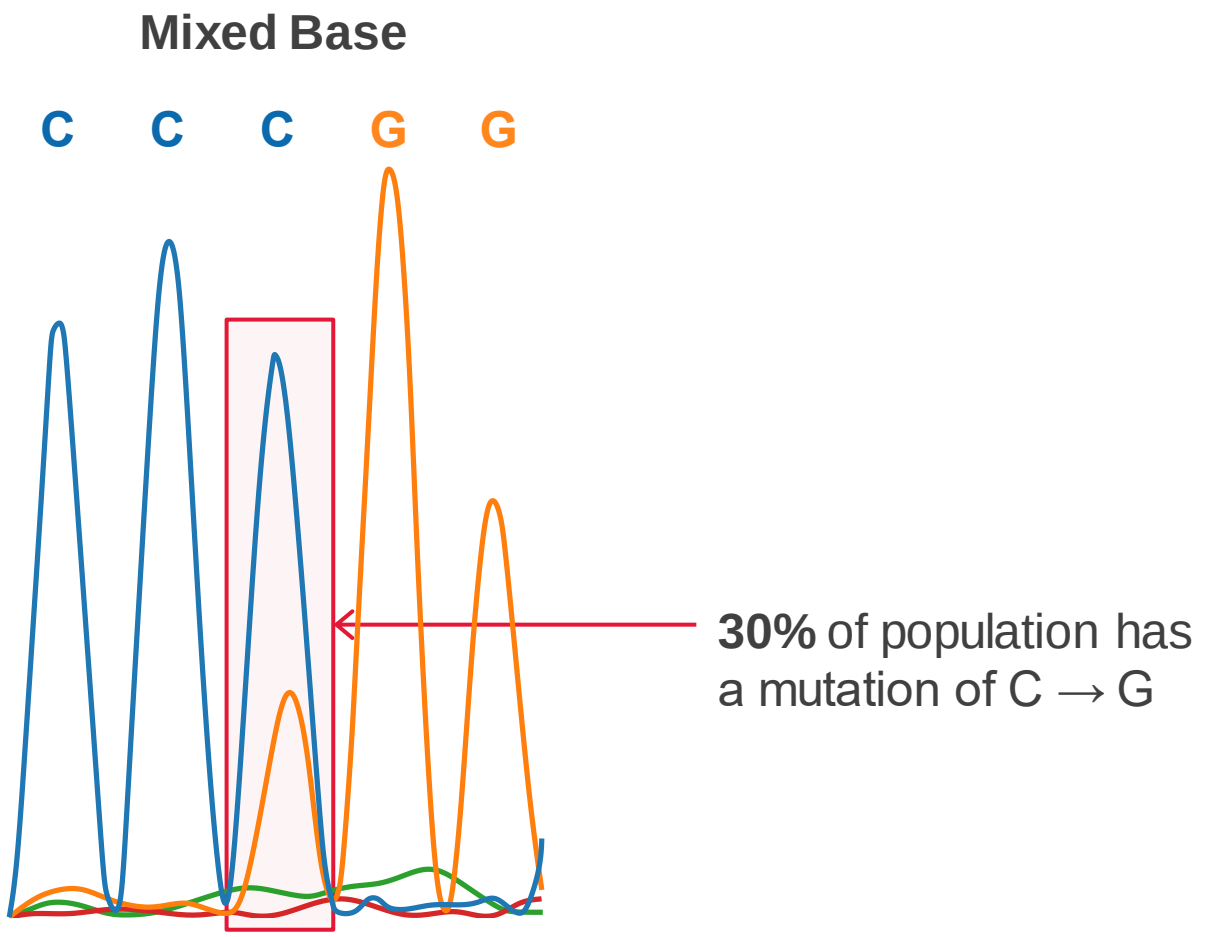
Other issues with current algorithm

- We've discovered many other failure modes that are not being handled correctly by the off-the-shelf algorithm:
  - Mixed bases
  - Contamination
  - Mispriming
  - Failed contigs
  - Peak drift
  - Etc.



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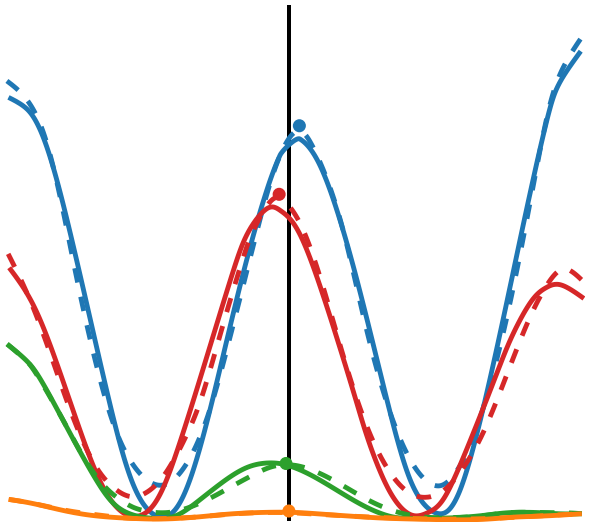
A new algorithm from the ground up

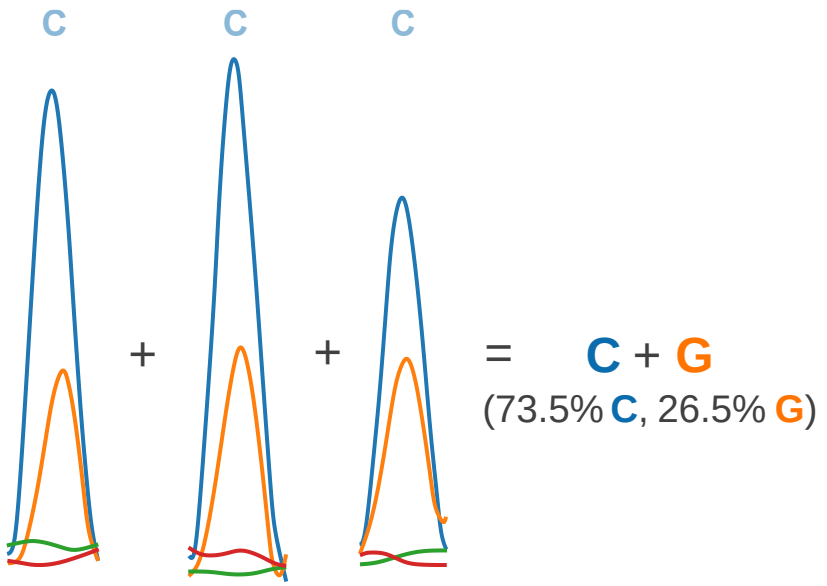
Peak Detection

- Using Bayesian MAP analysis, model peaks as superposition of gaussians
- Based on statistics of huge number of historical reads

Base Calling

- Use Bayesian Hypothesis testing, calculate probabilities of all possible base calls (including all mixtures)
- Calculates the cumulative evidence of a mixture from all reads





Takes 100x the computation power, but only ~10 mins to run

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AI use cases

Sanger Sequencing Analysis

- Automated analysis pipeline
- Poly-A tail neural network QC
- Bayesian inference algorithm

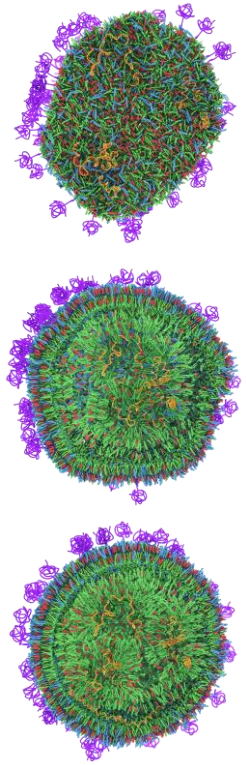
CryoEM Image Analysis

- Neural network image segmentation
- Detection/classification of particle types
- Nanometer scale LNP morphology

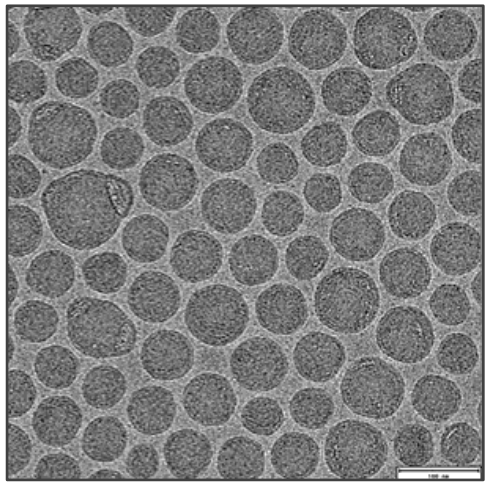
CryoEMs are images of our lipid nanoparticles

Components

Assembled LNPs



CryoEM Images



- Understand how process/components impact assembly
- Understand how LNP structure impacts in vivo performance
- Have generated 500k+ images across numerous conditions

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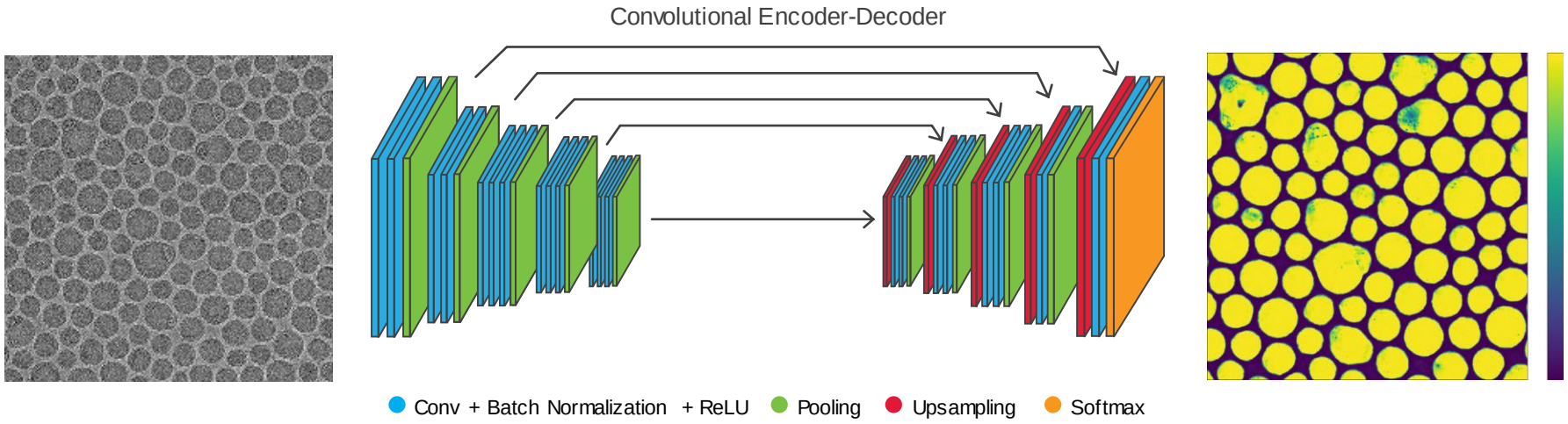
Neural network for image segmentation

- The first step is to segment the image into individual LNP particles
- We trained a state-of-the-art convolutional encoder-decoder neural network



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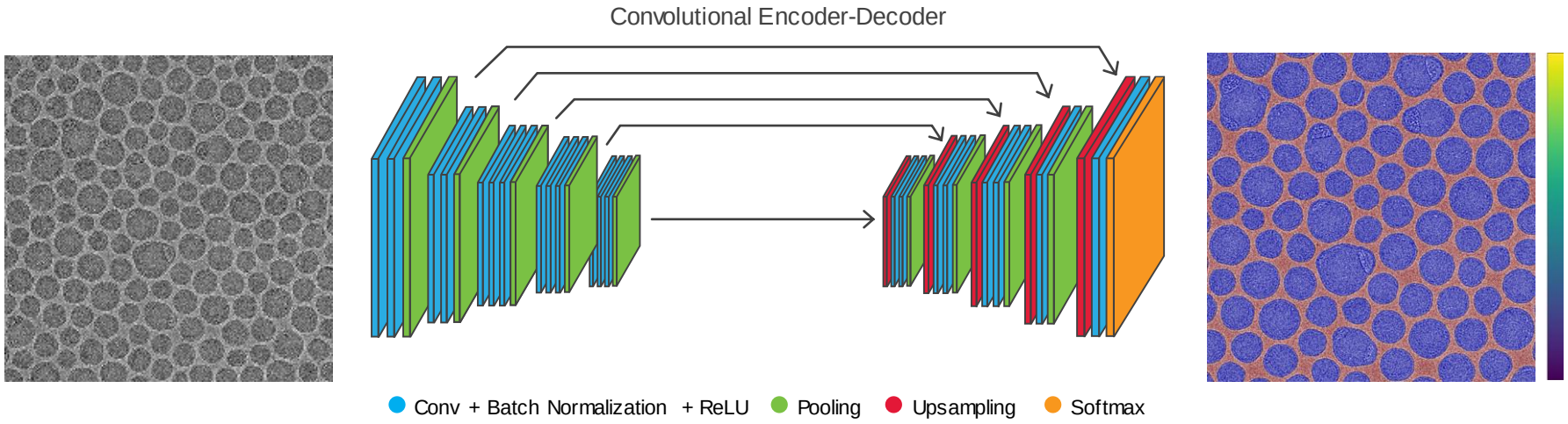
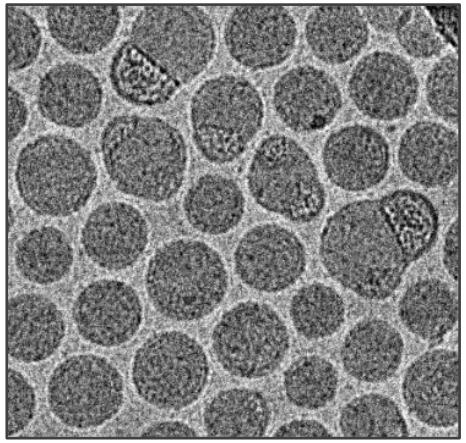
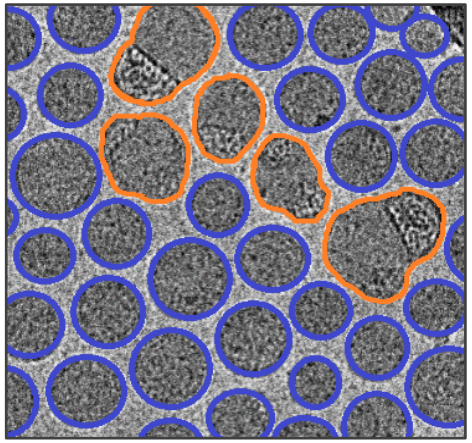
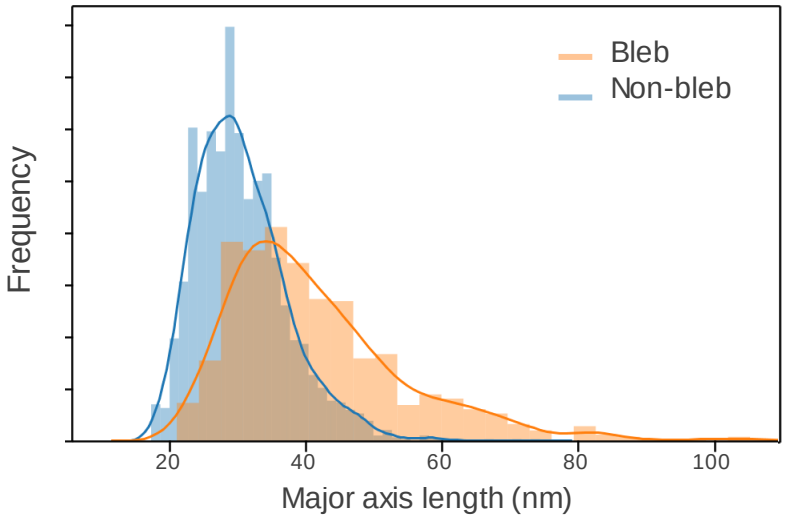


Automatic detection and classification of particle types







Model	Accuracy	Precision
Logistic Regression	0.87	0.75
Random Forest	**0.98**	**0.99**

- Pixel-value based random forest model achieves excellent performance
- Saves countless hours of manual analysis

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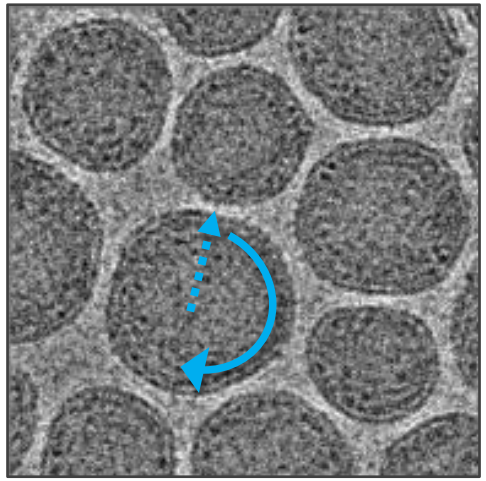
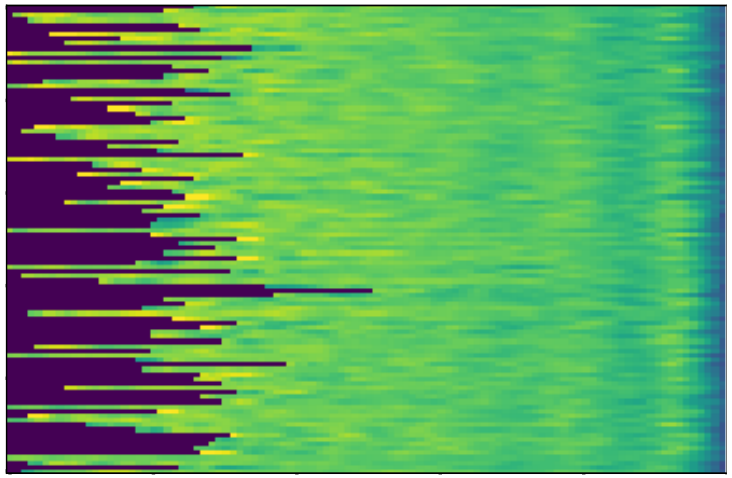
Measurement of nanometer scale LNP morphology

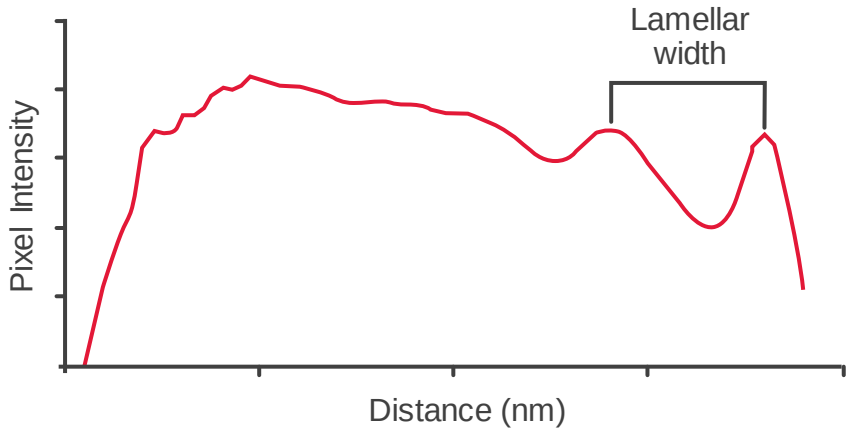


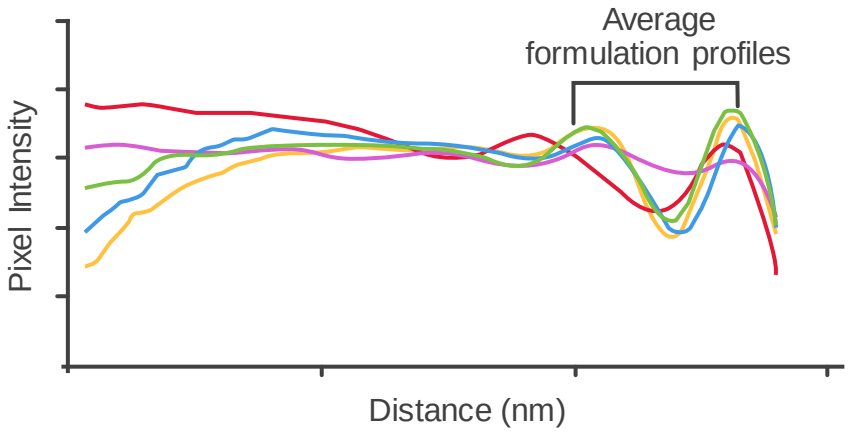
Extract radial profiles, align edges

Average **within** particles



Average **across** particles





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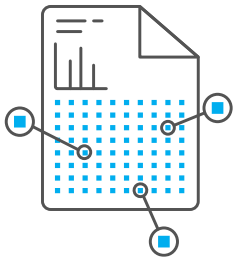
Moderna's AI factory

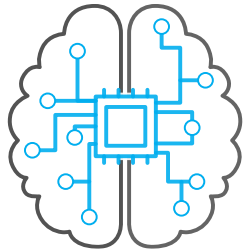
Data



Structured Data Capture & Integration

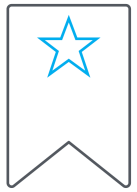
Algorithm Research & Development

Cloud & DevOps Infrastructure

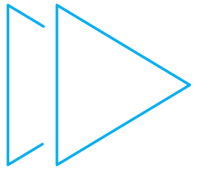


AI Model Design

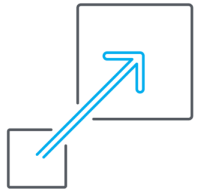
Rapid Production Deployment



Quality



Speed



Scale

Cost

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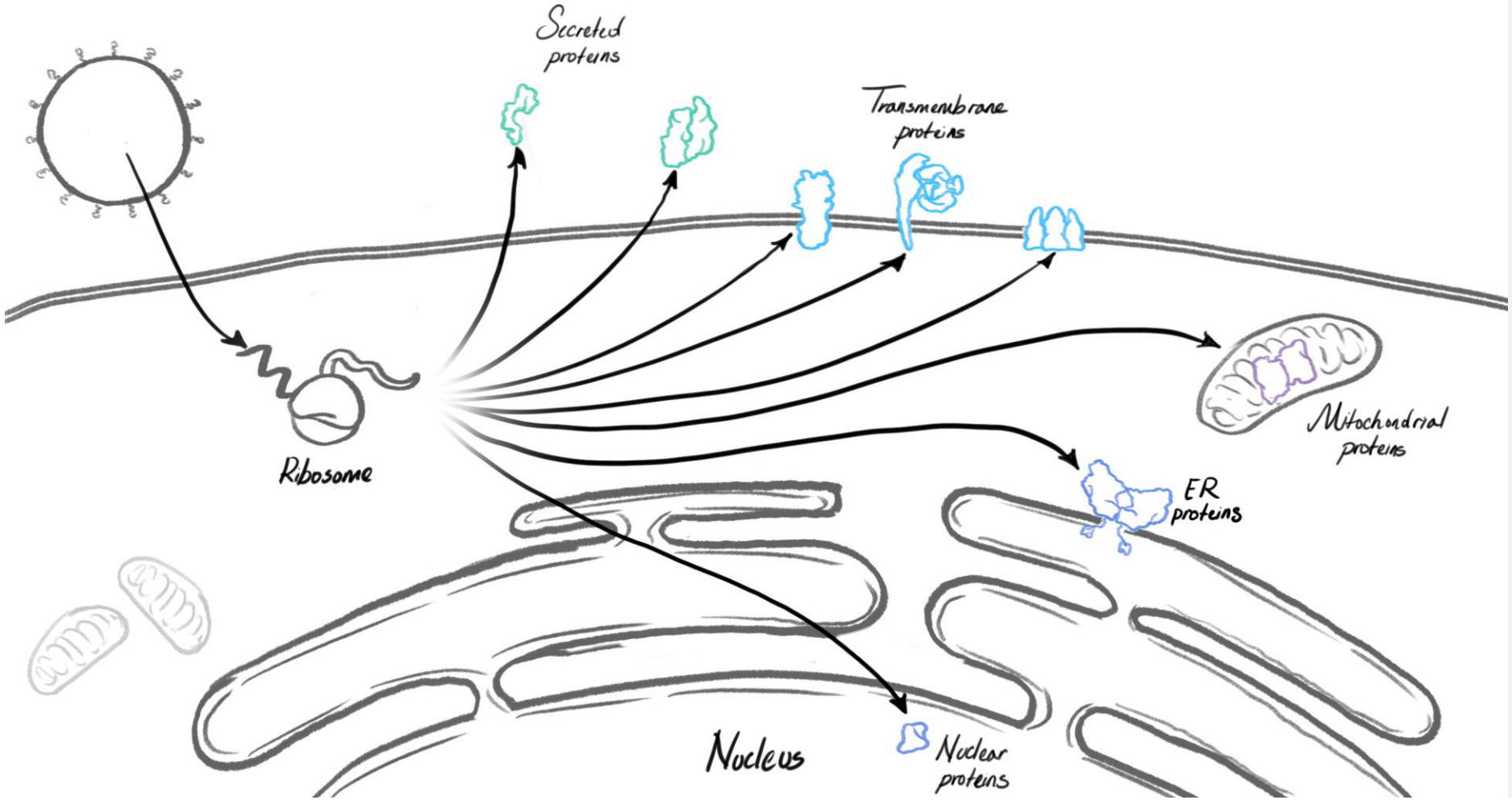
Q&A

mRNA as a potential new class of medicines



1. Large product opportunity
2. Higher probability of technical success
3. Accelerated research and development timelines
4. Greater capital efficiency over time vs. recombinant technology

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Thank you!