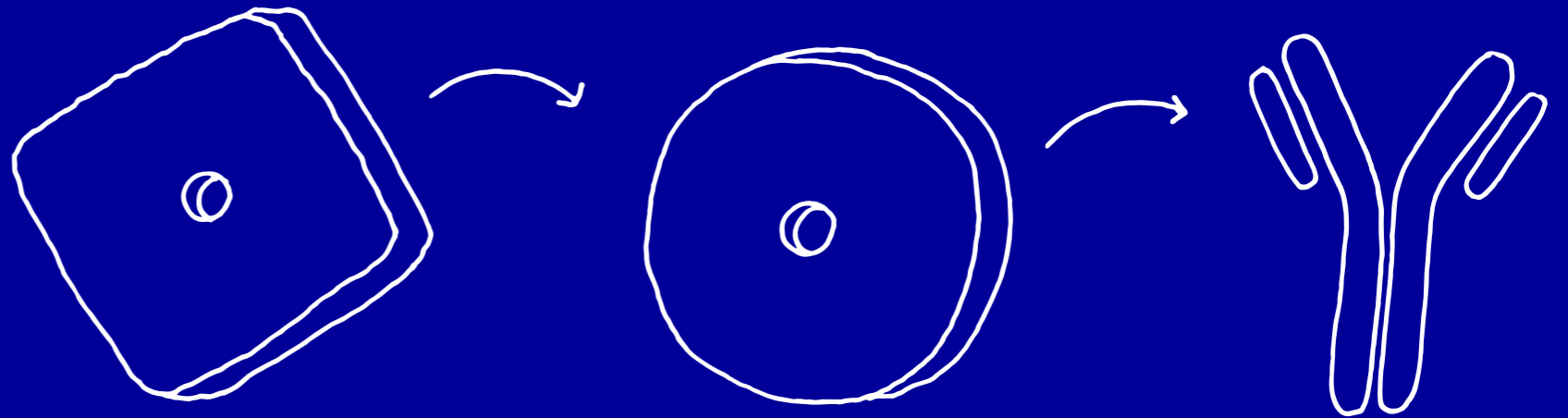


Paradigm shift in biologics





Cautionary statement regarding forward-looking statements

Information set forth in this presentation contains forward-looking statements, which involve a number of risks and uncertainties. All statements other than statements of historical fact are forward-looking statements, which are often indicated by terms such as “anticipate”, “believe”, “could”, “estimate”, “expect”, “goal”, “intend”, “look forward to”, “may”, “plan”, “potential”, “predict”, “project”, “should”, “will”, “would” and similar expressions. The forward-looking statements contained herein represent the judgement of Evotec as of the date of this presentation. Such forward-looking statements are neither promises nor guarantees, but are subject to a variety of risks and uncertainties, many of which are beyond our control, and which could cause actual results to differ materially from those contemplated in these forward-looking statements. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any such statements to reflect any change in our expectations or any change in events, conditions or circumstances on which any such statement is based. Given these risks, uncertainties, and other factors, you should not place undue reliance on these forward-looking statements.



Let's talk about biologics

2nd Capital Markets Day 2022



Werner Lanthaler
CEO



Matthias Evers
CBO



Craig Johnstone
COO



Linda Zuckerman
EVP, Global Head of
Biotherapeutic



Randal Ketchem
SVP Discovery &
Molecular Design



Randal Bass
SVP Process Design
Biotherapeutic Science



John Erickson
Veteran industry leader
in biologics
Guest Speaker



Welcome

Just – Evotec Biologics

Overview



A highly attractive market with challenges that we will master

Tremendous opportunity to make best molecules

Biologics CDMO (external)
market

>> **US\$ 10 bn**

CAGR through 2030

> **7%**

Top 10 medications

> **40%**

Unserved indications

7,000

High prices prohibitive for many

70%

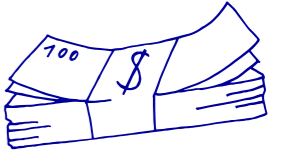
Underserved regions
without access

6 bn

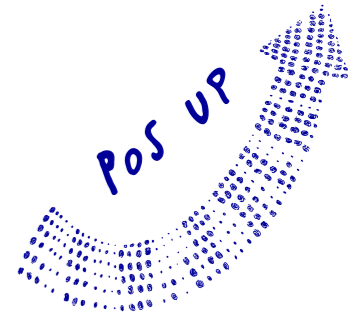
Preparedness & rapid response

> **12 months**

Lower costs



**Higher
probability
of success
(PoS)**



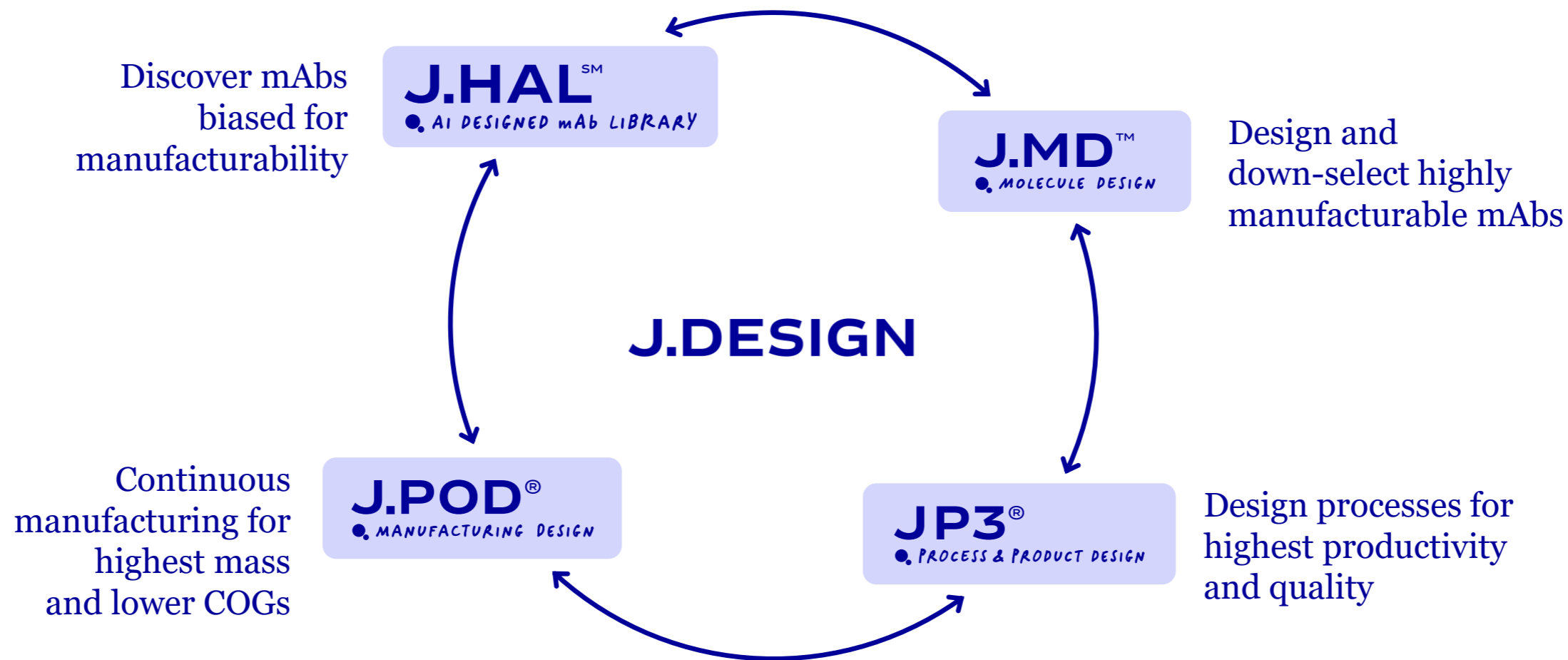
**Highest quality
& agility**





Combining critical capabilities to develop medicines that matter and provide access

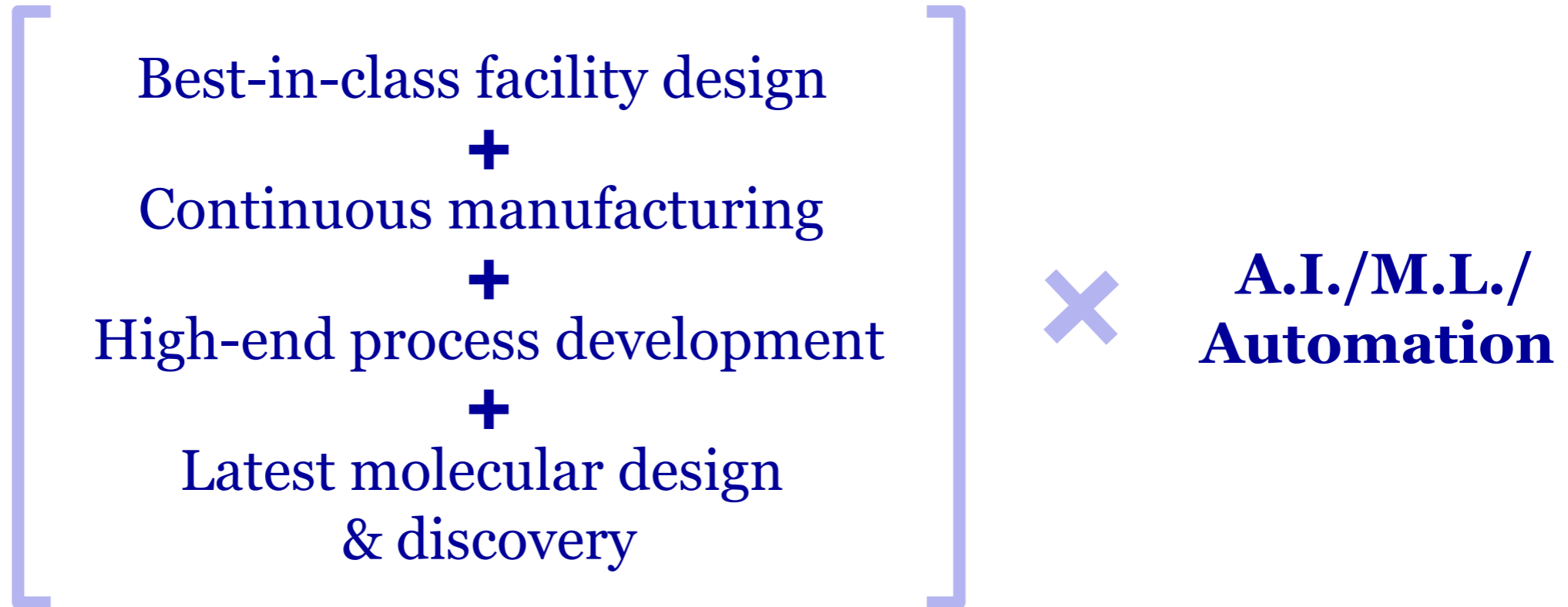
Capturing the market requires a paradigm shift





Leading across all relevant dimensions – A.I./M.L./Automation

Our underlying differentiators





For us A.I. & M.L. are not just buzzwords

Consistent implementation of A.I./M.L./Automation



Lisa Connell-Crowley

VP Process & Product Design & Seattle Site Head

“**Intensifying and shrinking production processes** are key factors for **improving the economics of biologics manufacturing** – rapid identification of **process parameters** for intensified, continuous manufacturing is critical for reducing time to the clinic – therefore we use and continue to **invest in HTS and automation technologies as part of process design.**”



Randal Ketchem

SVP Discovery & Molecular Design

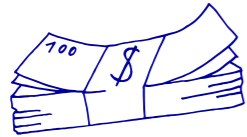
“*Before we invested in wet-lab equipment the very first thing we bought at Just – Evotec Biologics were computers – with those we have built an **integrated data infrastructure** to register, track, and utilize our data across projects – that is just one example of how we **apply data science and A.I./M.L. consistently.***”



J.POD® – best-in-class biologics facility worldwide

Three key points to remember on your tour

Lower costs



From

Cost/gram >US\$ 150

Large infrastructure footprint

Billion dollar facilities

Scale-up

Fixed capacity

Long construction time (5 years)

Screening for the best antibody

High level of manual labor

Long-time in media

To

Cost/gram <US\$ 50¹

Small J.PODs® for continuous manufacturing

Facilities that require less CAPEX

No scale-up

Flexible capacity

Short construction time

Designing the antibody fit for purpose via A.I./M.L.

High level of automation

Fresh out of the cell

Higher probability of success (PoS)



Highest quality & agility





Agenda

9.00 – 9.30 am	Registration
9.30 – 11.00 am	Site Tour – Overview and tour preparation
11.00 am	Start of webcast
11.00 – 11.30 am	Action Plan 2025
11.30 – 12.15 pm	Paradigm shift in biologics – From A.I./M.L.-based discovery to agile commercial manufacturing
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2.15 – 3.00 pm	Roundup & Q&A session



Action Plan 2025

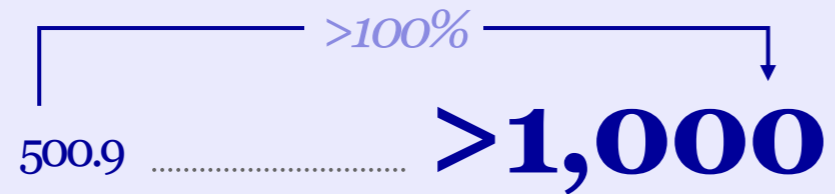
*... more than **Just** a beginning!*



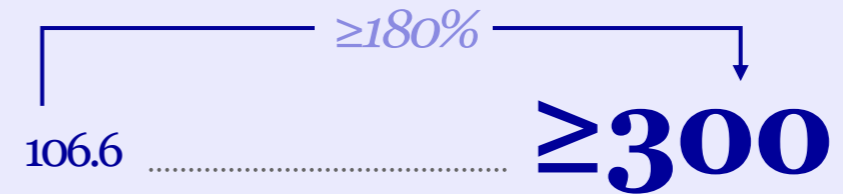
Recap: Our mid-term aspirations at a glance

2020-2025 estimated key performance indicator goals¹

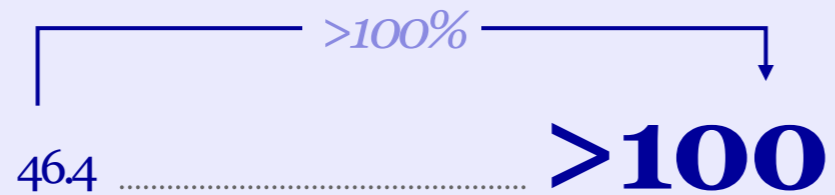
Group revenues
in € m



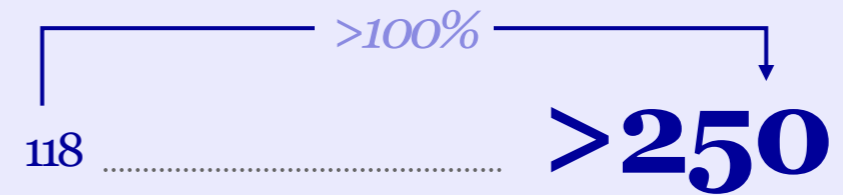
Adjusted group EBITDA
in € m



Unpartnered R&D
in € m



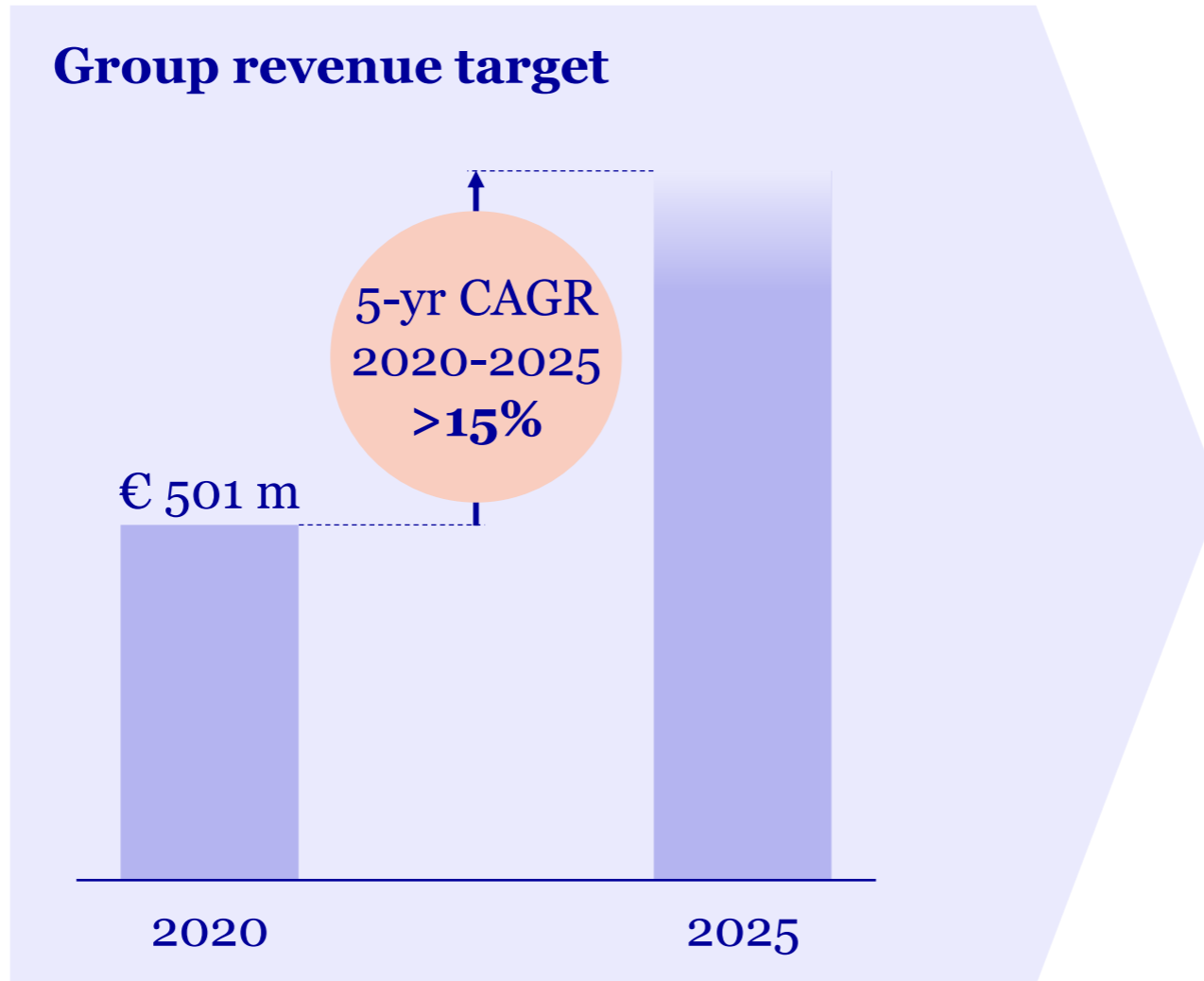
Co-owned projects²





Group revenue goal > € 1,000 m by 2025 well within reach

Action Plan 2025 in full swing



CAGR 2020-2022e

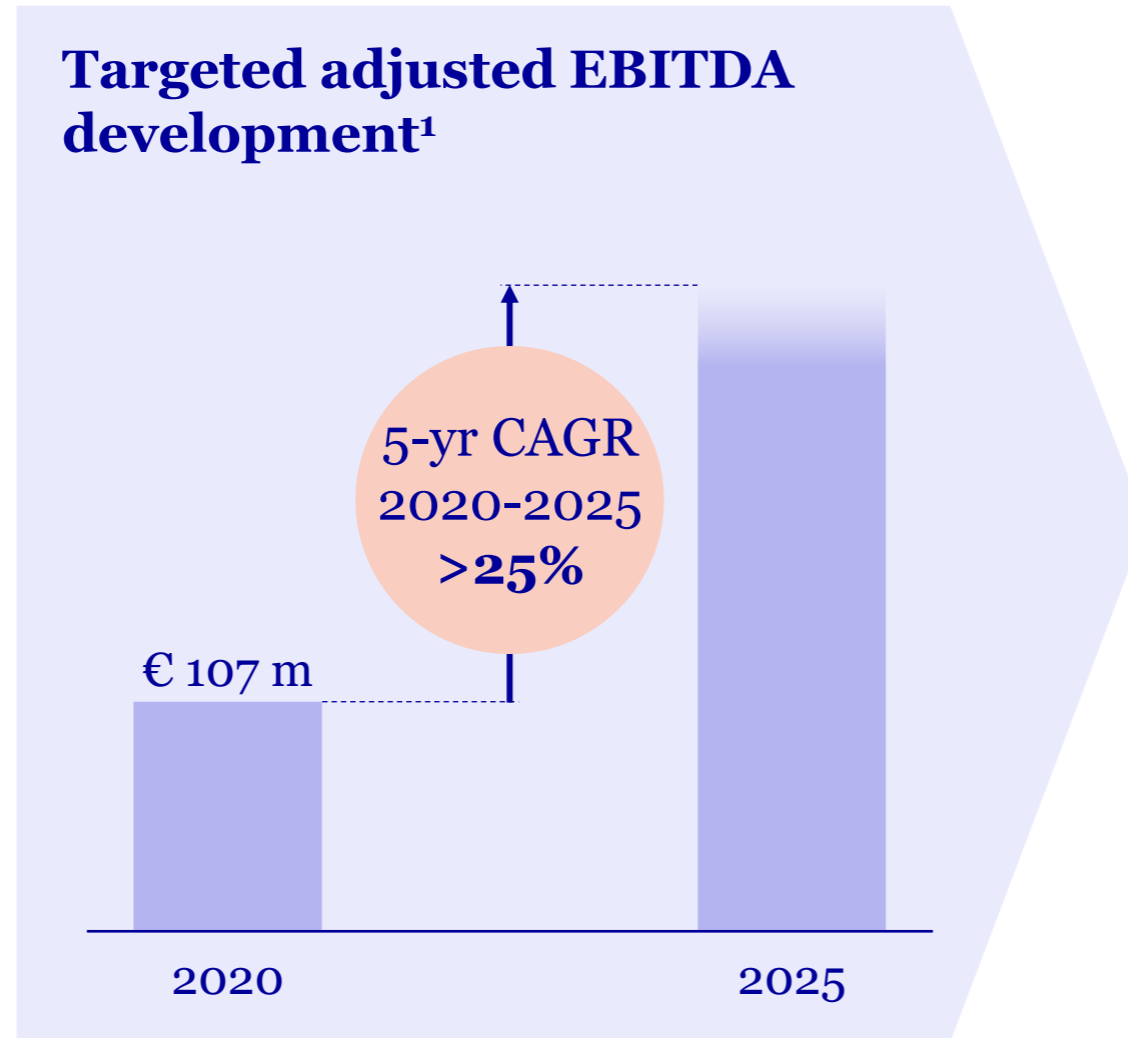
+20%

- Very strong growth of group revenues
- Shared R&D picking up further momentum despite biotech funding slow-down
- Just – Evotec Biologics in start-up phase



Commitment to innovation drives growth & long-term profitability

Targeting adjusted EBITDA \geq € 300 m by 2025



5-year adj. EBITDA CAGR 2020-2025 to reach >25% due to

- Operating leverage of broader platform and expanded manufacturing
- Growth of co-owned pipeline leading to increasing contribution from milestones
- Precision medicine platforms drive success sharing models



Industry at a pivotal moment

A shared economy platform in R&D

Need for more precision

Most drugs still provide benefit in only 50% of patients

Need for better disease understanding

Lifetime risk for cancer e.g. 44% in men & 38% in women

Need for wider access

Only 10% of world's population have access to life changing biotherapeutics

Our focus areas

PanOmics¹

iPSC-based Cell Therapies

Just - Evotec Biologics

End-to-End Shared R&D



Together for medicines that matter

Game changers

More precise medicine

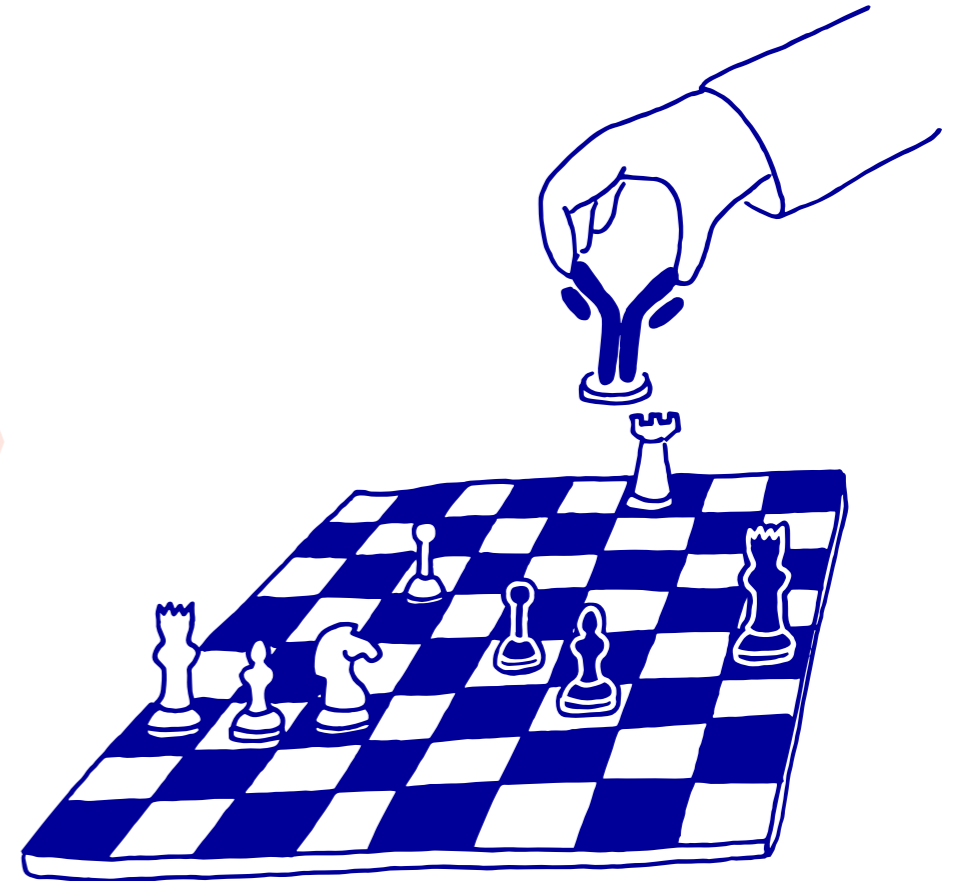
PanOmics databases, multi-modality end-to-end shared drug discovery & development

A.I./M.L. & technology convergence

Latest technologies coming together with drug discovery & development, molecular diagnostics

Best talent & right business model

*Innovation – Collaboration –
Entrepreneurship –
From fixed to variable costs*





Opportunity and right to win by focus area within Action Plan 2025

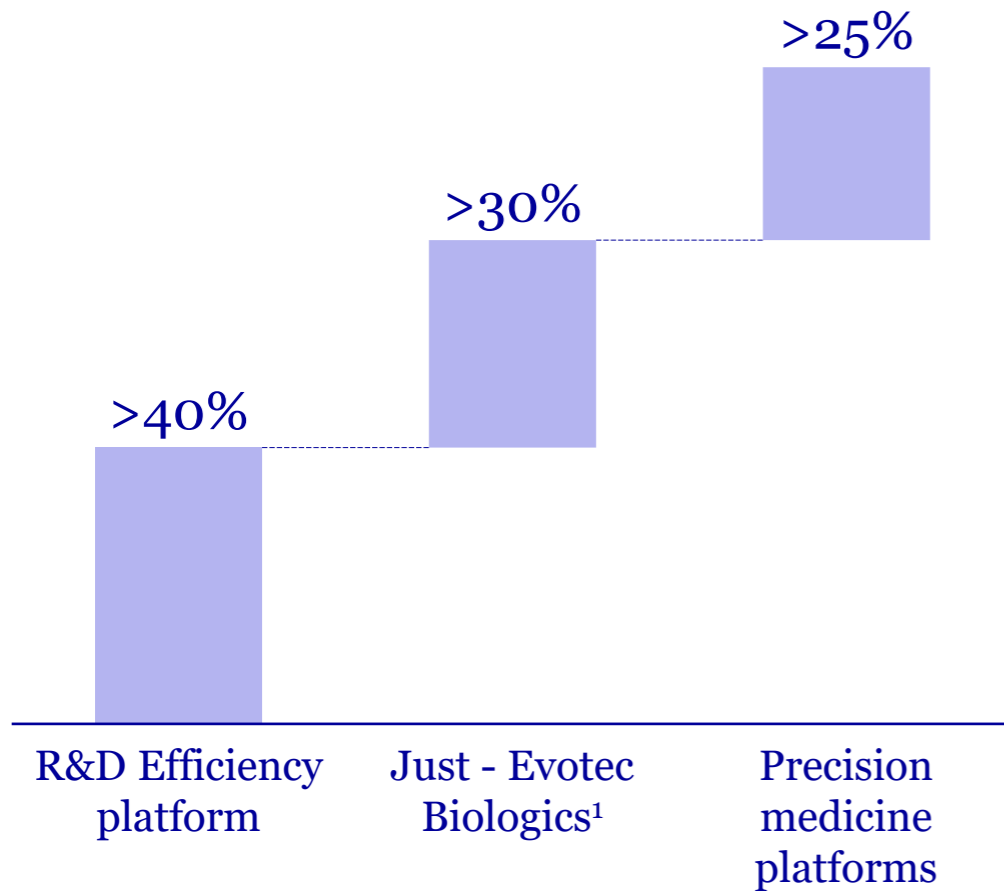
	What	How
<i>PanOmics</i>	Disease understanding to redefine diseases via multi-omics, patient-driven drug design; step-up probabilities of success & productivity	Leading footprint at scale, esp. in transcriptomics and proteomics, molecular patient databases with data analytics (PanHunter)
<i>iPSC-based Cell Therapies</i>	Potential for cures (e.g., diabetes, oncology) overcoming access challenges to cell therapies with off-the-shelf-solutions	Leading fully integrated iPSC capability at scale
<i>Just - Evotec Biologics</i>	Disruptive technology to offer lowest cost, highest quality biologics in fully flexible approach	First-to-industry continuous manufacturing; capacity available, expansion in progress
<i>End-to-End Shared R&D</i>	Most efficient, highest quality external R&D solutions	Industry leading problem understanding with best track record and latest technologies



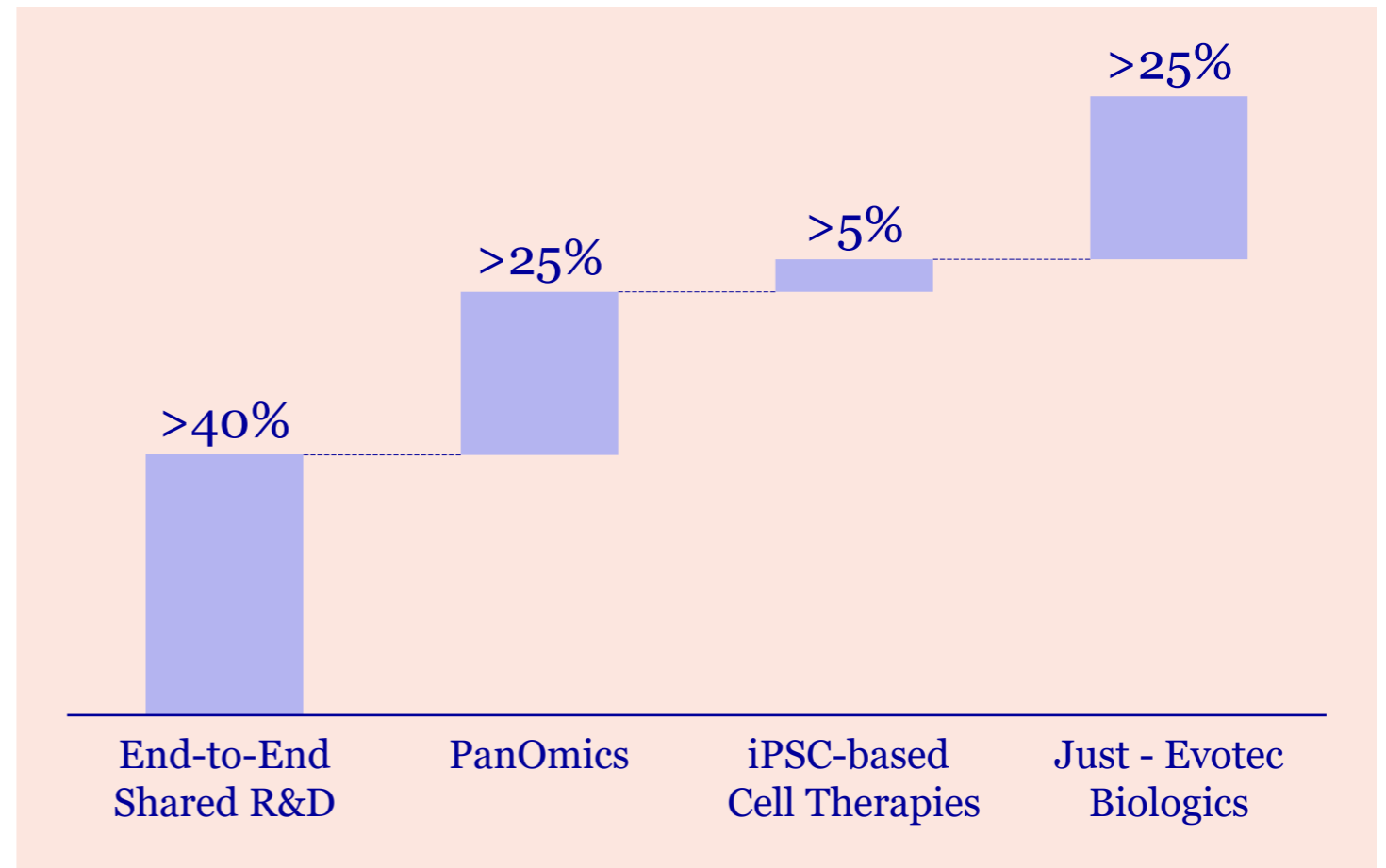
More balanced revenue mix at slightly higher than anticipated volume by 2025

Differentiating platforms show upside and long-term growth

Targeted revenue composition 2025



Contribution with focus areas by 2025

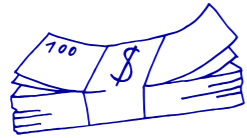




Today's focus is on better biologics derived from a new paradigm

The paradigm shift

Lower costs



From

Cost/gram >US\$ 150
Large infrastructure footprint
Billion dollar facilities

Scale-up
Fixed capacity
Long construction time (5 years)

Screening for the best antibody
High level of manual labor
Long-time in media

To

Cost/gram <US\$ 50¹
Small J.PODs[®] for continuous manufacturing
Facilities that require less CAPEX

No scale-up
Flexible capacity
Short construction time

Designing the antibody fit for purpose via A.I./M.L.
High level of automation
Fresh out of the cell

Higher probability of success (PoS)



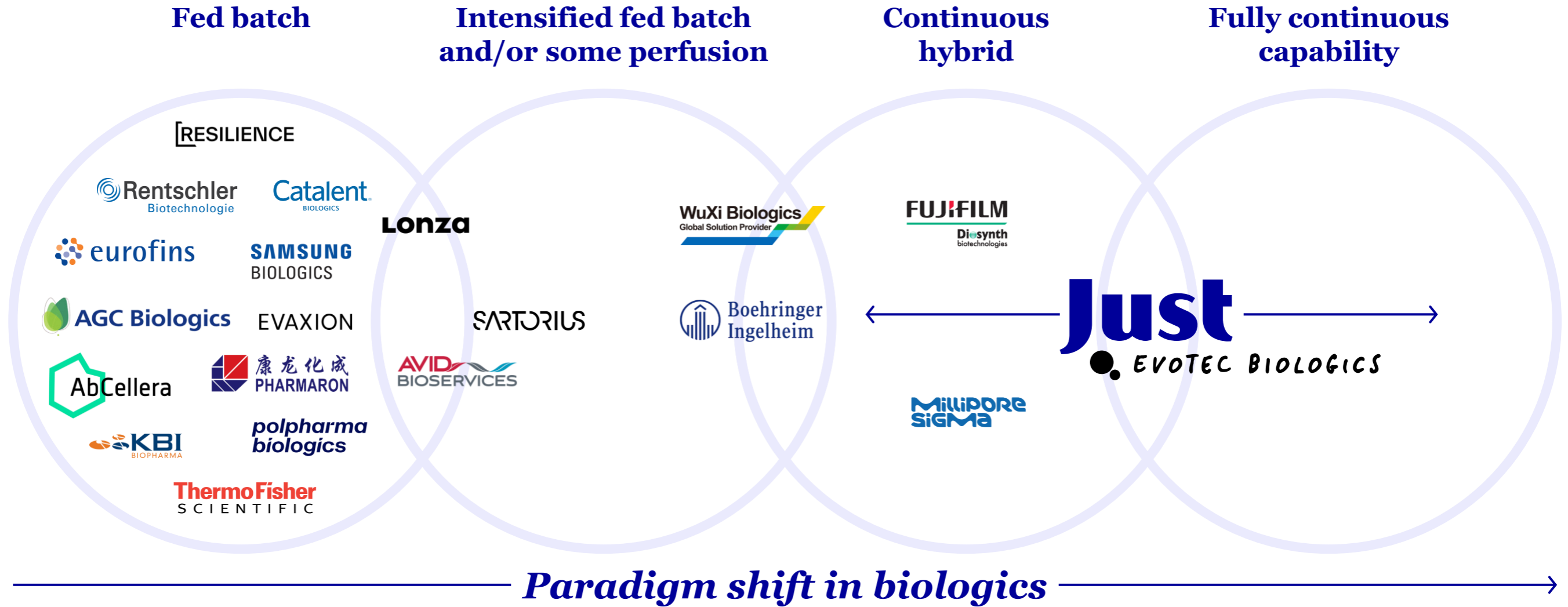
Highest quality & agility





Continuous manufacturing is at the center of our commercial value proposition

Illustrative assessment of capabilities across the industry (highly simplified)



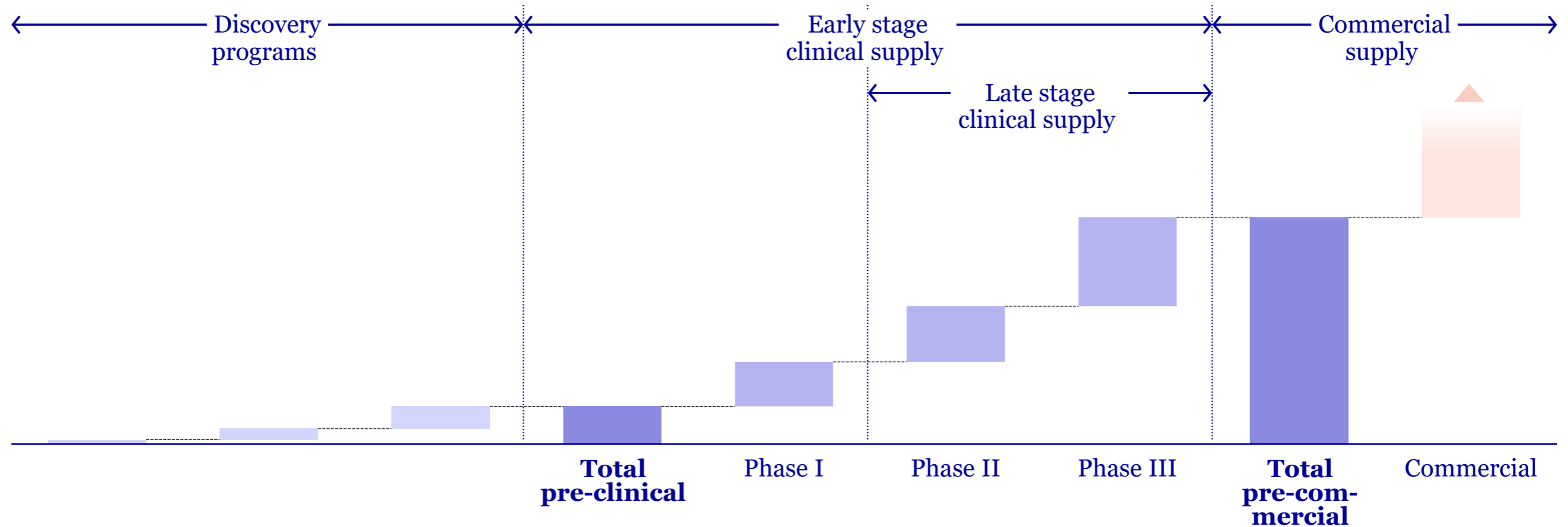


Advancing towards late stage and commercial programs over time

Just - Evotec Biologics supports full development vision for biologics

Archetypical development of revenue cascade

(non-probability weighted; illustrative)

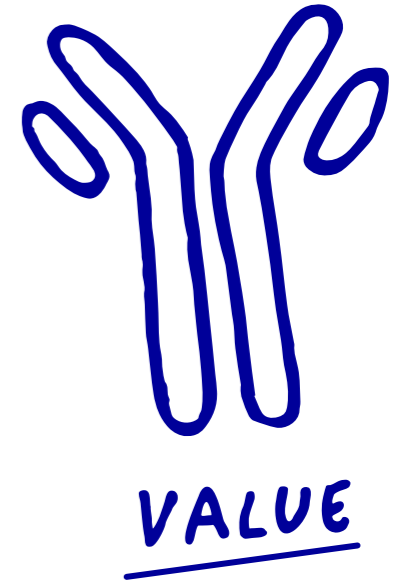
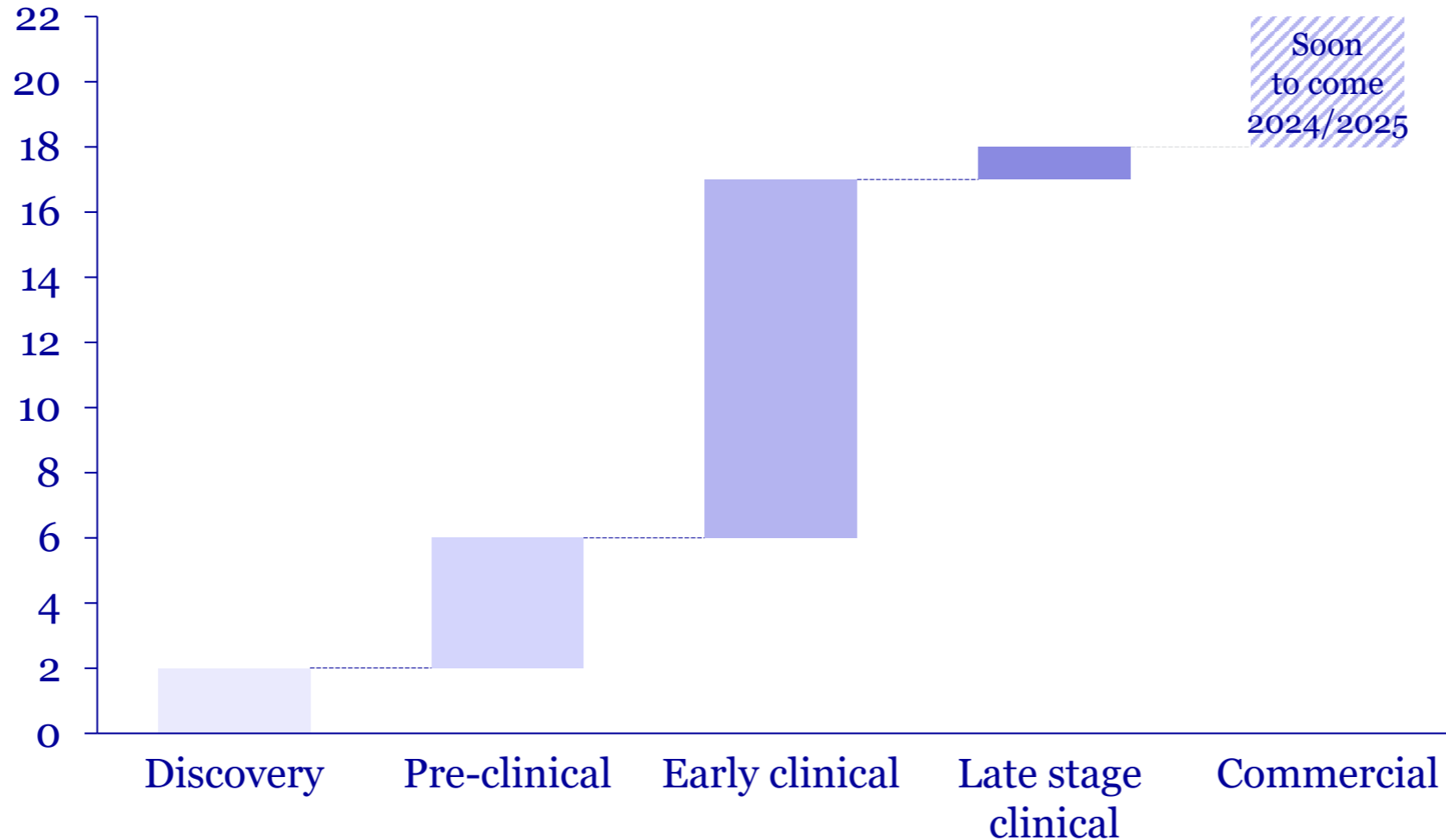




Rapid growth towards commercial programs together with our partners just started

Early discovery and pre-clinical programs build a robust pipeline towards commercial contracts

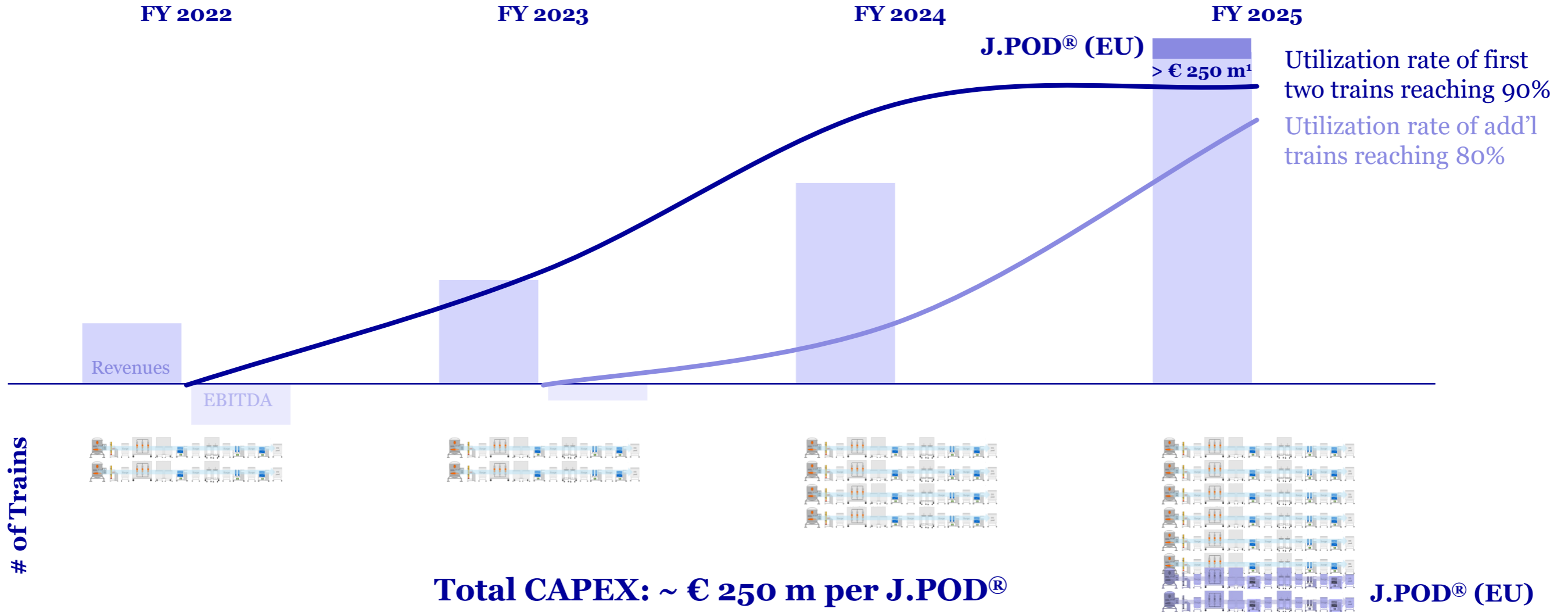
Number of programs





Capacity building up over time

Relation between capacity, utilization and revenues

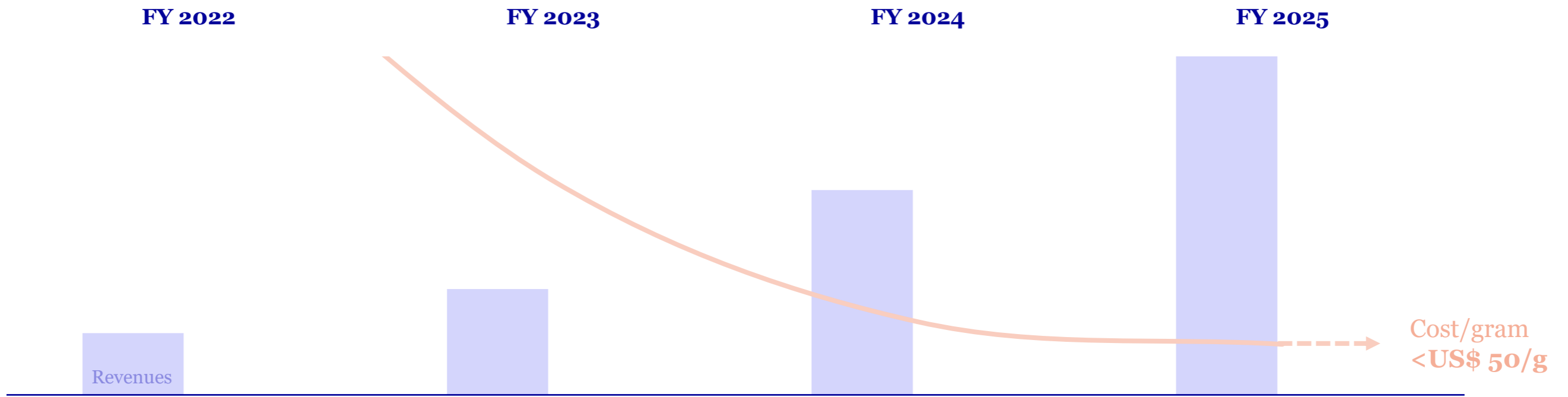


of Trains



Technology leadership leading to cost advantages

Relation between unit costs and revenues

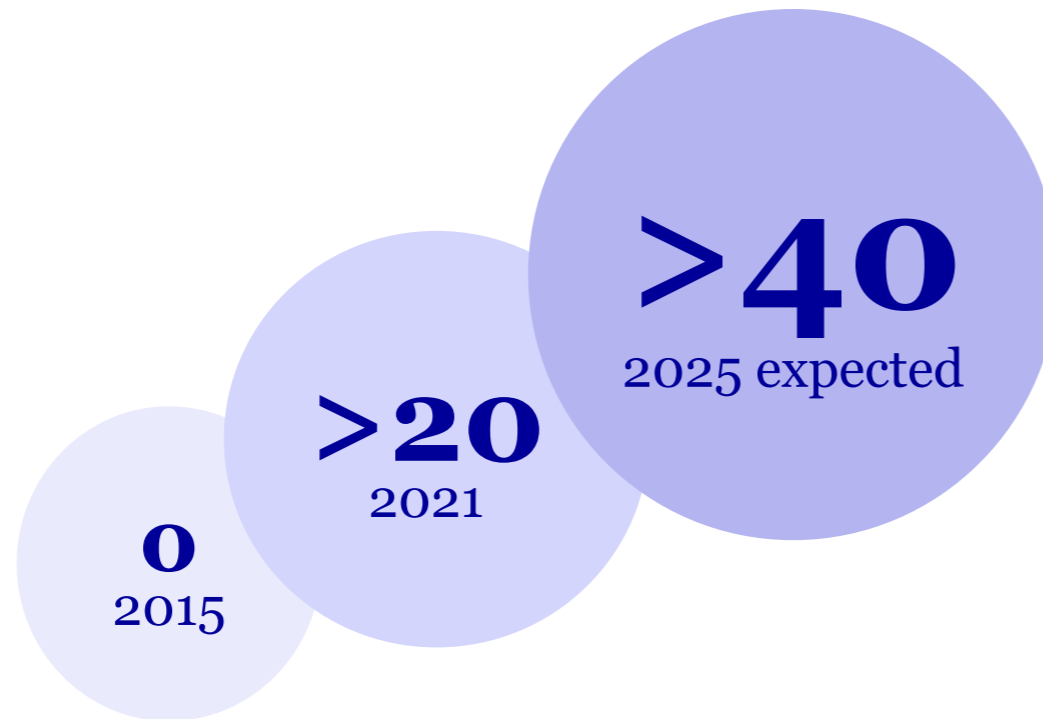




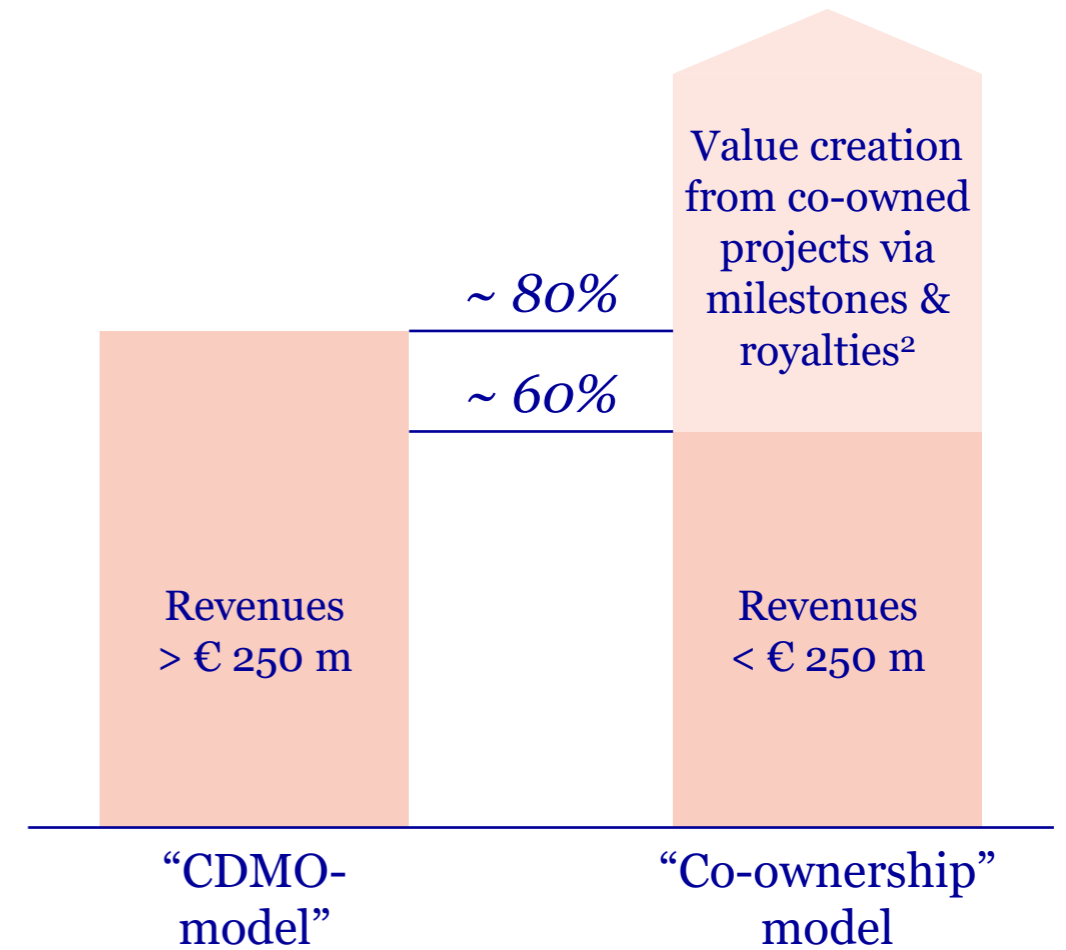
Co-ownership leading to value creation upside

High-value partnerships offer path to increased royalties

Co-owned biologics pipeline assets¹⁾



Business model options

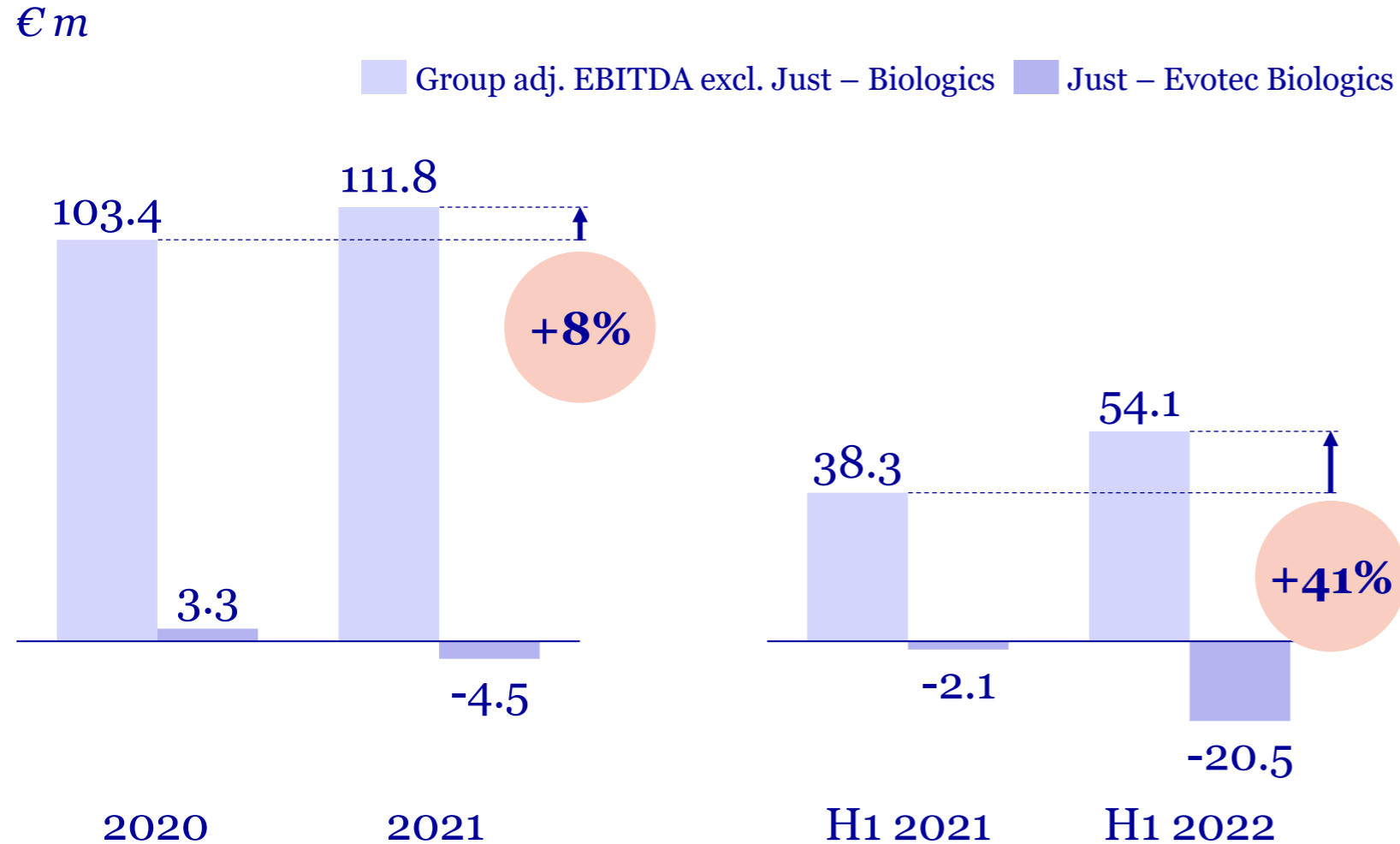




Evotec with strong base business momentum

Leading innovation at balanced risk

Accelerating EBITDA growth in first six months



Stronger than ever base business

Higher unpartnered R&D
spend

Profitable business even in
periods with lower milestones,
upfronts and licenses

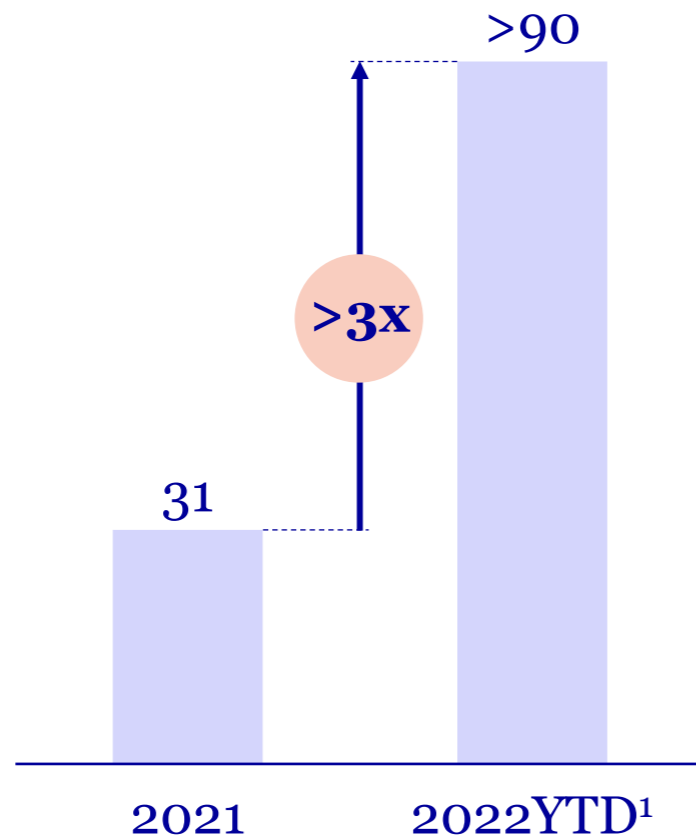
Start-up of
Just - Evotec Biologics in
full swing



We are making progress in expanding the partnering pipeline

Summary of commercial progress 2022

Just – Evotec Biologics Closed Sales *Sales in € m*



- Closed Sales is leading indicator of future 2023 and 2024 revenues
- Closes Sales 2022 show strong growth – indicates market entry progressing and future potential
- Business Development is ramping up further to maximize partnering opportunities, particularly in U.S. and Europe



A paradigm shift takes persistence and time

Case study: Tesla Inc.

Paradigm shifts take time

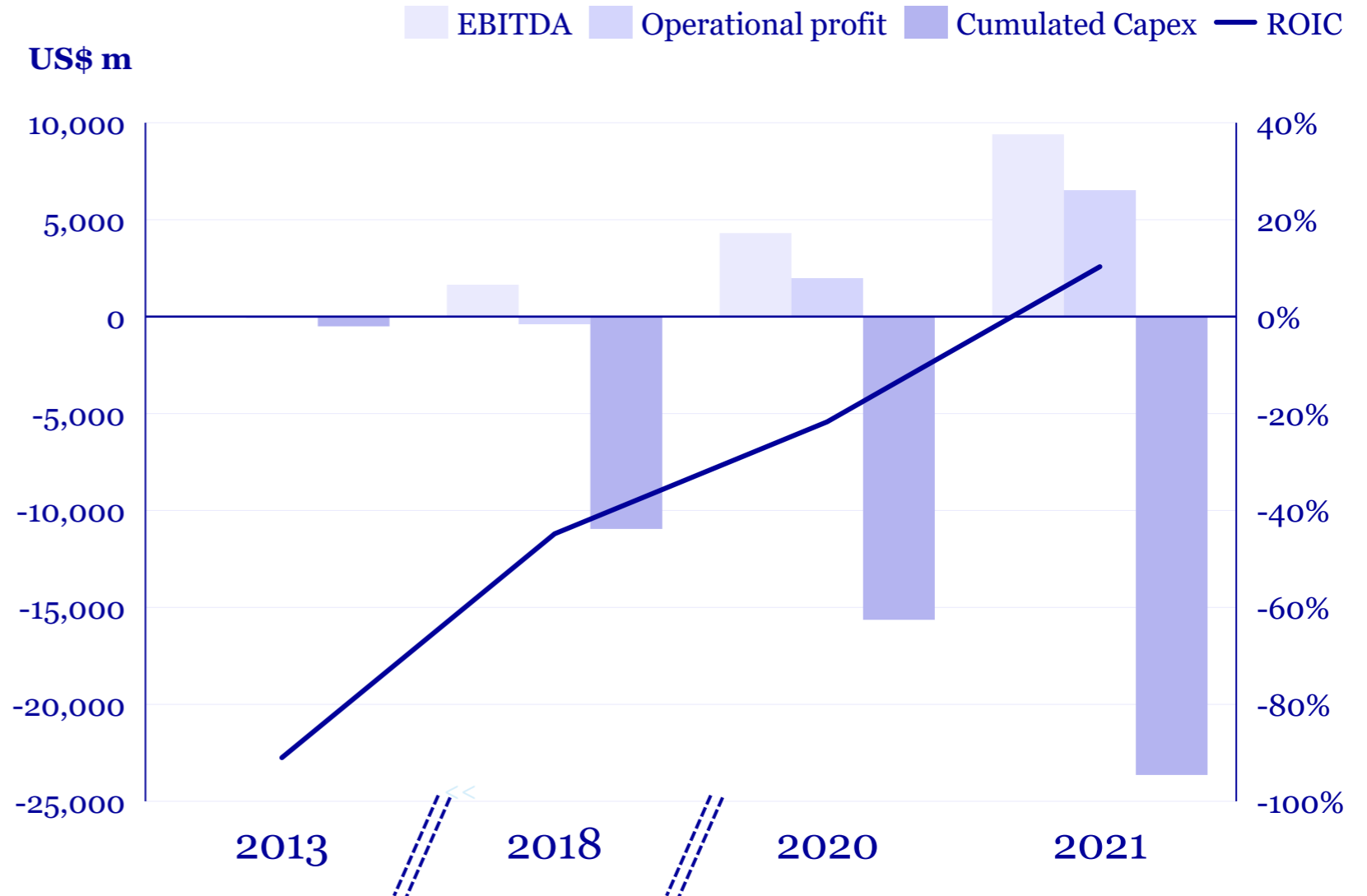
Foundation: 1 July 2003

> US\$ 23 bn capex in last 10 years

Sustained positive EBITDA as of 2018

2020 first year with positive operational result

First year with positive ROIC: 2021





Imagine if COGs was < US\$ 50 per gram?

- Underserved indications and multiple combination treatments
- Access to underserved populations and stress reduction for healthcare systems
- Access to life saving therapies for underdeveloped regions
- Rapid response in global health & pandemic situations

**Together
for medicines
that matter**





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Paradigm shift in biologics

*From A.I./M.L.-based
discovery to agile commercial manufacturing*



Experienced leadership team dared to dream

>500 combined years of expertise

Team (current role and experience)

Linda, Zuckerman, PhD

EVP, Global Head of Biotherapeutics, 20 years



Christelle Dagonneau, PhD

SVP Global BD Biologics, 21 years



Randal R. Ketchem, PhD

SVP Discovery & Molecular Design, 25 years



Randal Bass, PhD

SVP Process Design Biotherapeutic Science, 20 years



Sundar Ramanan, PhD MBA

SVP Global Biotherapeutic Quality, 22 years



Ben Castro

VP Manufacturing Ops & JPOD® Site Head, 26 years



Caren Tidwell, PhD

VP Grants and Contracts, 28 years



Lisa Connell-Crowley, PhD

VP Process & Product Design & Seattle Site Head, 23 years



Magnus Schroeder, PhD

VP Process & Product Design, 19 years



Eva Gefroh

VP Technical Ops, 24 years



Valerie Alvarado

VP Capital Projects, 25 years



Vasant Gandhi, PhD, ESQ

VP Corporate Development, 24 years



Caroline Chan

VP Human Resources, 26 years



Dan Rasmussen, MBA

VP Finance, 18 years



Debbie Banner

Chief of staff, 25 years



Alumni

Jim Thomas



Dean Pettit



Victor Fung

Consulting on supply chain resiliency

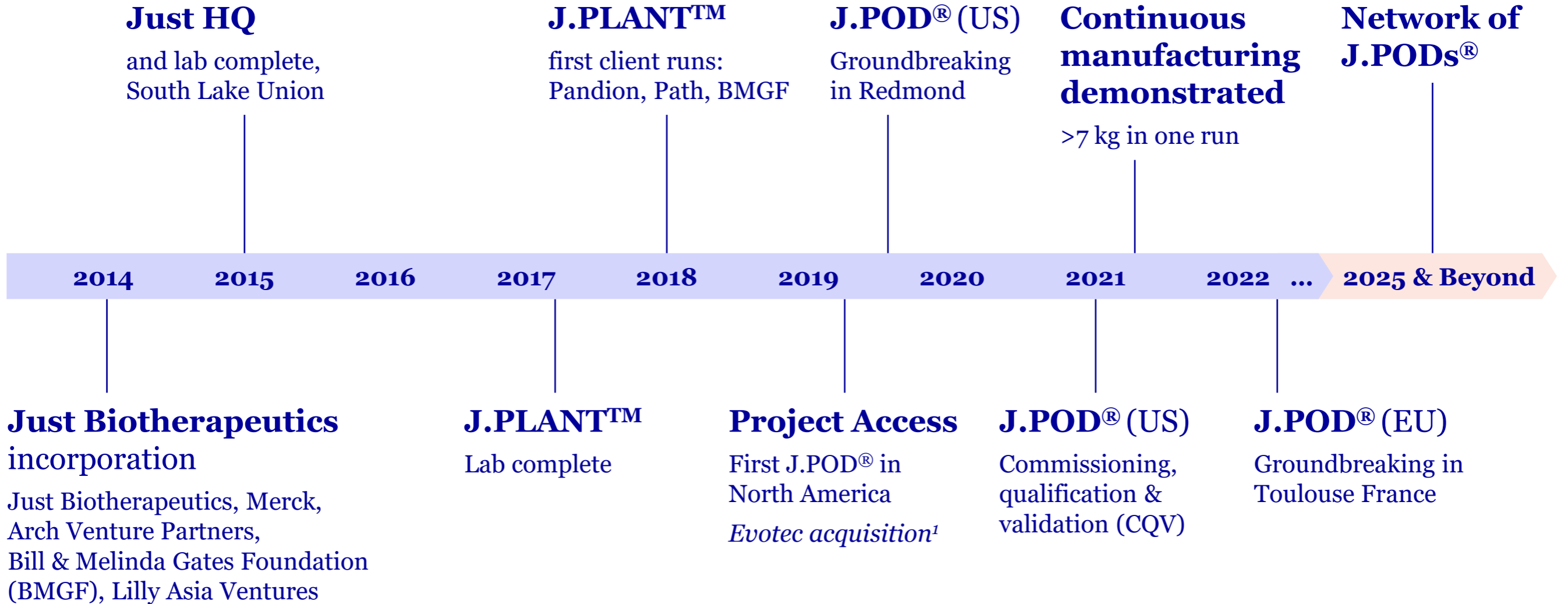


BLAs for Enbrel® , Vectibix® , Prolia® , Repatha® , XGEVA® , adalimumab (AMJEVITA™), bevacizumab (MVASI™)



We are on a journey to provide better access to biologics










Timeline





The paradigm shift is already in motion

Accelerating the paradigm shift in biologics day-by-day

Current state	Future state	Just EVO TEC BIOLOGICS	<i>Others</i>
 <p data-bbox="568 560 1134 608">Stainless steel fed batch</p> <p data-bbox="568 735 1176 783">Facility cost >US\$ 500 m</p> <p data-bbox="568 879 1134 991">Separate upstream & downstream processing</p> <p data-bbox="568 1086 950 1134">Fixed cost focus</p>	Flexible & agile capacity		
	Facility cost << US\$ 500 m		
	Fully integrated platform		
	Variable cost focused		



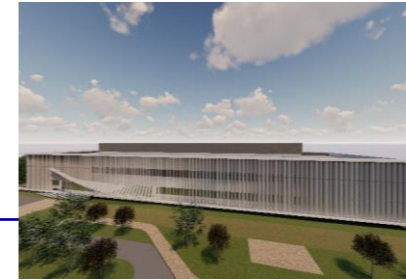
Global manufacturing network is “Just at the beginning”

J.POD® – Status and timing



J.PLANT Seattle, Washington, US

- 500L SUB
- Phase I – Clinical
- Over 34 runs
- 100% success 3 years



J.POD® Toulouse, France, EU

- 500L & 1,000L SUB
- Phase I – Commercial
- Groundbreaking 2022
- Expected CQV 2024



J.POD® Redmond, Washington, US

- 500L & 1,000L SUB
- Phase I – Commercial
- First cGMP run Oct 2021

Cloning of J.POD® facilities

Supply resilience

Facilitate global access

Global health & pandemic preparedness



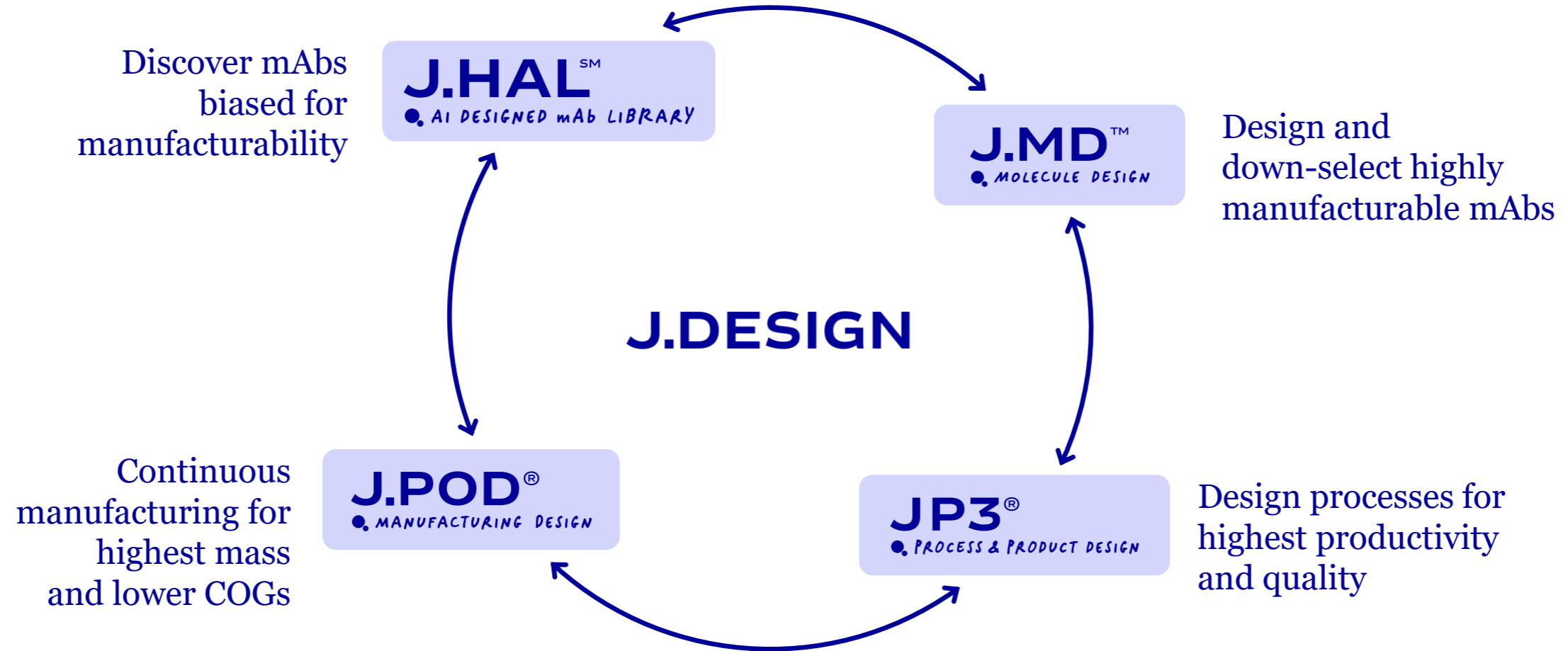
***Our technology:
Paradigm shift in biologics***

*From A.I./M.L.-based
discovery to agile commercial manufacturing*



We will capture the market by introducing a paradigm shift

Integrating critical capabilities to develop medicines that matter and provide access





How we change the biologics value creation paradigm

Just – Evotec Biologics value drivers





We change the value creation paradigm for biologics

Just – Evotec Biologics value drivers as proven in recent projects



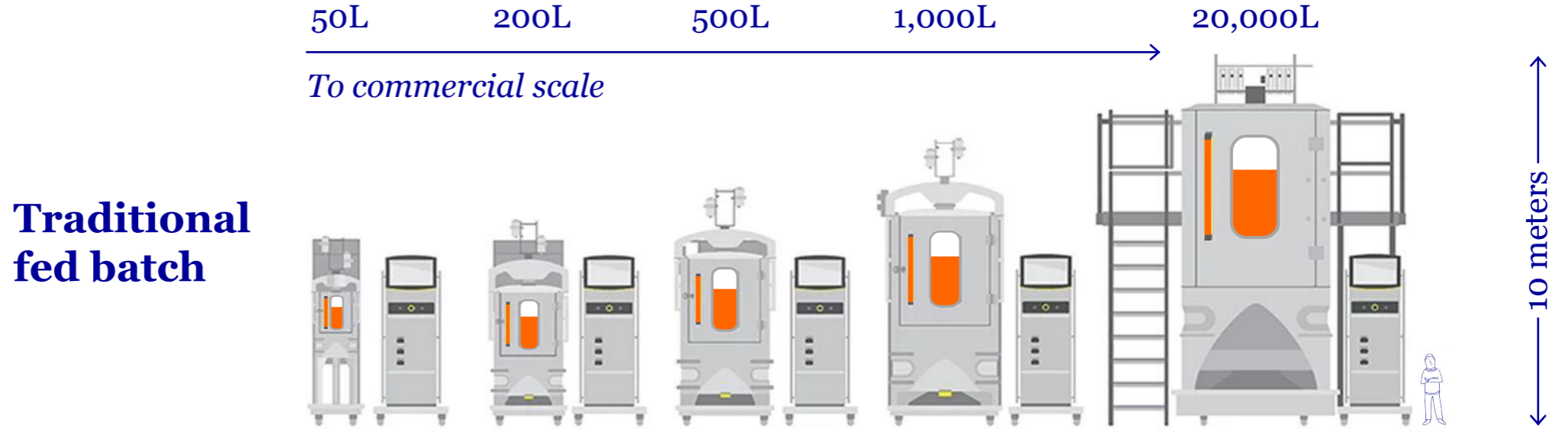
- 1.** No need to scale up from clinical to commercial
- 2.** Ability to build a new J.POD® facility < 24 months
- 3.** Add additional trains/capacity in < 12 months
- 4.** Change over time between products < 2 days



1. No need to scale up from clinical to commercial

Typical scale-up for a commercial mAb vs. Just - Evotec Biologics process

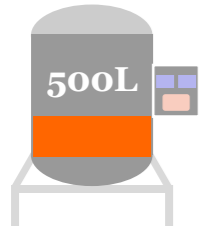
- For US\$ 1 bn mAb capability, every month lost during tech transfer is about US\$ 80 m¹
- Each scale up takes months and costs US\$ 100,000s - US\$ 1 m²
- Tech transfers to CDMOs or for larger scales are risky²





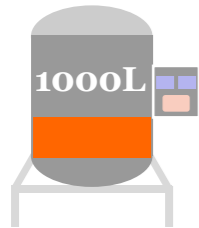
1. No need to scale up from clinical to commercial

Bioreactor duration can be extended with steady-state continuous perfusion technology



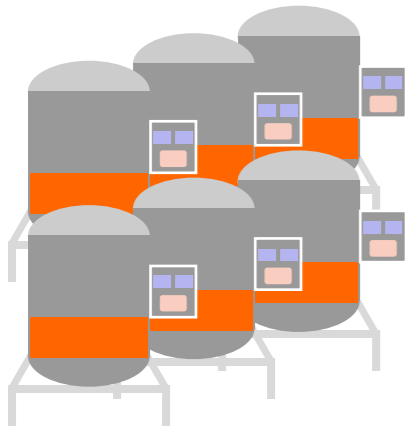
15-day process

Early-stage clinical trial
5-8 kg drug substance per run



25-day process

Late-stage clinical trial
35-38 kg drug substance per run



25-day process

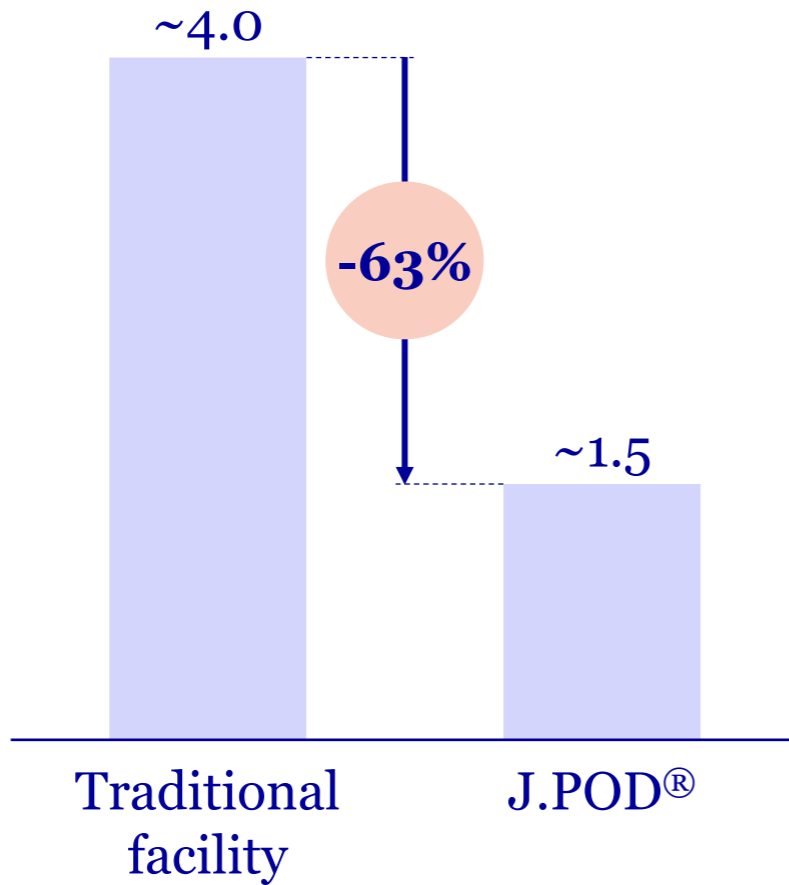
Commercial
2000 kg drug substance per year



2. Ability to build a new J.POD[®] facility < 24 months

Timelines to build a J.POD[®] or add capacity

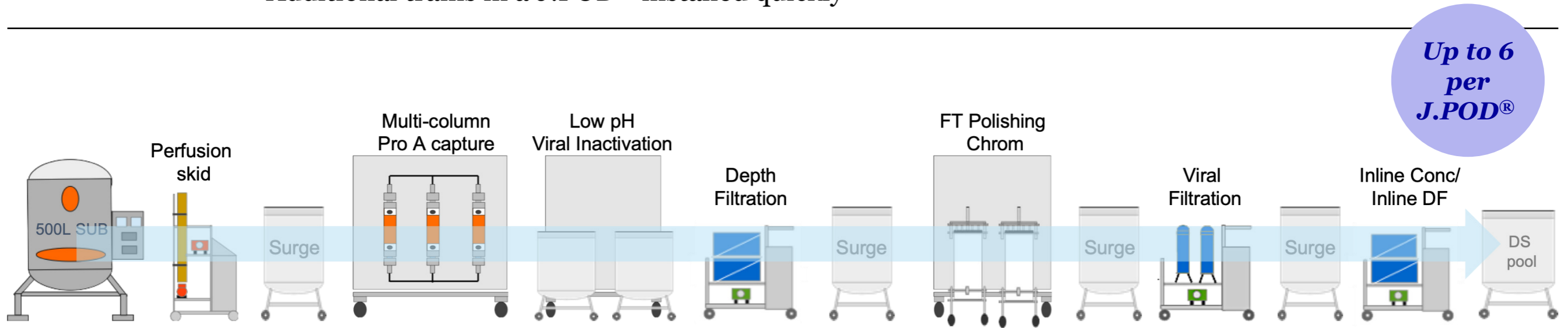
Time to set up a J.POD[®] is short
Years





3. Add additional trains/capacity in < 12 months

Additional trains in a J.POD® installed quickly



Additional trains can be added into an existing facility

- Maximum flexibility for build out of facilities
- Limited CAPEX at the beginning
- Fully adjustable to clinical and market needs

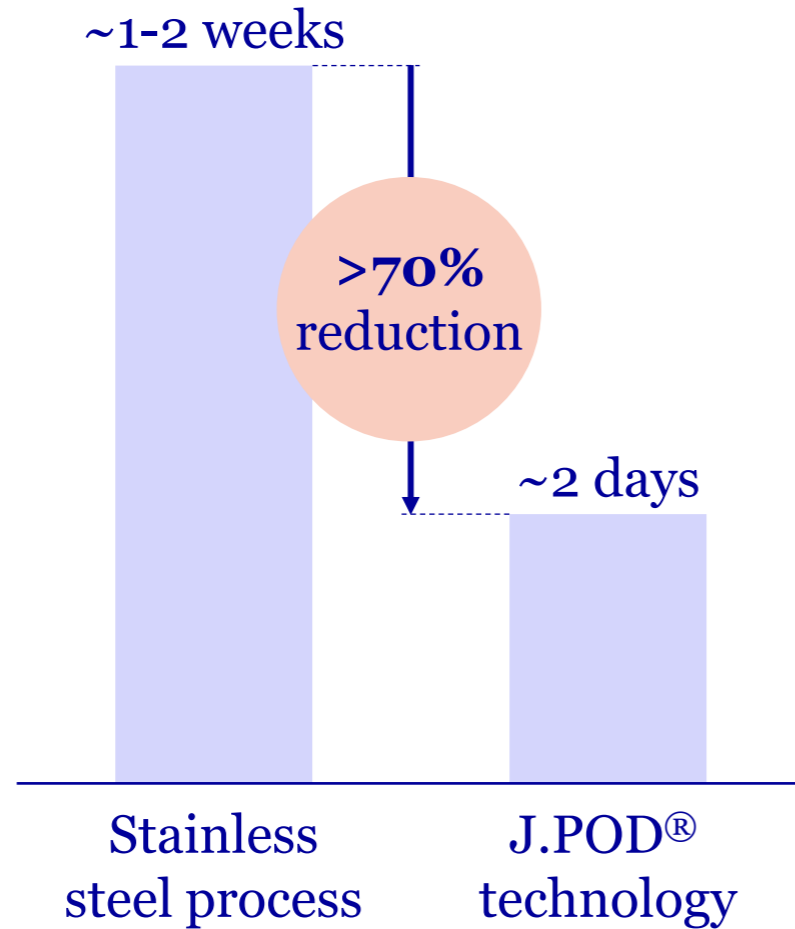
Less than
12 months



4. Change over time between products < 2 days

Timeline to change from product A to B

Change over in manufacturing is fast

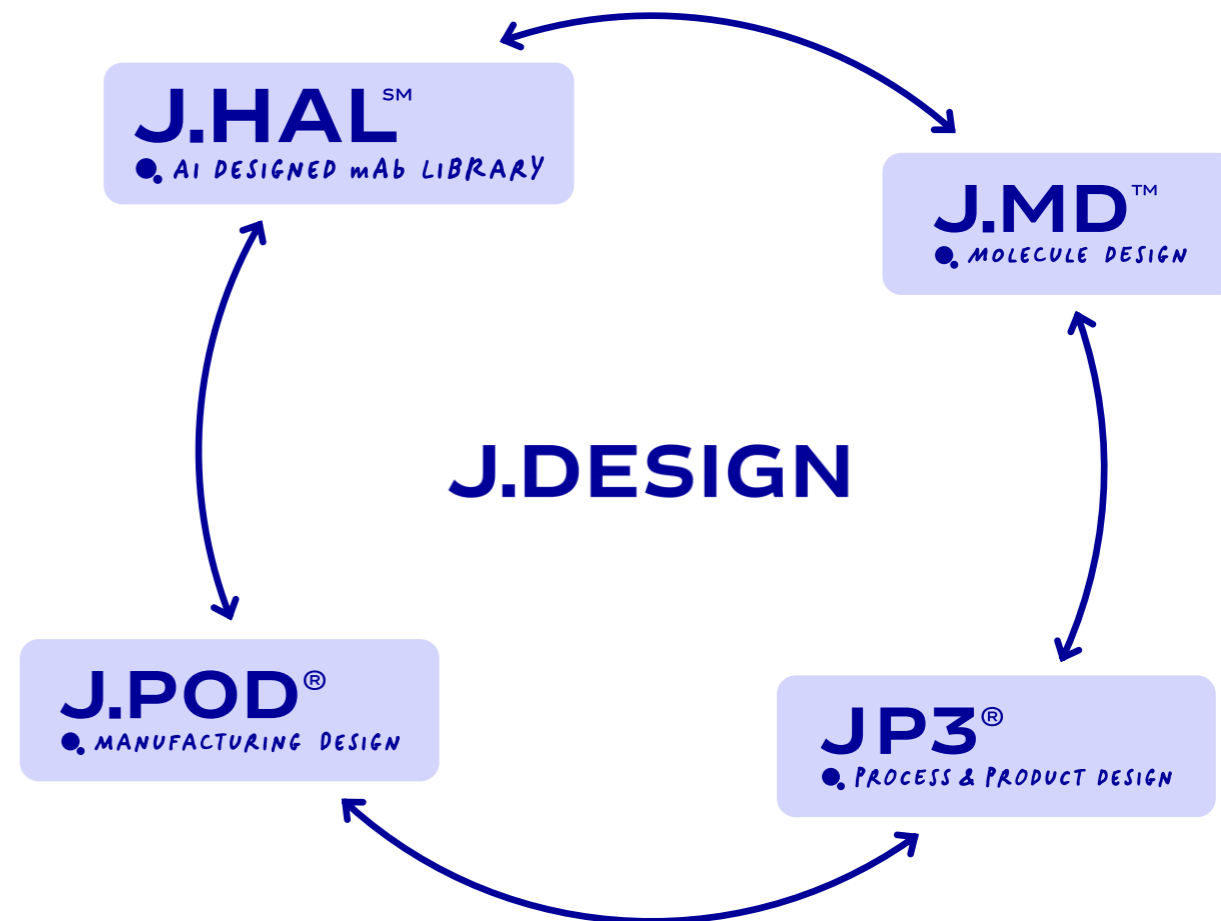




We will capture the market introducing a paradigm shift

Integrating critical capabilities to develop medicines that matter and provide access

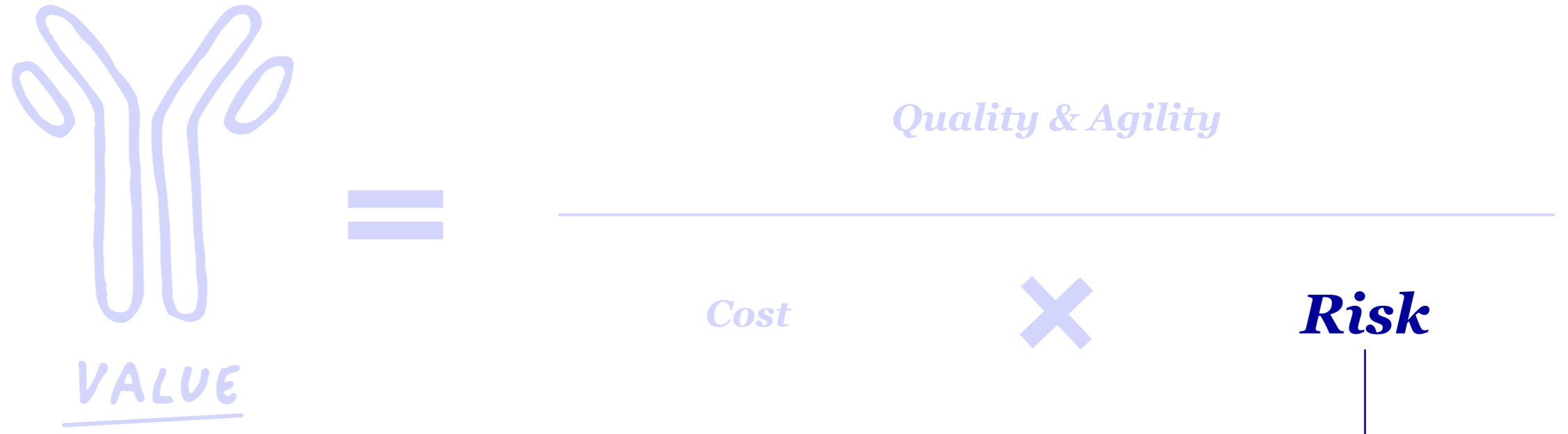
- No need to scale up from clinical to commercial
- Ability to build a new J.POD[®] facility < 24 months
- Add additional trains/ capacity in <12 months
- Change over time between products <2 day





We change the value creation paradigm

Just – Evotec Biologics value drivers as proven in recent projects



1. Select the best therapeutic candidate out of >1,000 possibilities via A.I./M.L./Automation
2. Increased automation with less human intervention will reduce the risk of failure & increase Probability of Success (PoS)
3. Higher quality product produced
4. Lower environmental impact with smaller footprint facility

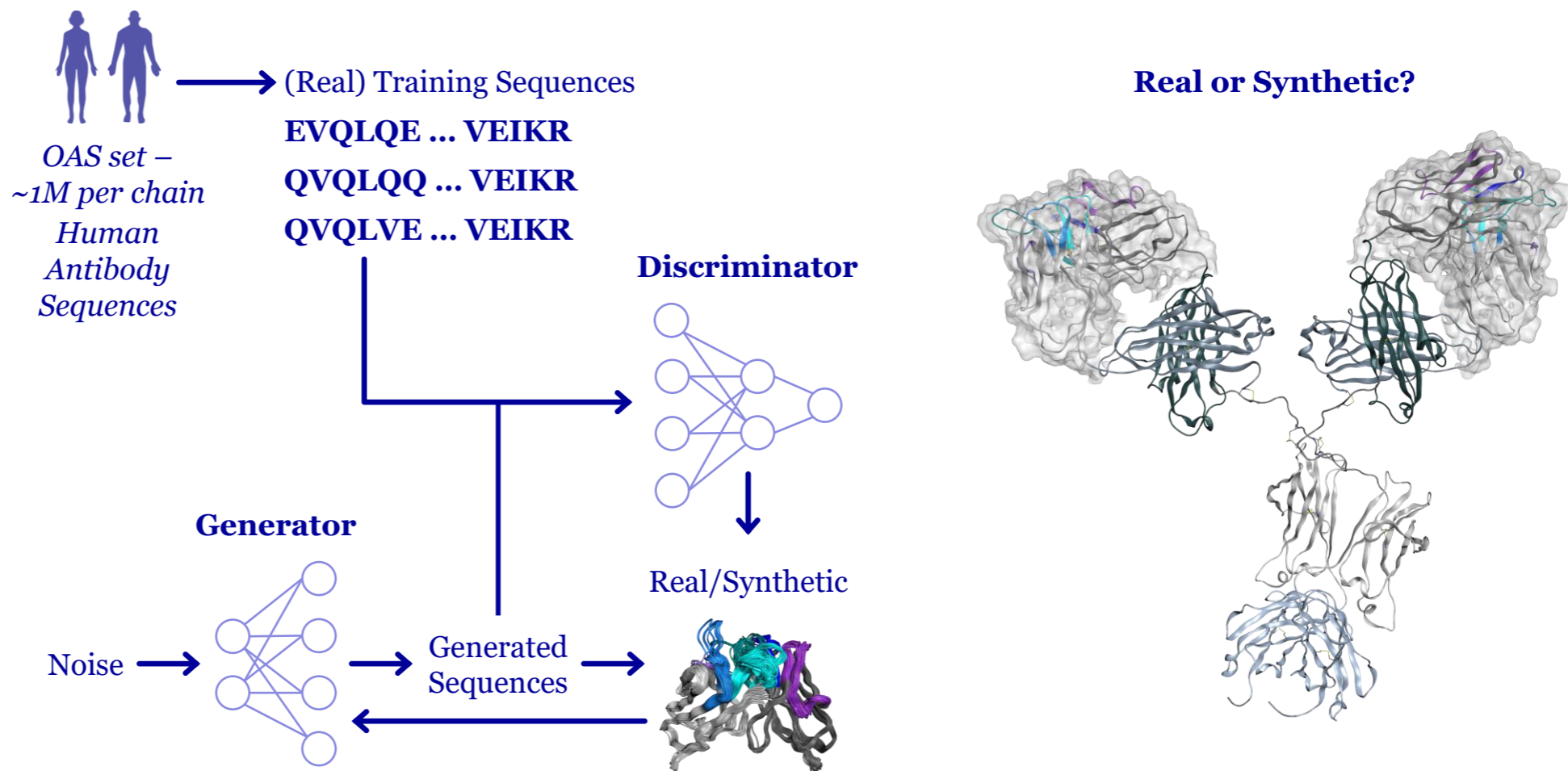


1. Select the best therapeutic candidate via A.I./M.L./Automation

Deep dive on our proprietary tool to reduce attrition early on

J.HALSM technology is a GAN application for antibody sequences

- Large, human-derived antibody sequence training set
- Use GAN training models
- Ability to generate synthetic humanoid large, diverse, combinatorial germline pairings for library creation





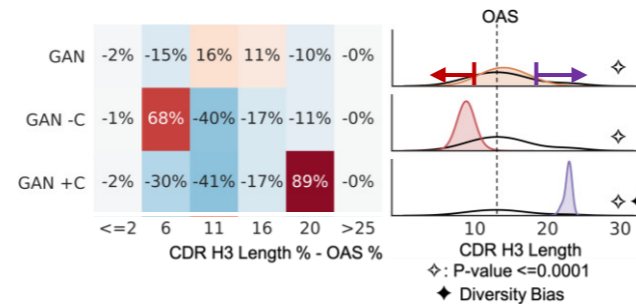
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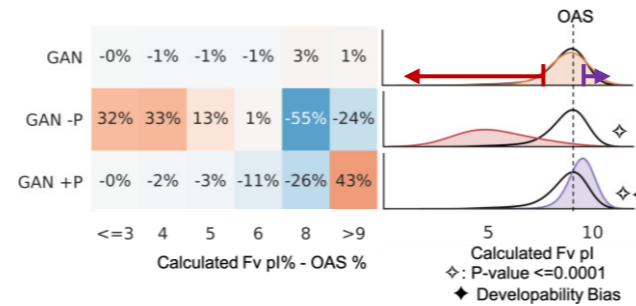
GANs control design through transfer learning

- Properties are transfer learned to bias for exhibit the desired property
- Mechanism of the property could be known or unknown
- A known mechanism could be CDR length, charge, pI, predicted immunogenicity, etc.
- An unknown mechanism could be temperature or pH stability, long pharmacokinetics, etc.
- J.HALSM under continuous development and growth

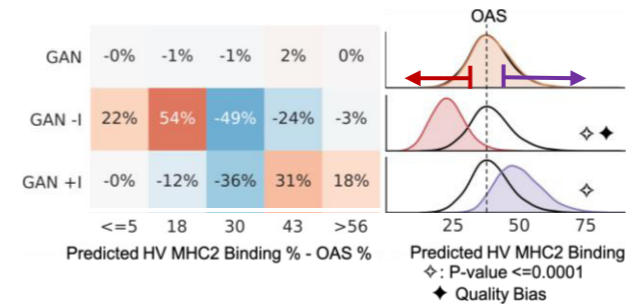
Δ CDR H3 Length vs training Set



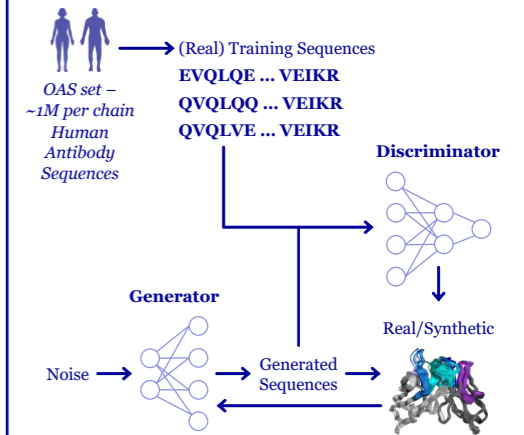
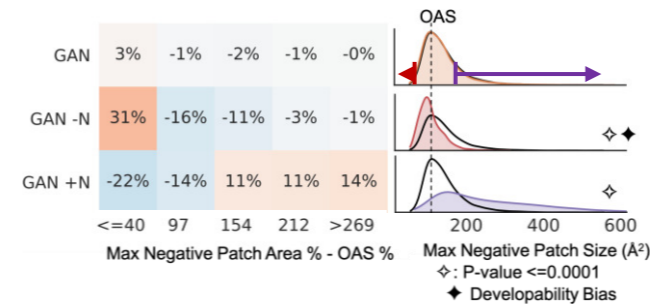
Δ Calculated Fv pI vs training Set



Δ Immunogenicity vs training Set



Δ Max Negative Patch vs training Set

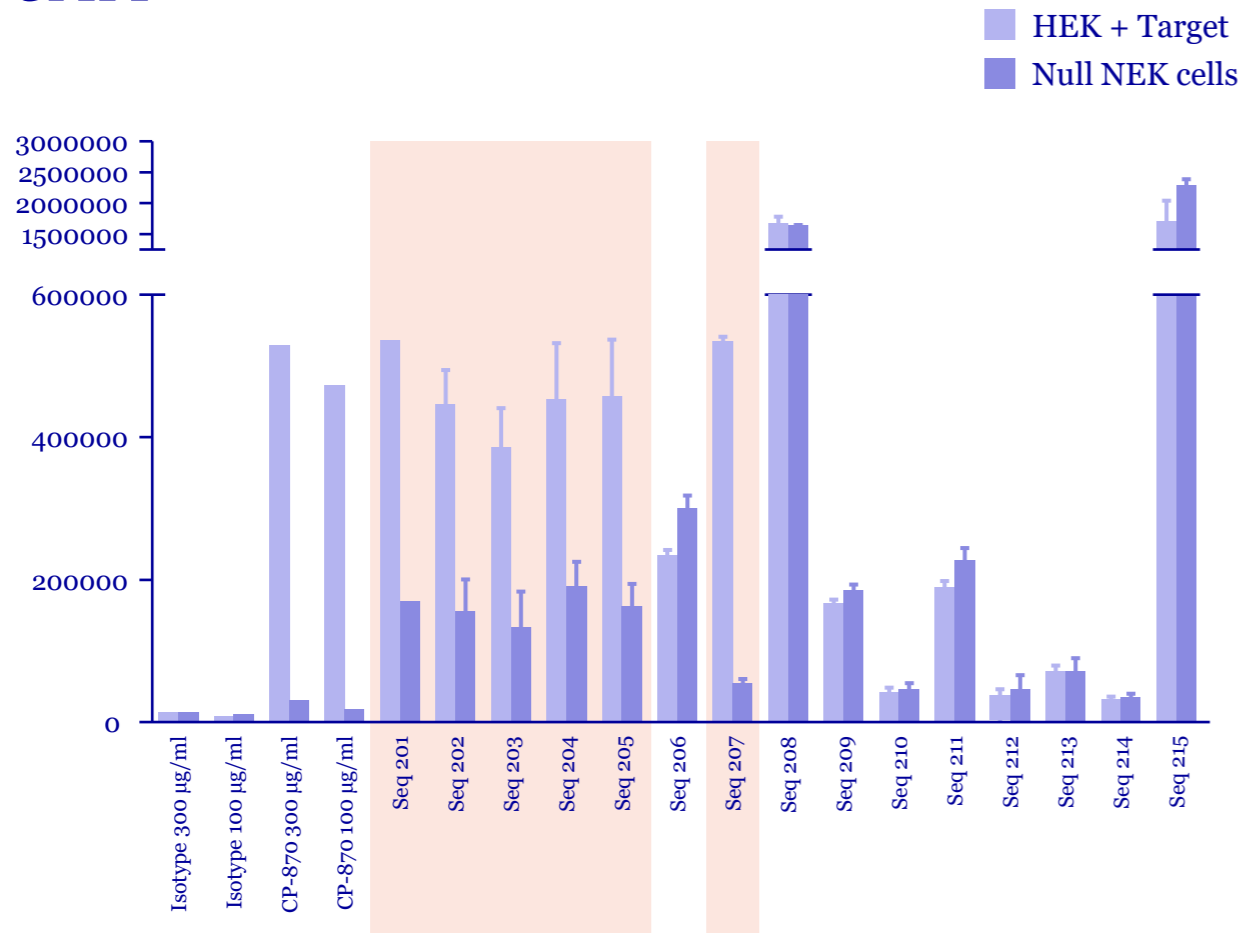




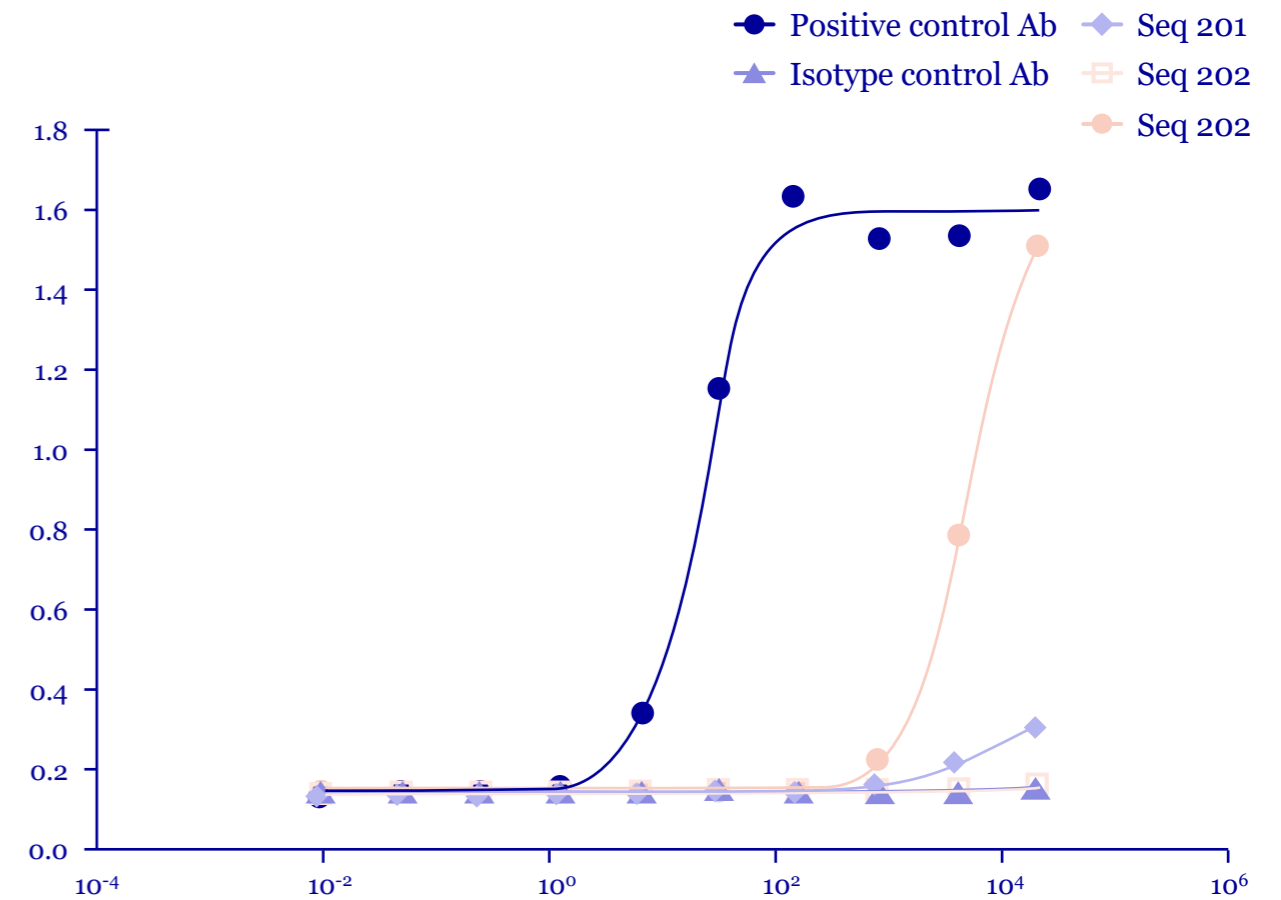
1. Select the best therapeutic candidate via A.I./M.L./Automation

In vitro assay data demonstrating mAbs binding, A.I. driven discovery

Agonist: Binding activity GMFI



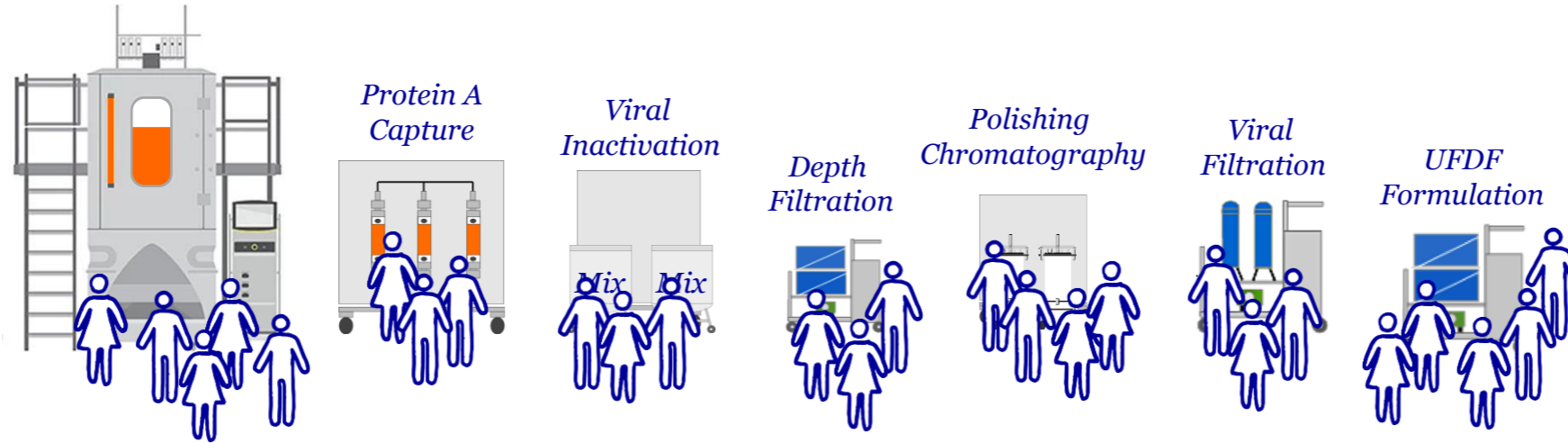
Agonist: Functional activity OD 620-655



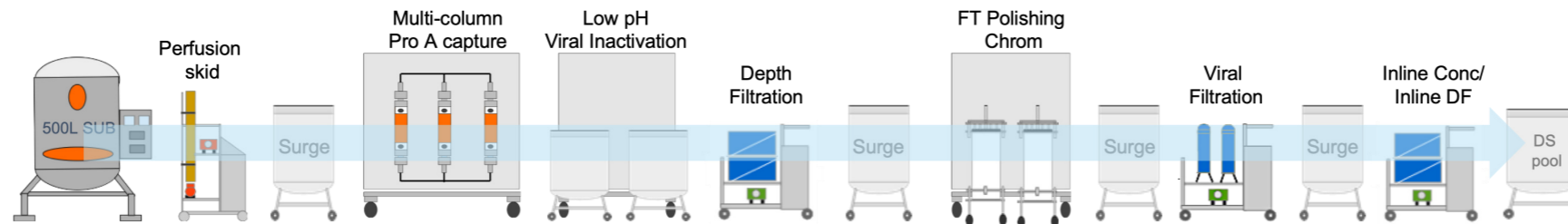


2. “Lights-out manufacturing” – Less human intervention will reduce risk of failure

Traditional fed batch



- Manual operations
- Each of the operations is an individual batch



Highly connected and automated continuous process allows for

- Minimal intervention
- Remote monitoring



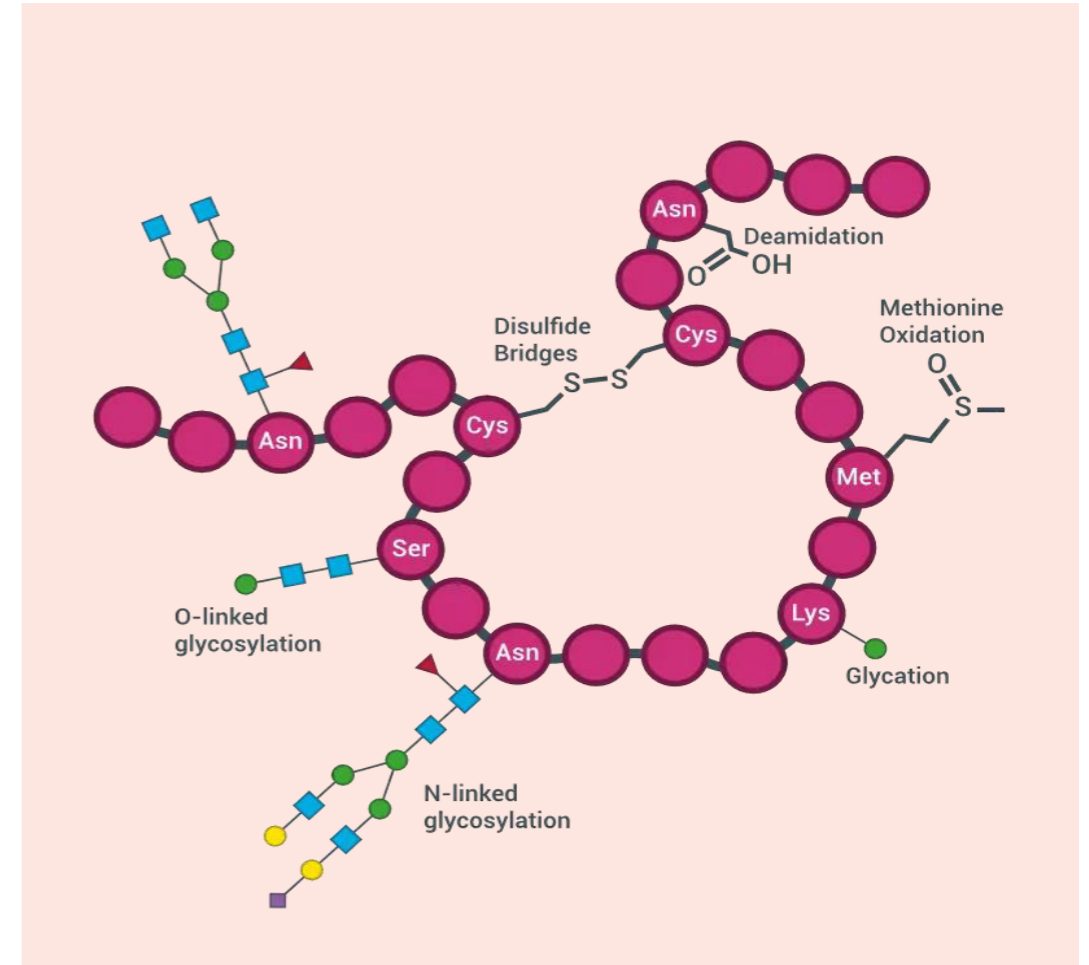
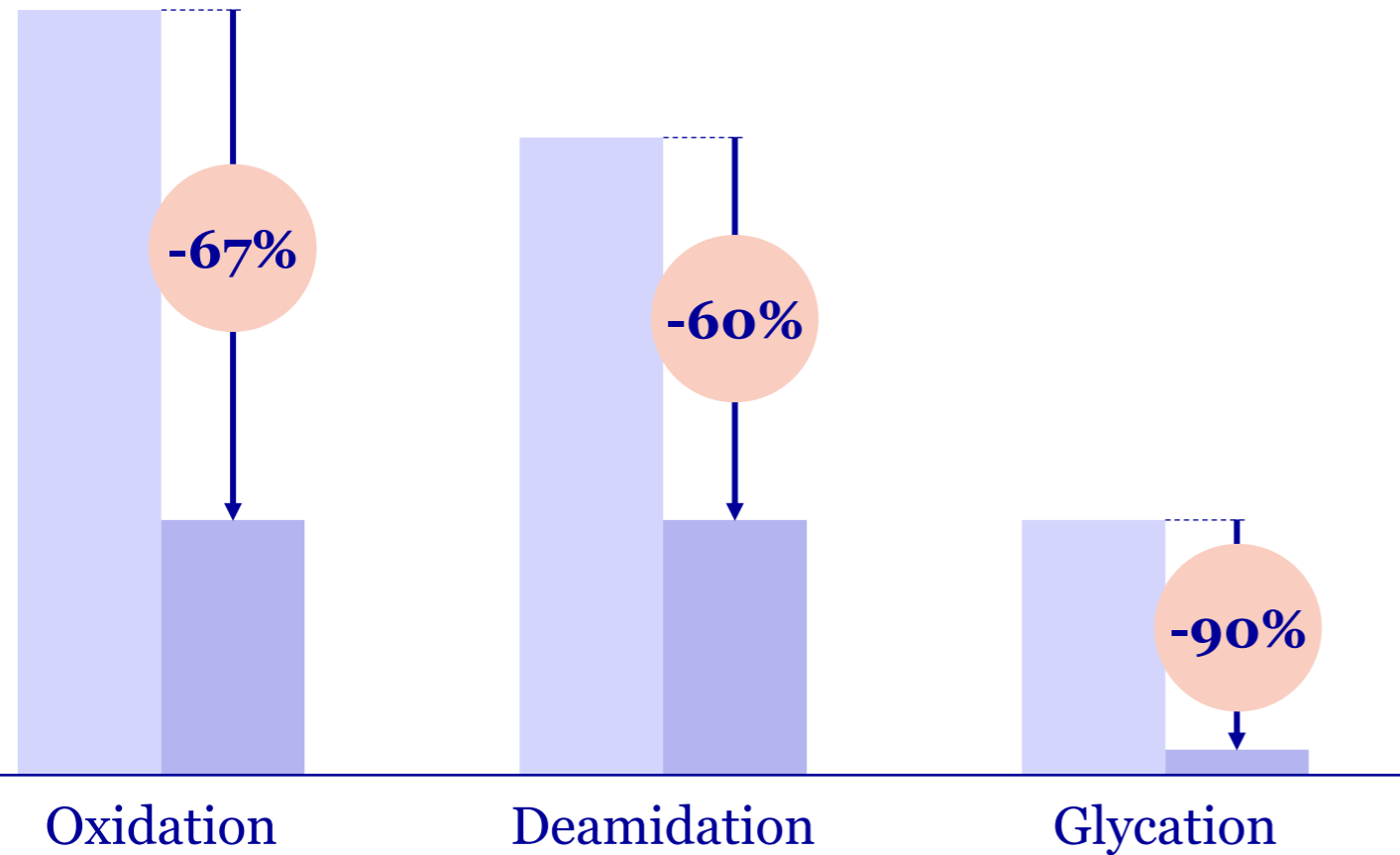


3. Higher quality product produced

Example, heavy chain post-translational modifications are reduced

Level of post translational modification

■ Fed batch ■ Just – Evotec Biologics





4. Lower environmental impact with smaller footprint facility

Just - Evotec Biologics leads industry in minimizing environmental impact

Utilities & HVAC¹

- No steam-in-place or clean-in-place utilities needed
- Water for injection generated by reverse osmosis
- Heat recovery strategies boost energy efficiency by 90%
- Small footprint facility and small cleanroom PODs in Grade D ballroom reduces energy requirements
- Right-sized air changes/hour in labs

No Steam-in-place/Clean-in-place =
reduction in water usage

>50%

Water for injection by reverse osmosis:
Cost savings of
US\$ 0.7 m - US\$ 2.1 m per year

90%

Other

- LED lighting and occupancy sensors
- Low flow fixtures for showers/restrooms; Aquasense faucets
- 16 EV charging stations

450 cubic/feet plastic film and
30 cubic/feet of styrofoam/year

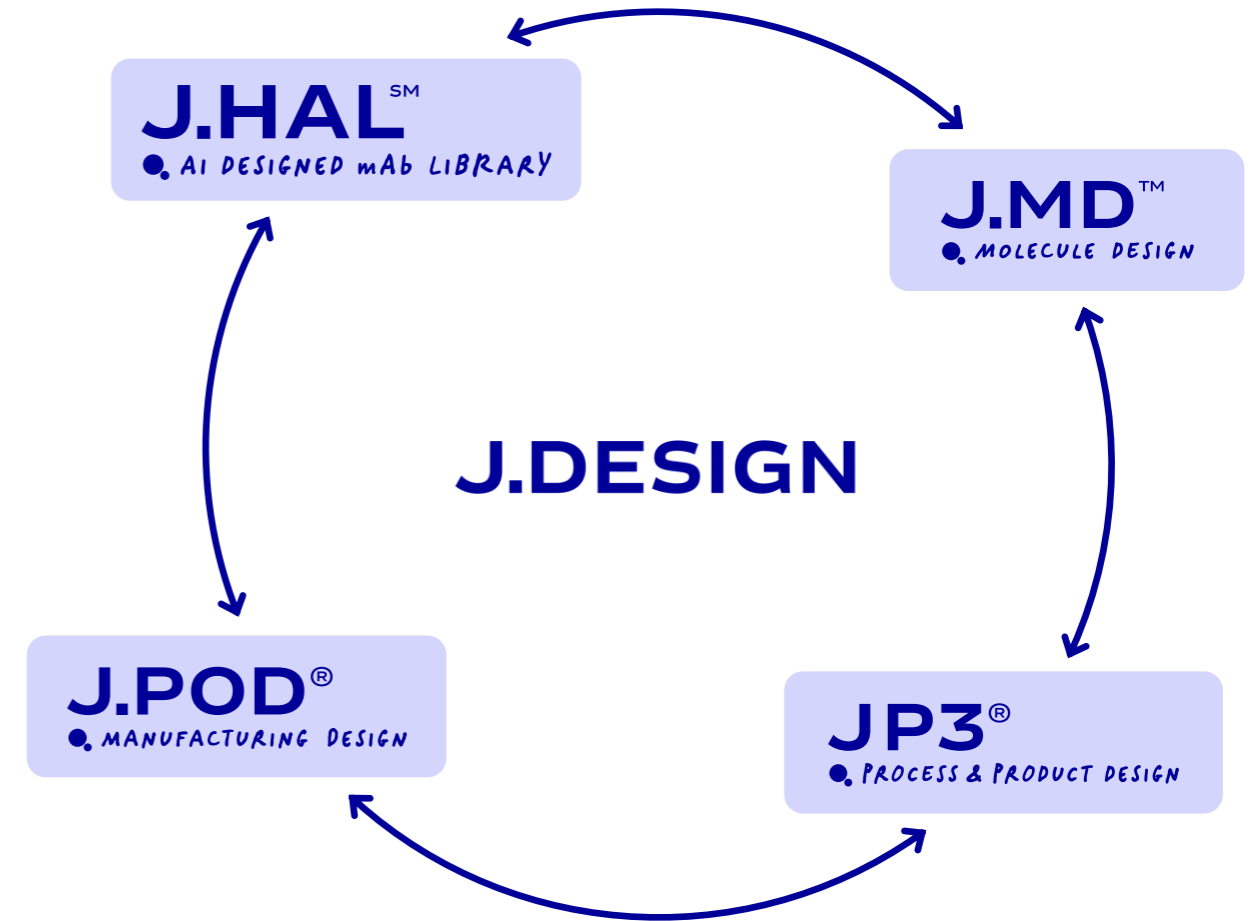




We will capture the market introducing a paradigm shift

Integrating critical capabilities to develop medicines that matter and provide access

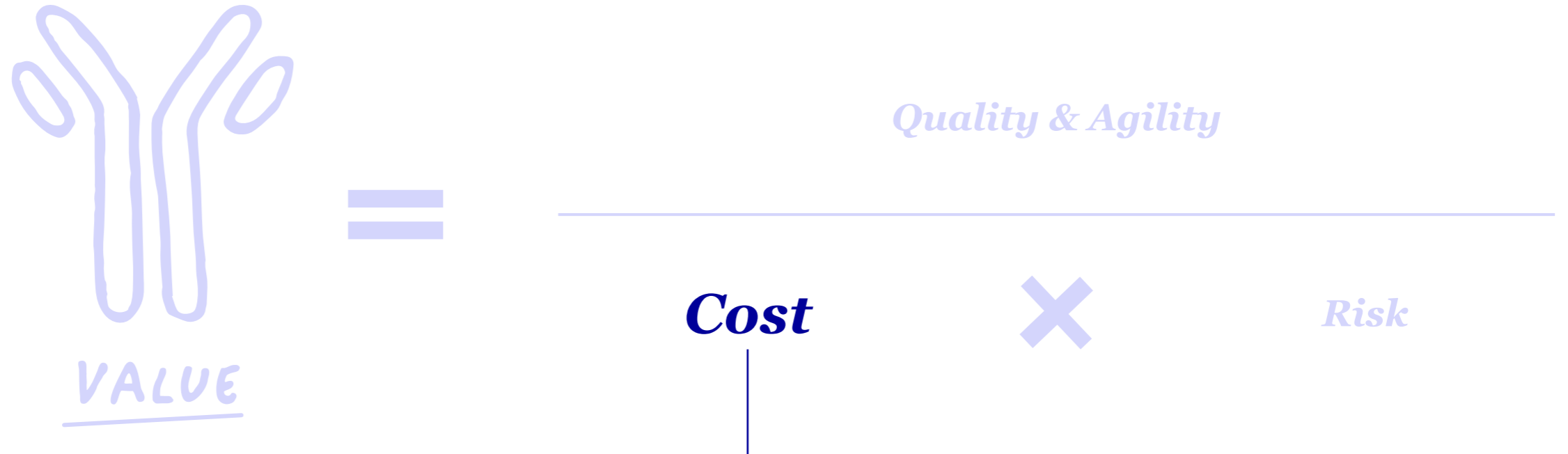
- Select the best therapeutic candidate out of >1,000 possibilities via A.I./M.L./Automation
- Increased automation with less human intervention will reduce the risk of failure & increase Probability of Success (PoS)
- Higher quality product produced
- Lower environmental impact with smaller footprint facility





We change the value creation paradigm for biologics

Just - Evotec Biologics value drivers as proven in recent projects

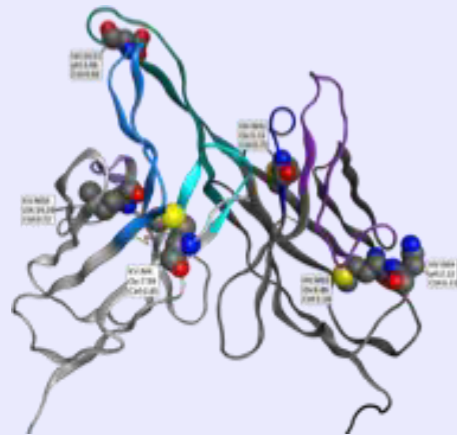


1. Selection of best antibody (J.HALSM or J.MDTM) enables highest productivity
2. Highly intensified processing yields lowest possible COGs
3. Ability to skip engineering runs for first-in-human programs saves time and costs
4. Substantially lower costs in the range of millions compared to billions for setting up the facility



1. Selection of best antibody (J.HALSM or J.MDTM) enables highest productivity

Case study: *In silico* selection of best two mAbs using J.MDTM



- *In silico* validation: Rank ordered and down selected from 283 mAbs
- 4 selected for biophysical characterization
 - Conformational stability
 - Colloidal stability

High throughput biophysical characterization of mAbs

mAb	Conformational stability						Colloidal stability						
	DSF WSS	DSF1 T1	DSF2 T2	Thermal Hold Ave	Low pH HMW	Unfold	SINS	Zenix RT	9.5% PEG	CL	KLH	dsDNA	Insulin
mAb 1	Undefined	No violation	No violation	No violation	No violation	No violation	No violation	No violation	No violation	No violation	No violation	No violation	No violation
mAb 2	No violation	No violation	No violation	No violation	No violation	No violation	No violation	No violation	No violation	No violation	No violation	No violation	No violation
mAb 3	No violation	No violation	No violation	No violation	No violation	No violation	Violation	Undefined	No violation	No violation	No violation	No violation	Undefined
mAb 4	Violation	No violation	Violation	Violation	No violation	No violation	Undefined	Violation	No violation	No violation	No violation	No violation	No violation

mAb 1 and 2 had best profile → chosen for cocktail
 Both highly productive at 4g/L/day, Highly stable, Easily formulated

mAb 3 and 4 eliminated

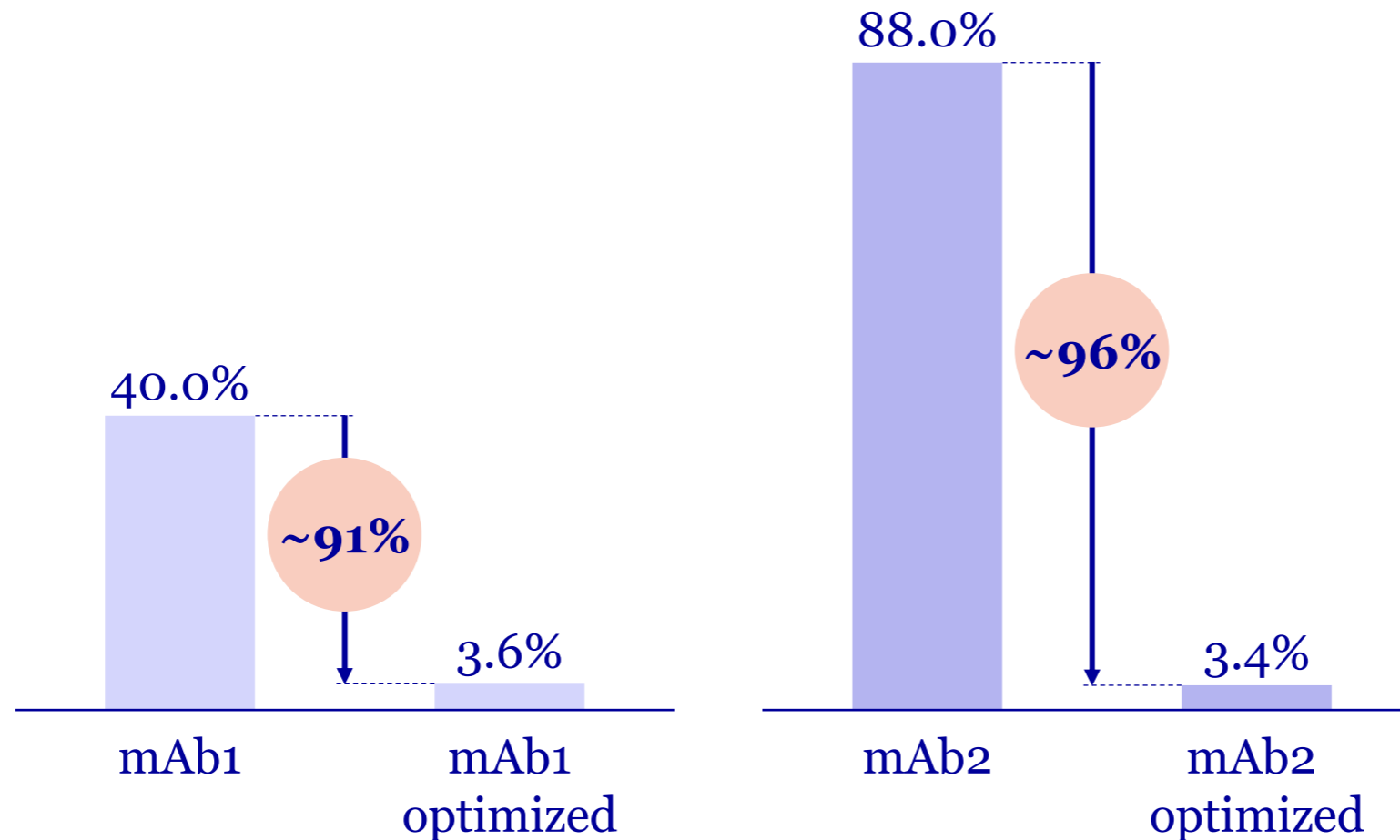
■ No violation
 ■ Violation
 ■ Undefined



1. Selection of best antibody (J.HALSM or J.MDTM) enables highest productivity 2/3

Sequence optimization reduces pH induced aggregation

Low pH aggregation



High levels of aggregation at low pH would be a potential stopper in development

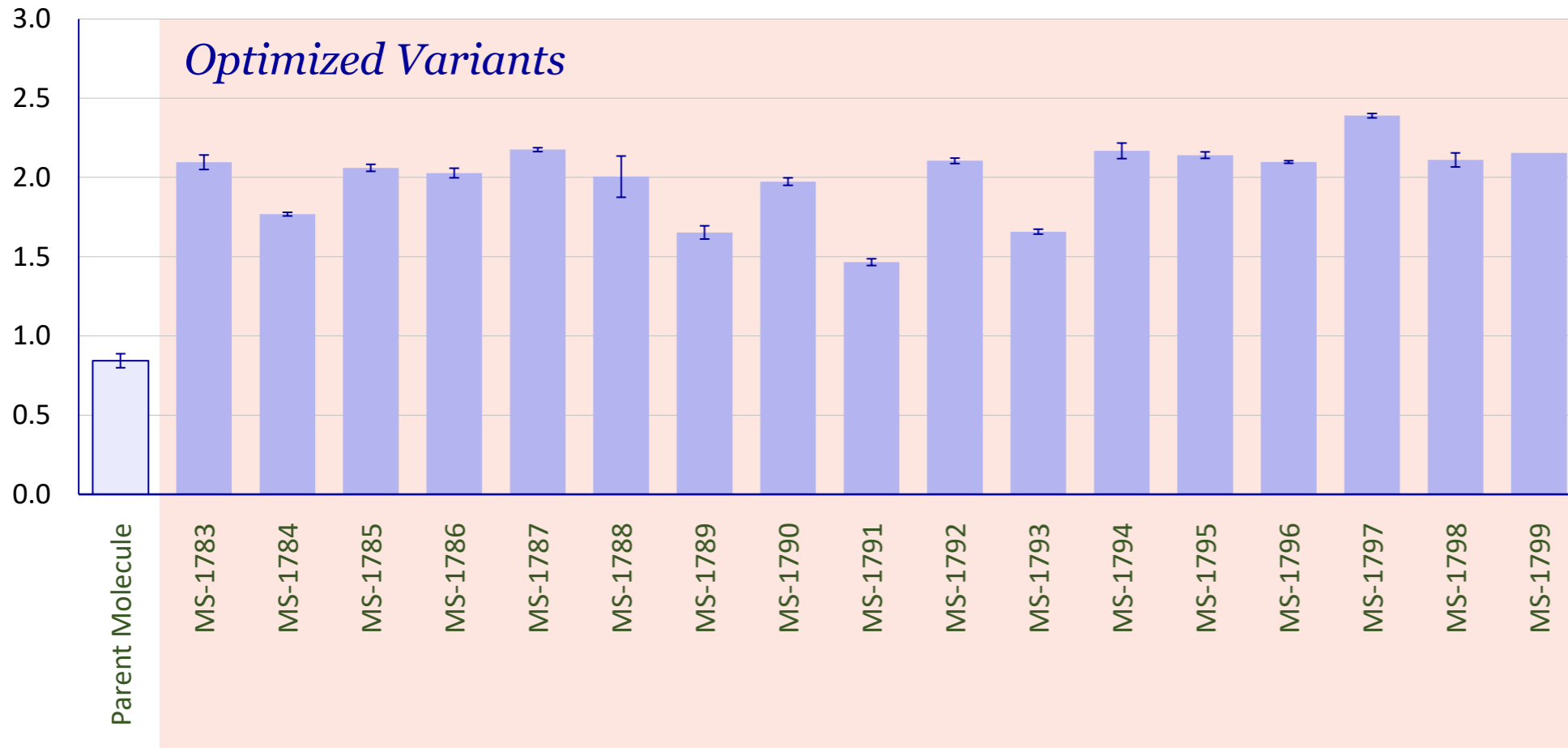
Redesign of problematic regions increases PoS



1. Selection of best antibody (J.HALSM or J.MDTM) enables highest productivity

Optimization of titer is one of the keys to achieving high productivity at later stages

Titers achieved with variant designs, x-fold increase



A panel of variant designs compared to the parental molecule in 24-deep well plates, assessed via high throughput screening technology

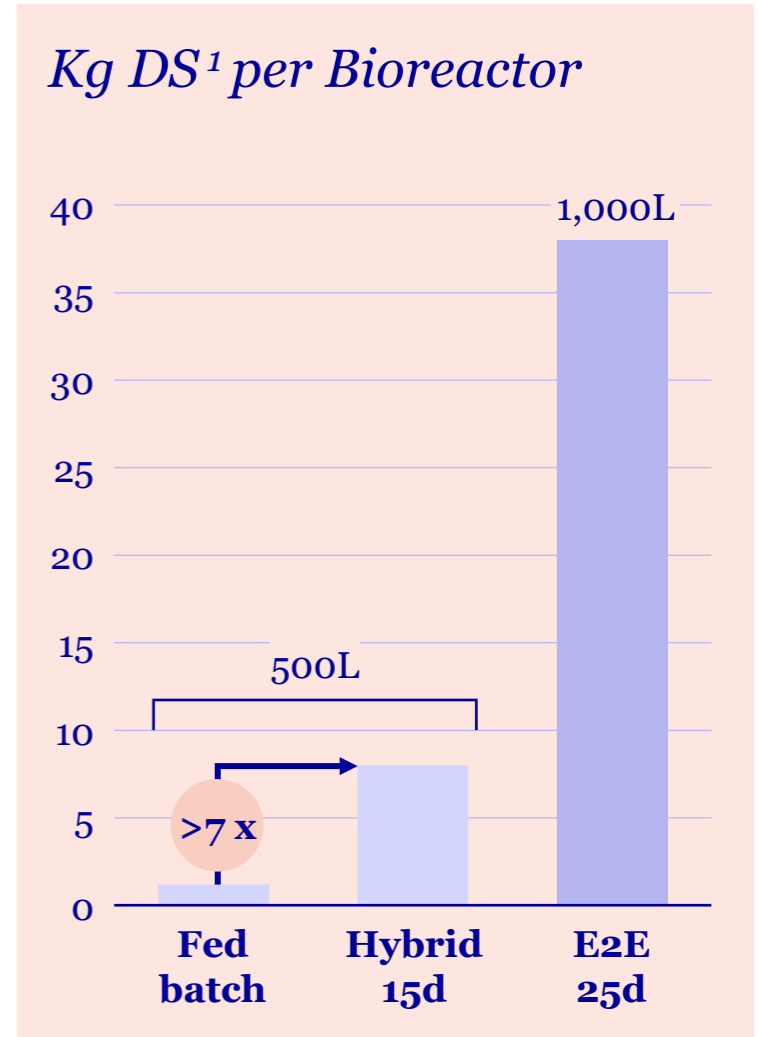
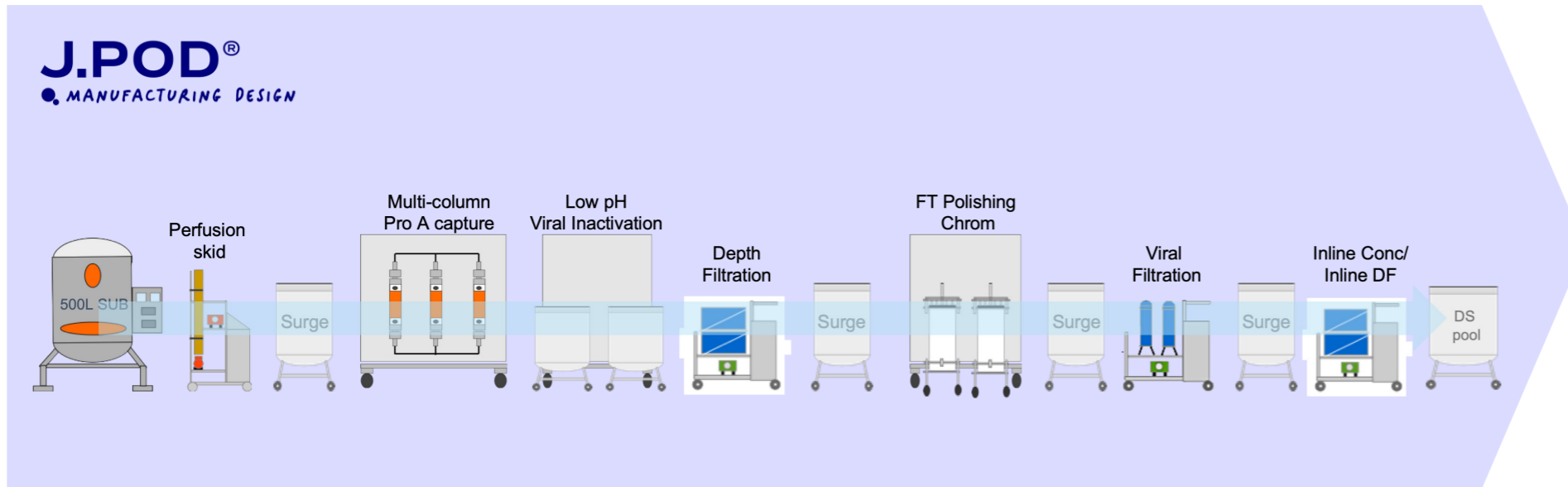
Select the optimal antibody to ensure highest productivity



2. Highly intensified processing yields lowest possible COGs

Case study: Comparison of fed batch to continuous end-to-end mass output

Fully end-to-end continuous process for late-stage products > 25-day production



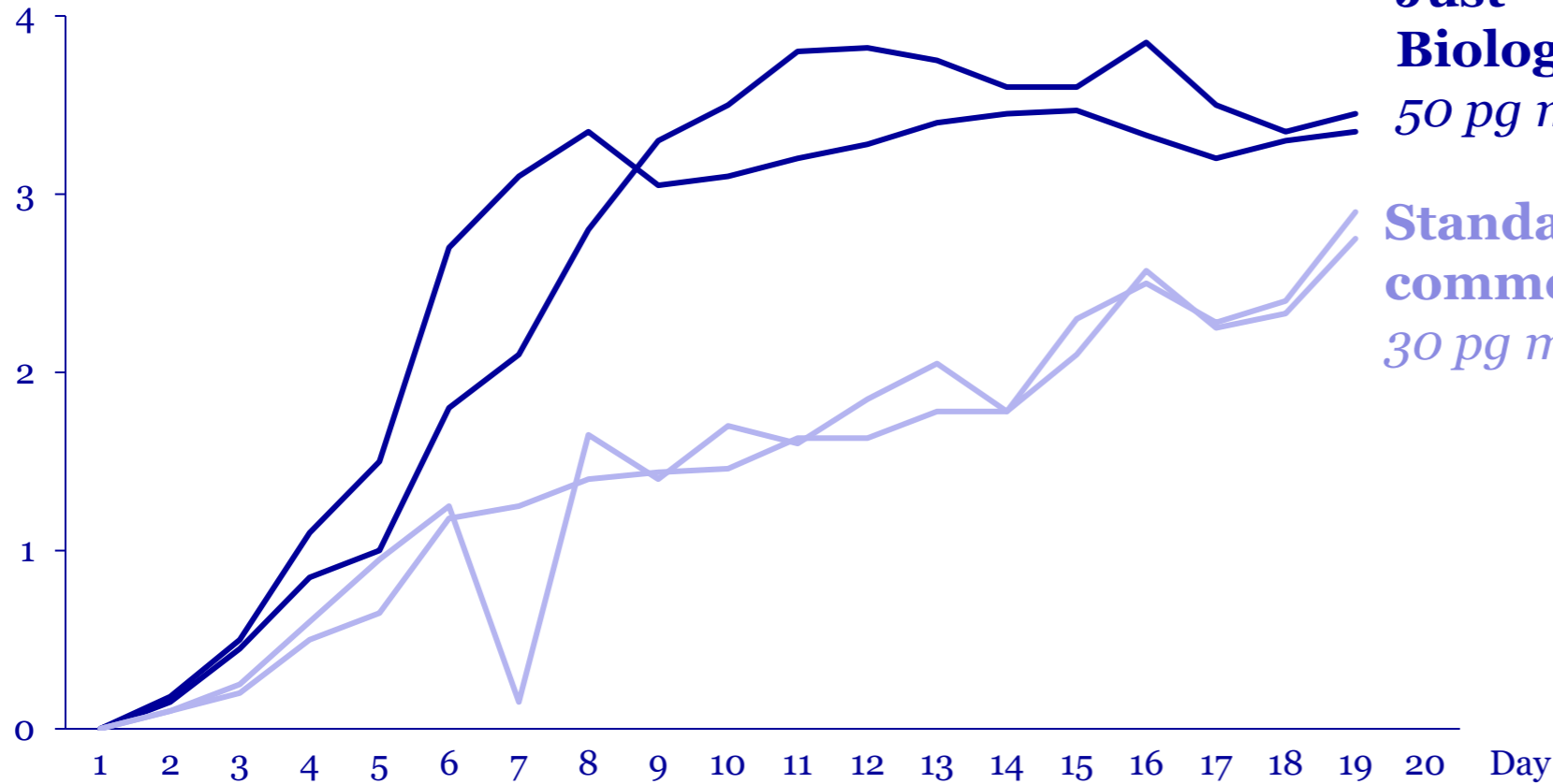


2. Highly intensified processing yields lowest possible COGs

Comparison of proprietary cell line CL-72 with industry standard

Productivity of proprietary Just – Evotec Biologics cell lines vs standard commercial cell lines

Permeate Productivity (g/L/d)



Just – Evotec Biologics (CL-72)
50 pg mAb / cell / day

Standard commercial cell line
30 pg mAb / cell / day

Same DNA sequence was transfected into both standard commercial cell line and Just - Evotec Biologics

CL72 cell line and two sets of pools were compared for productivity across 20+ days of culture

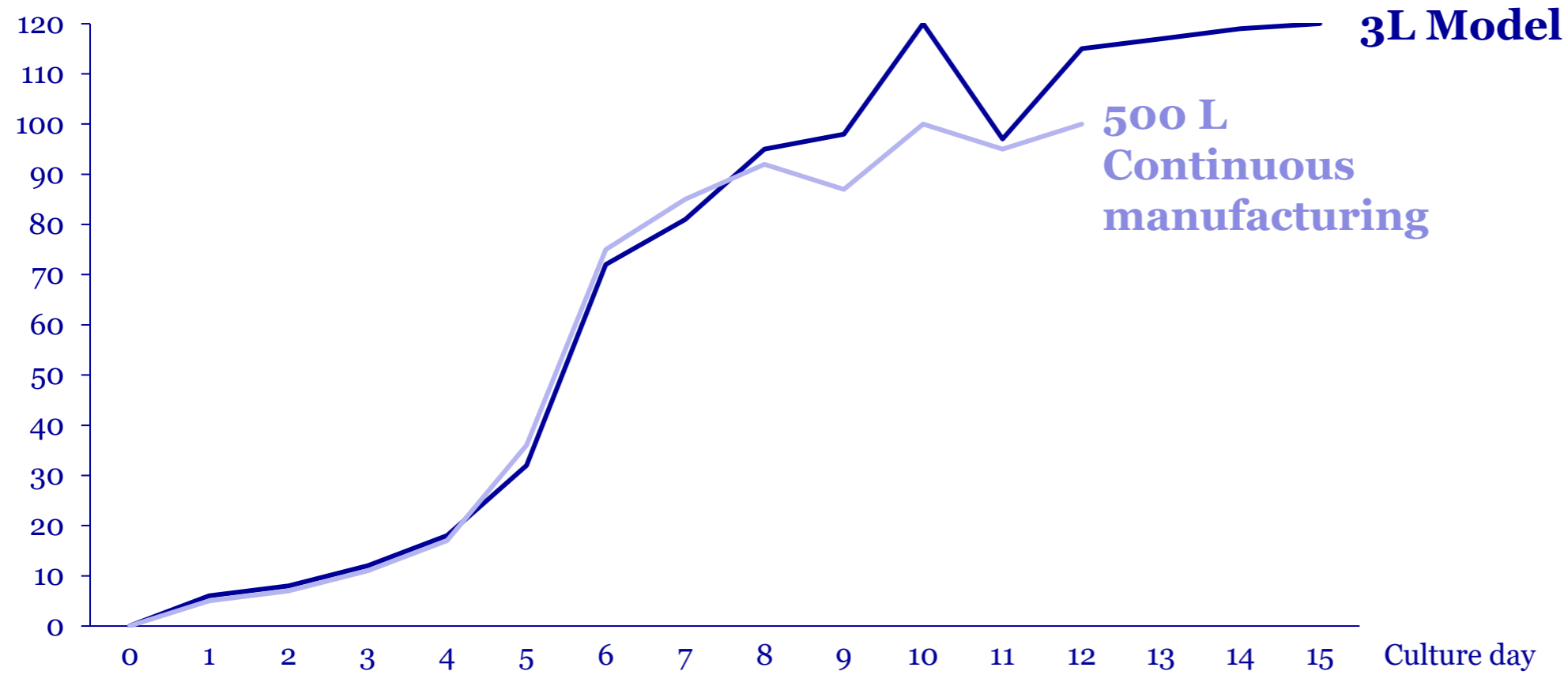


2. Highly intensified processing yields lowest possible COGs

Illustrative example of model compared to manufacturing scale reactor

Productivity of proprietary Just – Evotec Biologics cell lines vs traditional cell lines

in 10^6 cells/ml



3L model system gives high confidence for seamless transition to 500L

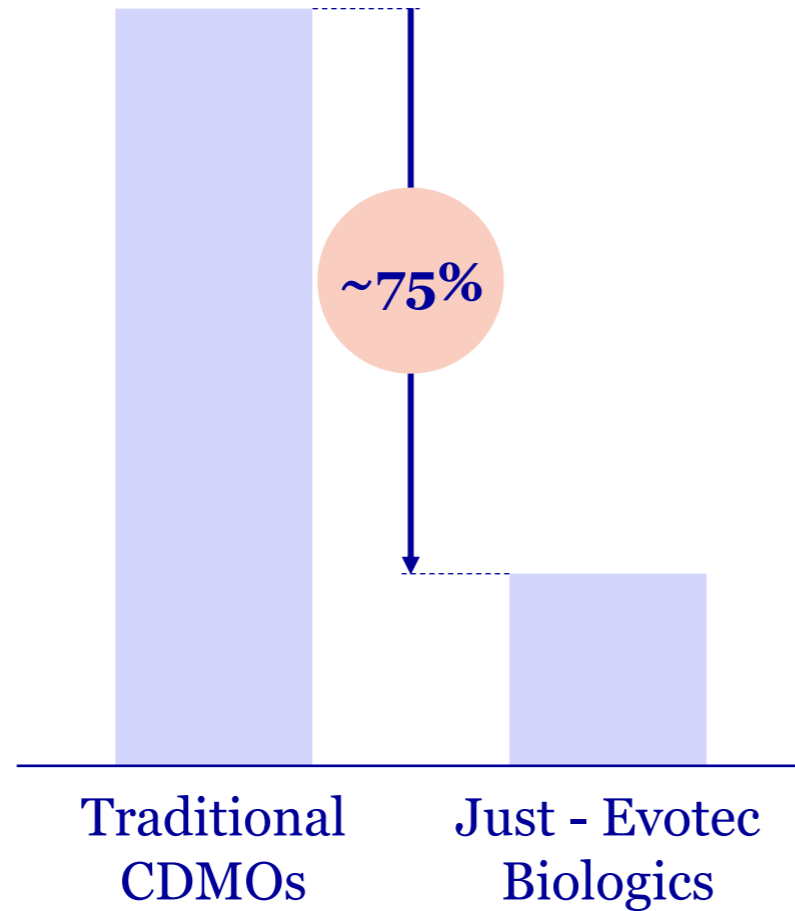
High productivity:
3-4 grams product / L / day



2. Highly intensified processing yields lowest possible COGs

J.POD[®] based COGs will facilitate our aspiration for this target

COGs





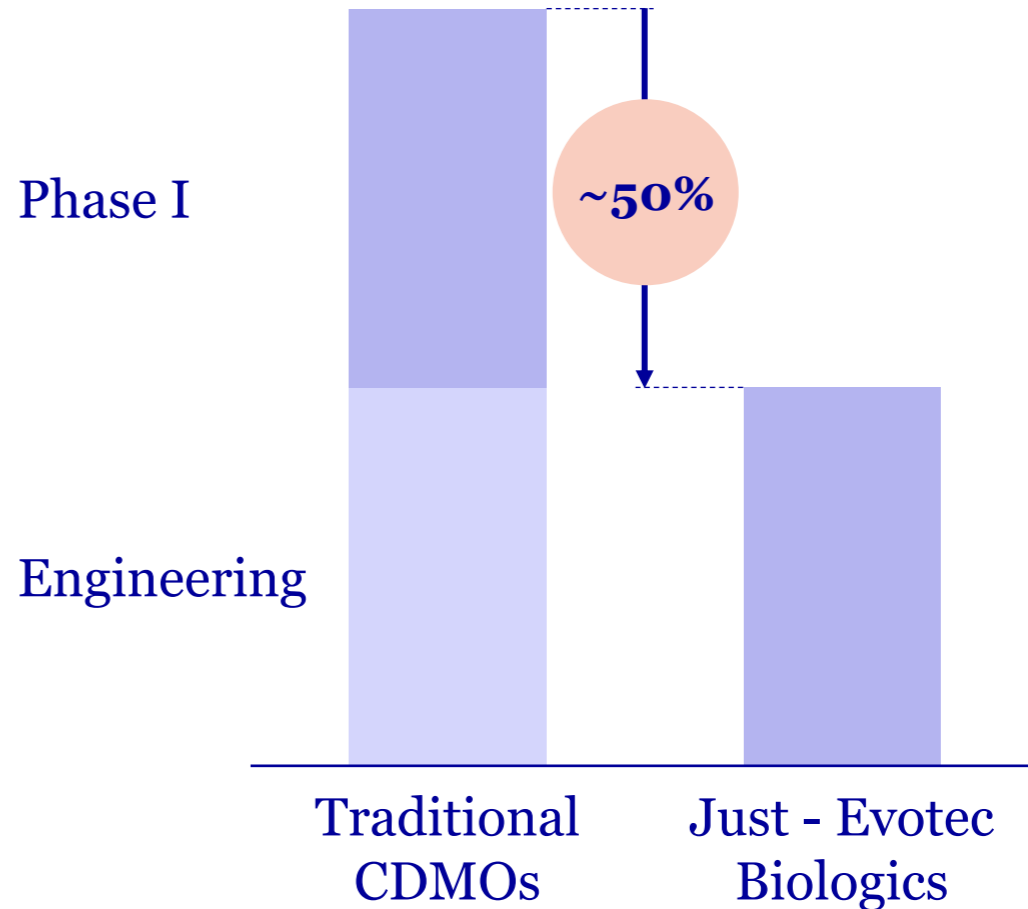
3. Ability to skip engineering runs for first-in-human programs saves time and costs

Simplified for majority of FIH programs

First-in-human programs (FIH)

- Scale down models are representative of 500L scale
- Thereby reduces need for engineering run(s)
- Scale from 3L to 500L cGMP run(s)

Manufacturing for FIH



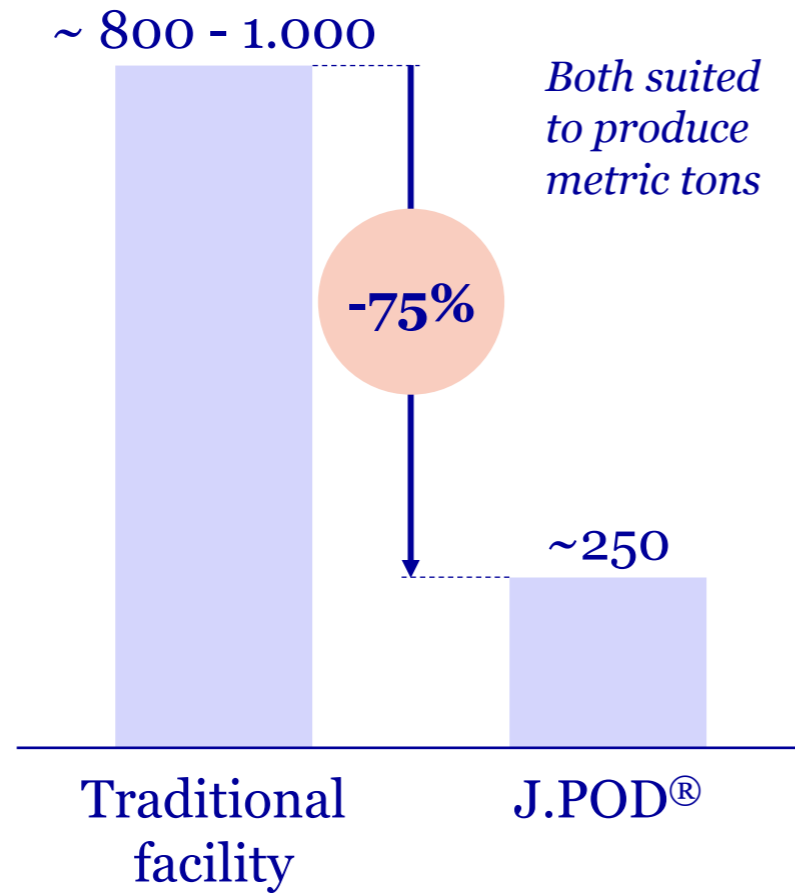


4. Substantially lower costs – J.PODs[®] come with a disruptively low capital need

Comparison between traditional facility and J.POD[®]

Cost of a J.POD[®] facility

US\$ m

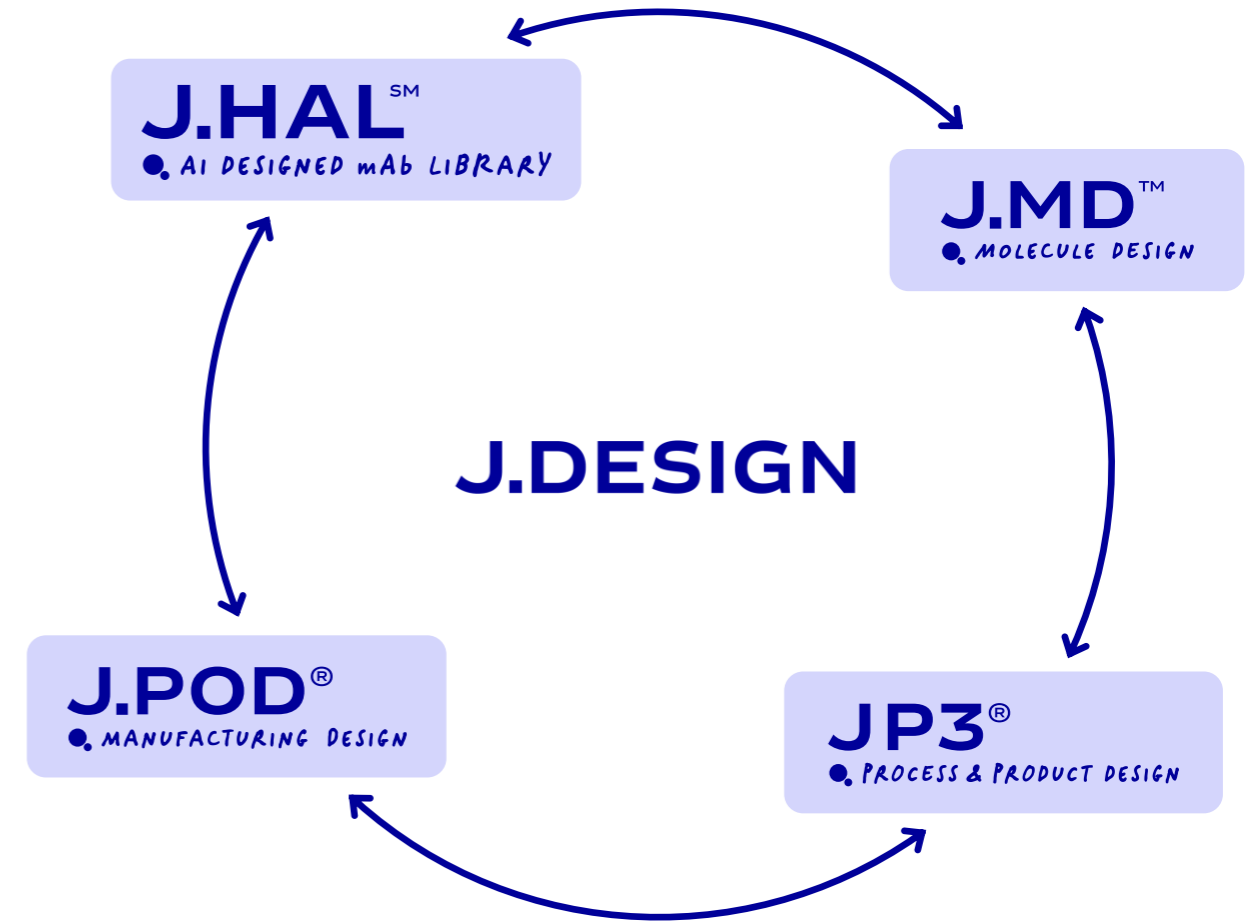




We will capture the market introducing a paradigm shift

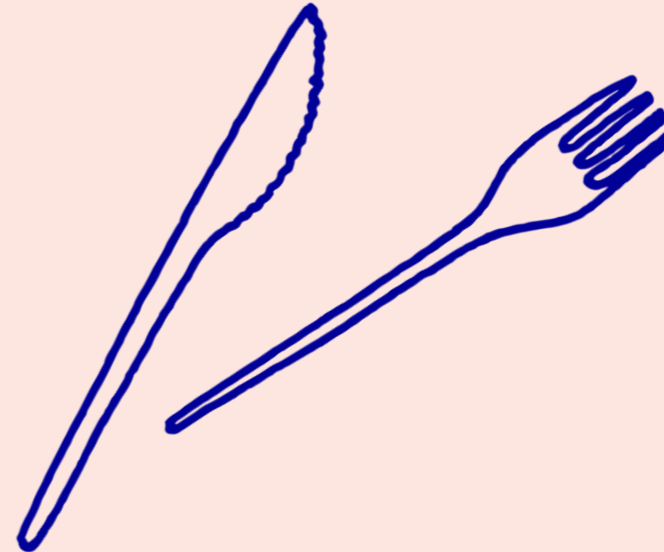
Integrating critical capabilities to develop medicines that matter and provide access

- Selection of best antibody (J.HALSM or J.MDTM) enables highest productivity
- Highly intensified processing yields lowest possible COGs
- Ability to skip engineering runs for first-in-human programs saves time and costs
- Substantially lower costs in the range of millions compared to billions for setting up the facility





Let's have lunch together
30 min lunch break










Agenda

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9.30 – 11.00 am	Site Tour – Overview and tour preparation
11.00 am	Start of webcast
11.00 – 11.30 am	Action Plan 2025
11.30 – 12.15 pm	Paradigm shift in biologics – From A.I./M.L.-based discovery to agile commercial manufacturing
<i>12.15 – 12.45 pm</i>	<i>Lunch Break</i>
12.45 – 1.15 pm	A shared vision for biomanufacturing – John Erickson
<i>1.15 – 2.15 pm</i>	<i>Markets' needs – Access to medicines that matter</i>
2.15 – 3.00 pm	Roundup & Q&A session

End-to-end collaboration to transform biopharmaceutical development and manufacturing

John Erickson¹  | Jeffrey Baker² | Shawn Barrett³ | Ciaran Brady⁴ | Mark Brower⁵ | Ruben Carbonell⁶ | Tim Charlebois⁷ | Jon Coffman⁸  | Lisa Connell-Crowley⁹ | Michael Coolbaugh³  | Eric Fallon¹⁰ | Eric Garr⁴ | Christopher Gillespie⁵ | Roger Hart¹¹ | Allison Haug¹ | Gregg Nyberg⁵ | Michael Phillips¹² | David Pollard¹³ | Maen Qadan¹⁴ | Irina Ramos⁸ | Kelley Rogers¹⁵ | Gene Schaefer¹⁶ | Jason Walther³  | Kelvin Lee¹ 

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³Global CMC Development, Sanofi, Framingham, Massachusetts, USA

⁴Biologics MS&T, Bristol-Myers Squibb, Devens, Massachusetts, USA

⁵Biologics Process Research and Development, Merck & Co., Inc., Kenilworth, New Jersey, USA

⁶National Institute for Innovation in Manufacturing Biopharmaceuticals, Raleigh, North Carolina, USA

⁷BioTx Pharmaceutical Sciences, Pfizer, Andover, Massachusetts, USA

⁸Biopharmaceutical Development, AstraZeneca, Gaithersburg, Maryland, USA

⁹Process Design, Just-Evotec Biologics, Seattle, Washington, USA

¹⁰Manufacturing Science and Technology, Drug Substance, Genentech, Inc., Oceanside, California, USA

¹¹Process Development, Amgen, Cambridge, Massachusetts, USA

¹²Next Generation Processing R&D, MilliporeSigma, Bedford, Massachusetts, USA

¹³Sartorius Corporate Research, Sartorius, Boston, Massachusetts, USA

¹⁴Biologics Research and Development, Eli Lilly and Company, Indianapolis, Indiana, USA

¹⁵Material Measurement Laboratory and Office of Advanced Manufacturing, National Institute of Standards and Technology, Gaithersburg, Maryland, USA

¹⁶API Large Molecule BioTherapeutics Development, Janssen R&D, Malvern, Pennsylvania, USA

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Email: erickson@udel.edu

Funding information

U.S. Department of Commerce, Grant/Award Numbers: 70NANB17H002, 70NANB20H037

Abstract

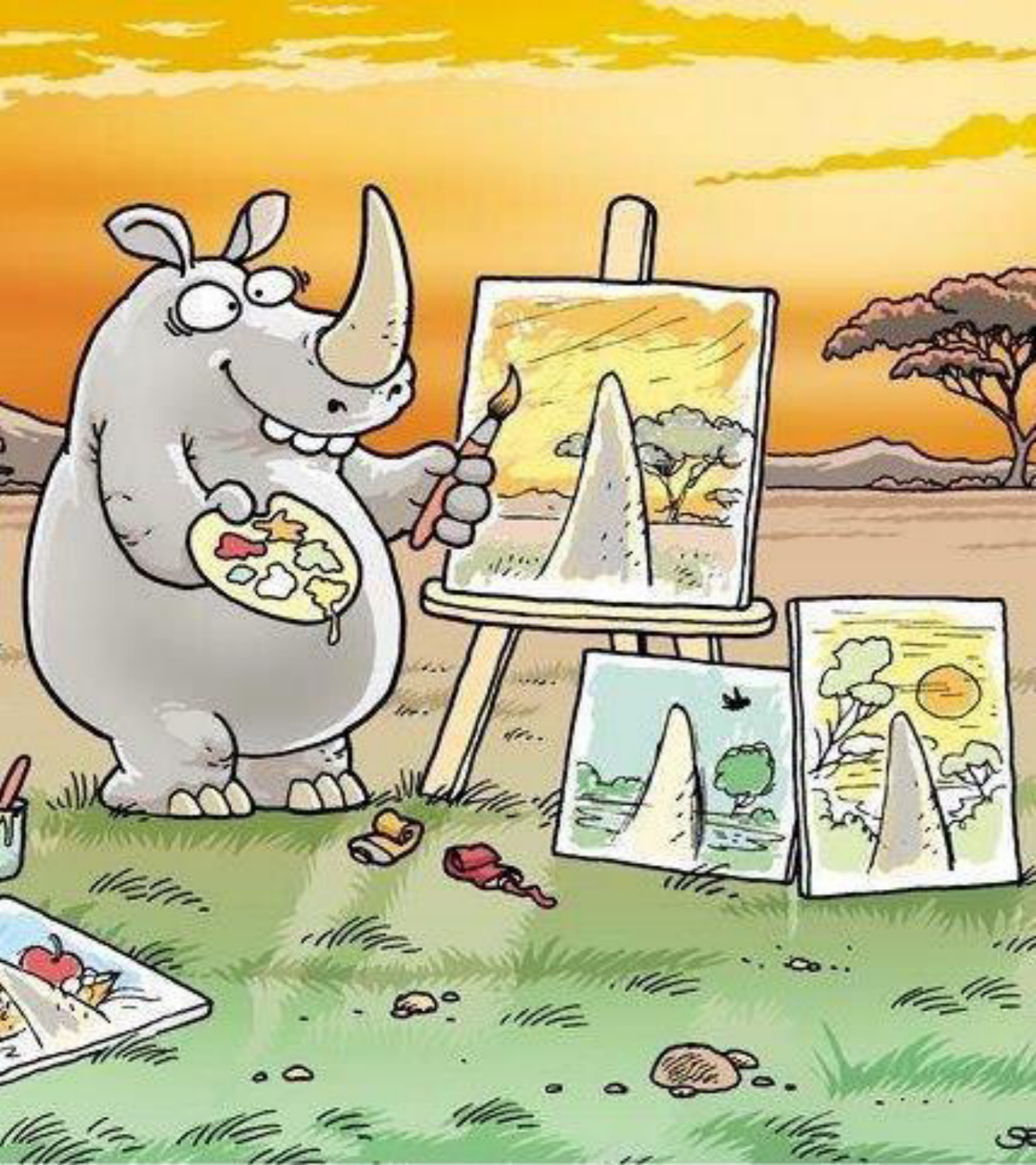
An ambitious 10-year collaborative program is described to invent, design, demonstrate, and support commercialization of integrated biopharmaceutical manufacturing technology intended to transform the industry. Our goal is to enable improved control, robustness, and security of supply, dramatically reduced capital and operating cost, flexibility to supply an extremely diverse and changing portfolio of products in the face of uncertainty and changing demand, and faster product

This article reflects the views of the author and should not be construed to represent FDA's views or policies.

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SHARED VISION FOR BIOPHARMACEUTICAL MANUFACTURING

- John C. Erickson, PhD
- November 2, 2022
- **DISCLAIMER:**
- Views expressed by authors on the paper represent themselves, not their companies.
- Key Opinion Leaders from critical mass of biopharmaceutical manufacturers
 - Sanofi, BMS, Merck, Pfizer, AZ, Just-Evotec, Genentech, Amgen, MilliporeSigma, Sartorius, Lilly, Janssen, FDA, NIST and NIIMBL



IS HIGH COGS A PROBLEM? DEPENDS ON YOUR POINT OF VIEW

✗ Sales – Not often biggest issue

- On time, in full delivery, more important
- Diminishing returns at high GM
- Significant Selling Cost
- Don't launch in low margin markets

✓ Corporate—Yes!

- Save money in mfg to spend in R&D
- Reduce COGS and inventory
 - Innovator COGS = >\$100 Billion > R&D
- Access to medicines and markets

? Manufacturing –Conflicted

- Recover costs from Commercial-predictability more important.
- Incremental YOY savings targets

✓ Emerging Markets

- Yes, but need dramatic reduction



DISCUSSIONS ABOUT COGS



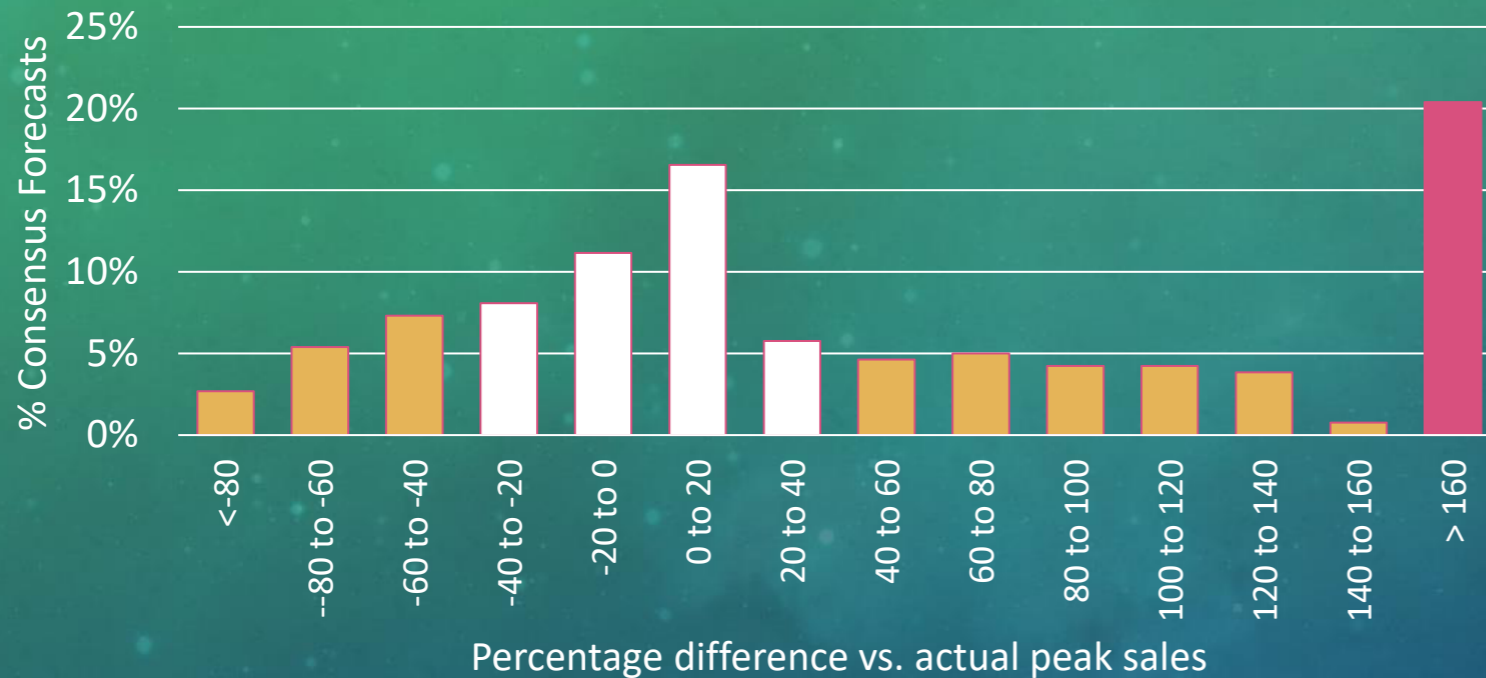
DISCUSSIONS ABOUT CAPEX

EVERYONE WANTS TO REDUCE CAPITAL COST OF FACTORIES

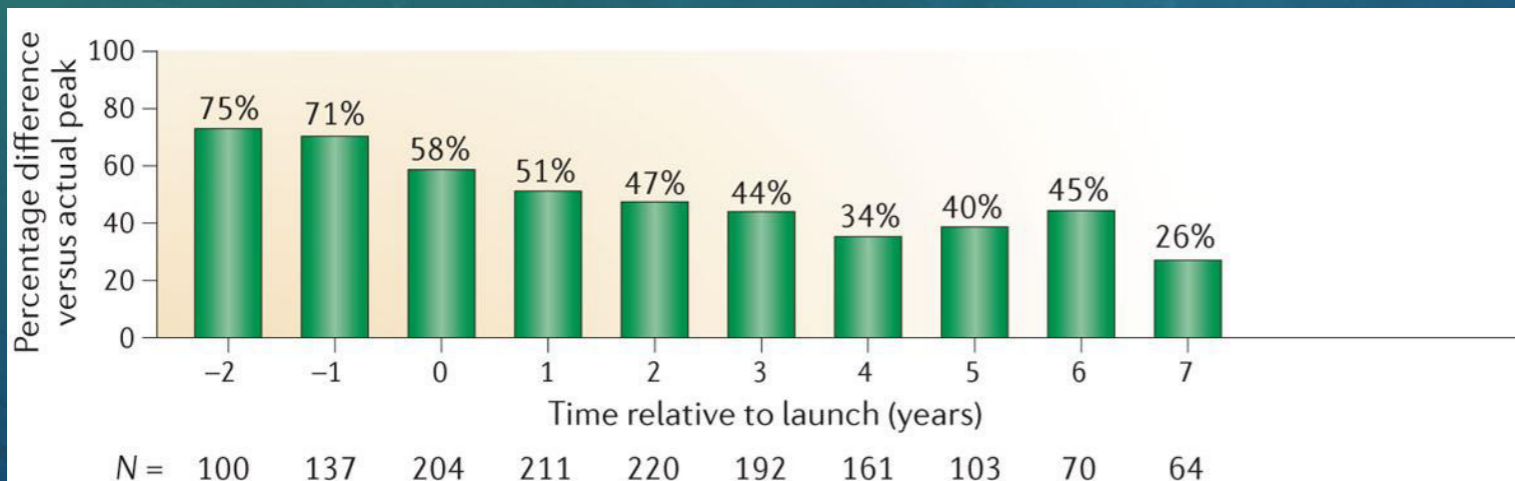


- $COGS = CapEx/lifetime + RM + Labor$
 - $COGS = \$100/g = \$40(dep) + \$60 (RM+L)$
 - CapEx can be high even if COGS is low.
 - Price: \$1,000/g, dep = 4% sales
 - CapEx: \$500mm
- People with \$500mm have choices and don't like CapEx. Top reasons:
 1. Forecast is usually wrong
 2. Hundreds of millions needed at once
 3. Competition with developing more drugs
 4. Decades of depreciation and risk of writeoff if technology changes
 5. Risk of drug not approved or delayed
 6. Need to build years before demand

PROBLEM #1: THE FORECAST IS USUALLY WRONG



- 260 drugs launched 2002-2011
- “...most ...forecasts were wrong, often substantially”
- >60% off by > 40%
- 20% overly optimistic by >160%
- Still wrong years post-launch
- If actual < expected
 - Underutilized Factories
 - Excessive Depreciation
 - Breaks mfg budget
- If actual > expected
 - Stockout, lost sales...



Cha, M., Rifai, B. & Sarraf, P. Pharmaceutical forecasting: throwing darts?. *Nat Rev Drug Discov* 12, 737–738 (2013).
<https://doi.org/10.1038/nrd4127>

PROBLEM #2 HIGH CAPEX



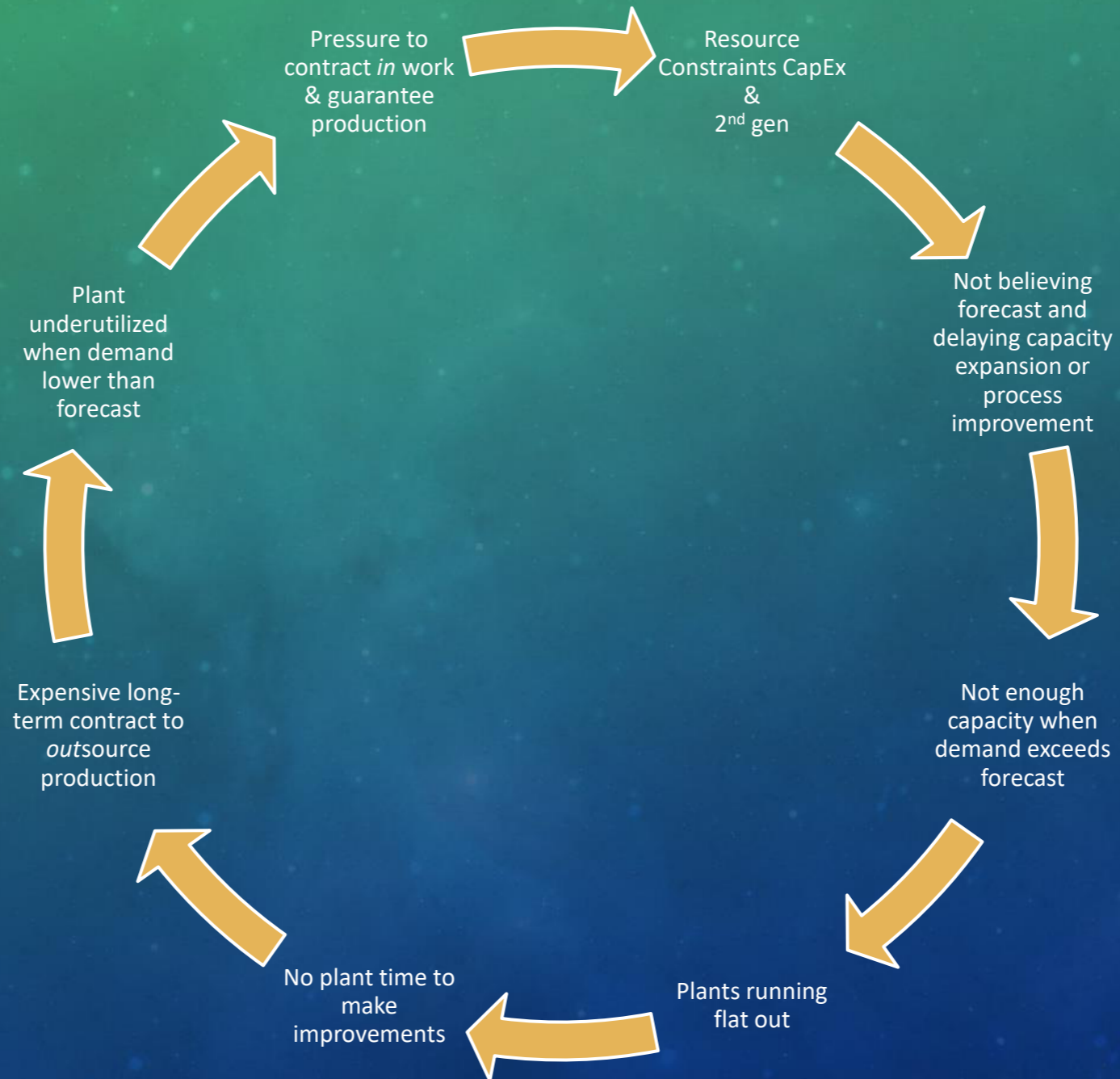
- Biopharm vs. small molecule
 - More CapEx
 - Produce a lot less
- 1,000 x more expensive on \$/capacity basis
- Equipment usually empty or mostly water

TABLE 1 Estimated capital costs for biopharmaceutical and small molecule API facilities

	Biopharmaceutical		Small molecule API ^a	
	6-pack	2k SUB	Batch	Continuous
Capital (\$)	500 MM	125 MM	73 MM	31 MM
Capacity (kg/year)	4000	4000	200,000	200,000
Normalized Capital \$/((kg/year)	125,000	31,000	370	160

^aAPI capital figures include working capital, while biopharmaceutical figures only include the cost of the facility.

BIOPHARM TECHNOLOGY VISCIOUS CYCLE



SOLUTION

- Don't complain about forecasts & R&D pipeline
- Mitigate forecast variability through ***Flexibility***
- Lower CapEx to reduce impact of low utilization

FLEXIBILITY TO MAKE A VARIETY OF PRODUCTS IN THE FACE OF UNCERTAINTY AND CHANGING DEMAND

- Problems to solve
 - Forecast variability
 - Facility fit differences for new products
 - Personalized/targeted medicine
 - changeover eats into plant time
- What
 - Delay capital until just before needed
 - More fully utilized facilities/reduced capital
- How: Build only what's needed now
 - Equipment that allows flexibility in
 - Rate of production (turndown)
 - Type of product
 - Reconfigurability
 - Portability
 - Interchangeability
 - Fast change-over
 - Automated qualification

CAPITAL & OPERATING COST AND SUSTAINABILITY NOT A BARRIER TO AVAILABILITY OF CAPACITY, INNOVATION OR CHANGE

- What

- >100X capital reduction for DS & DP
- No need to expand building footprints because process intensifies faster than need to build out.
- COGM low enough to increase patient affordability access
- Fully recyclable SUS, carbon neutral process

- How

- Intensified, integrated, continuous processes
- Standardized off-the-shelf equipment

1. Initial	2. Expand	3. Qualify new																																																
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VISION: BY 2029 INVENT, DESIGN, BUILD AND HELP COMMERCIALIZE DRUG SUBSTANCE AND PRODUCT MANUFACTURING CAPABILITY ENABLING:

- **Flexibility** to supply extremely diverse and changing portfolio of products in the face of uncertainty and changing demand
- Improved **Control, Robustness** and **Security of Supply**
- Faster Product Development and Supply Chain **Velocity**
- **Sustainable** plastic and energy use
- **Capital & Operating Cost** dramatically reduced
 - No longer barrier to availability of capacity, innovation or change
- DS & DP expertise and thinking **integrated** vial to vial



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<i>12.15 – 12.45 pm</i>	<i>Lunch Break</i>
12.45 – 1.15 pm	A shared vision for biomanufacturing – John Erickson
1.15 – 2.15 pm	Markets' needs – Access to medicines that matter
2.15 – 3.00 pm	Roundup & Q&A session



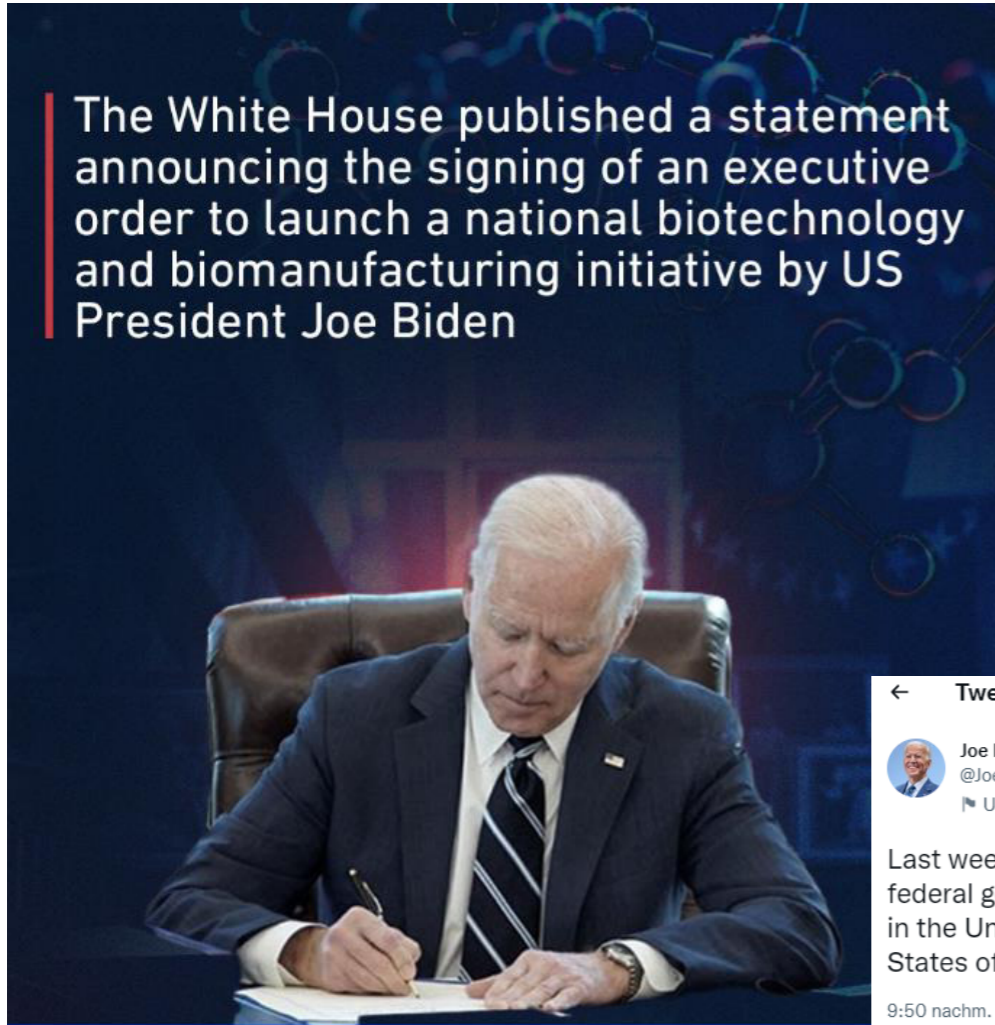
***Markets' needs –
Access to medicines that matter***



Access to high-quality medicines is today's top-of-mind issue

From patient access to building critical biotechnology and biomanufacturing capabilities

Selected examples



← Tweet



 **The White House**  @WhiteHouse

Today, @POTUS signed an Executive Order to launch a National Biotechnology and Biomanufacturing Initiative.

Learn how this Initiative will create jobs at home, build stronger supply chains, and ensure the United States' global leadership in biotechnology:



← Tweet

 **Joe Biden**  @JoeBiden
United States government official

Last week, I signed an executive order that directs the federal government to ensure biotechnologies invented in the United States of America are made in the United States of America.

9:50 nachm. · 21. Sep. 2022 · Sprout Social

The New York Times

TheUpshot

THE NEW HEALTH CARE

How to Decrease Prices for an Expensive Class of Drugs

Latest Issues **SCIENTIFIC AMERICAN** Cart 0 Sign In |

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THE CONVERSATION

MEDICINE

Biologics: The Pricy Drugs Transforming Medicine

Rather than being designed by chemists, this class of pharmaceuticals is produced by living cells. Here's where they come from and how they work

By Ian Haydon, The Conversation US on July 26, 2017



Biologics have become foundational therapies

Antibody-based therapies within top-10 drugs in disease by value, number / selected examples



Transformed the treatment of **AMD**



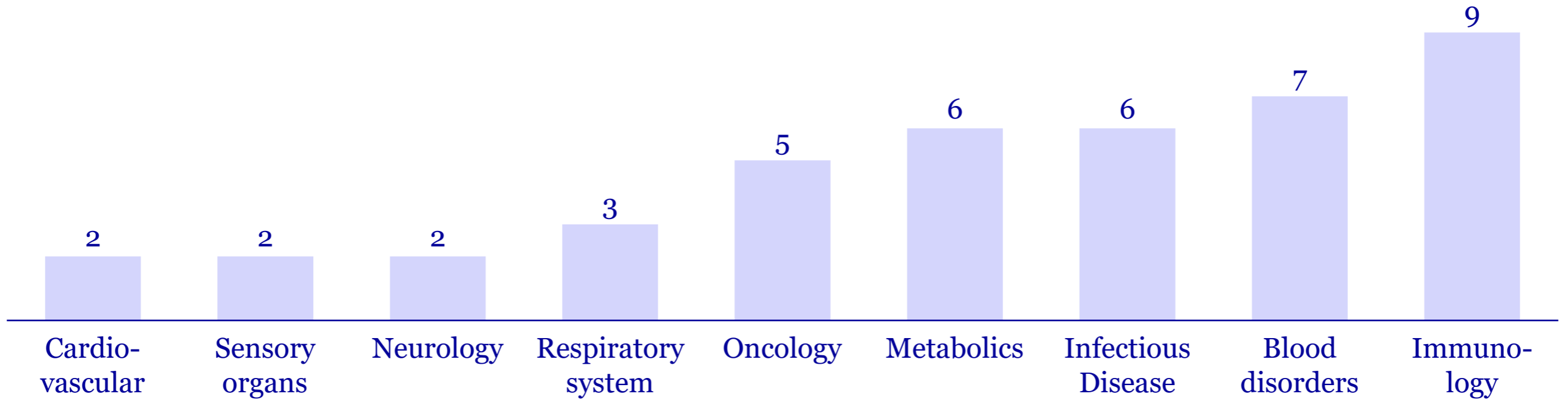
Propelled a paradigm shift in **Oncology**



Significantly improved care standards in **Hemophilia**



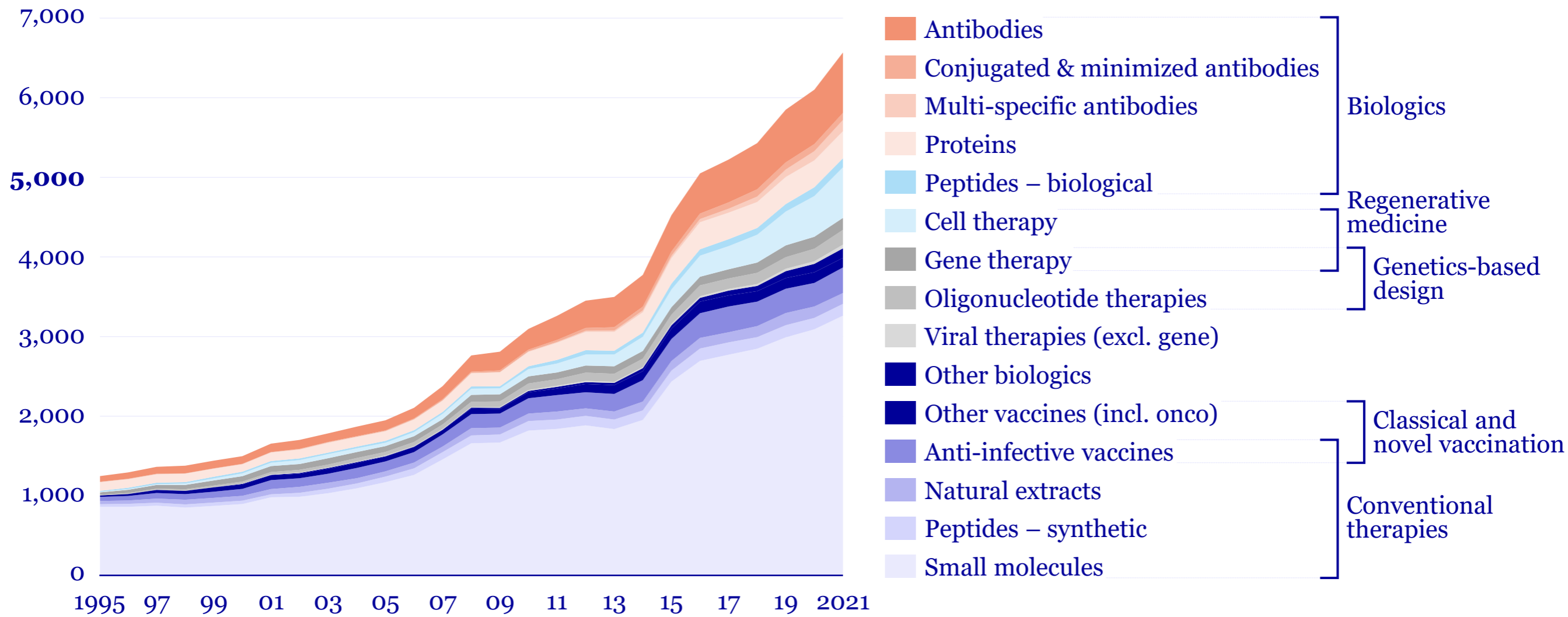
Transformed approach towards **autoimmune diseases**





Also, biologics will play a major role in the future

Number of pipeline products¹ in industry R&D pipeline, from Phase I to III





Do these important therapies reach everyone?

Our contribution to meet UN Sustainable Development Goal 3



7,000
underserved
rare indications

Underserved indications



70%
higher prices for antibodies
vs. small molecules

Underserved populations



6 bn
without access

Underserved regions¹



12 months
to first Ab therapy
in COVID

Global health &
pandemics²



What if COGS could be below US\$ 50 per gram?

Potential against access opportunity areas

Access opportunity areas	Critical factors preventing access		
	Cost	Agility	Risk
Serve underserved indications including combination treatments	High / can unlock access	High / can unlock access	High / can unlock access
Provide access to underserved populations while providing stress and reduce economic burden for healthcare systems	High / can unlock access	Low	Low
Serve regions with limited / no access to life saving therapies	High / can unlock access	High / can unlock access	Low
Provide rapid and effective pandemic response	High / can unlock access	High / can unlock access	High / can unlock access

Legend: High / can unlock access



Solving one access challenge at a time: underserved indications

Illustration of challenge and solution elements

50%

of the people affected by rare diseases are **children**

30

million people in **Europe** are living with rare disease

7,000

rare disease & disorders have been identified

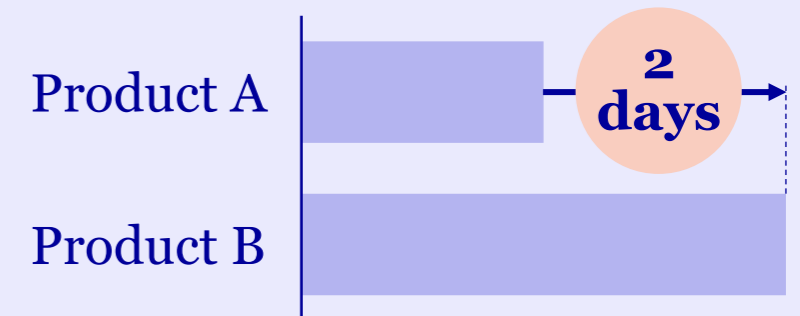
30

million people in **US** are living with rare disease

Just
EVOTEC BIOLOGICS

1. High titer cell lines

2. Rapid turn around





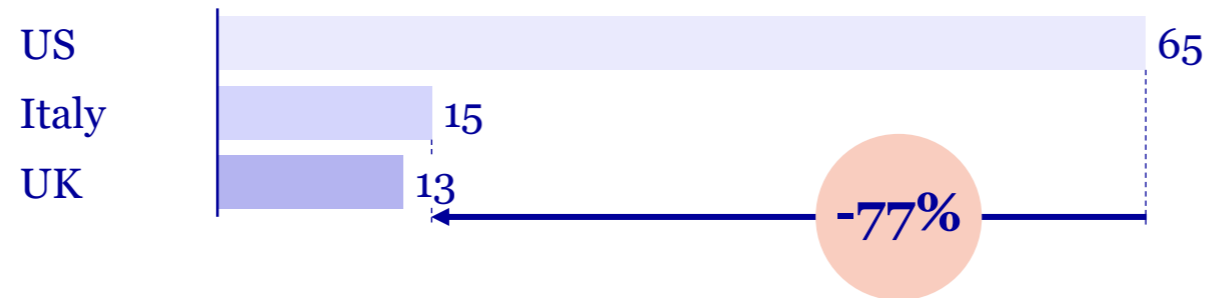
Solving one access challenge at a time: underserved populations

Illustration of challenge and solution elements

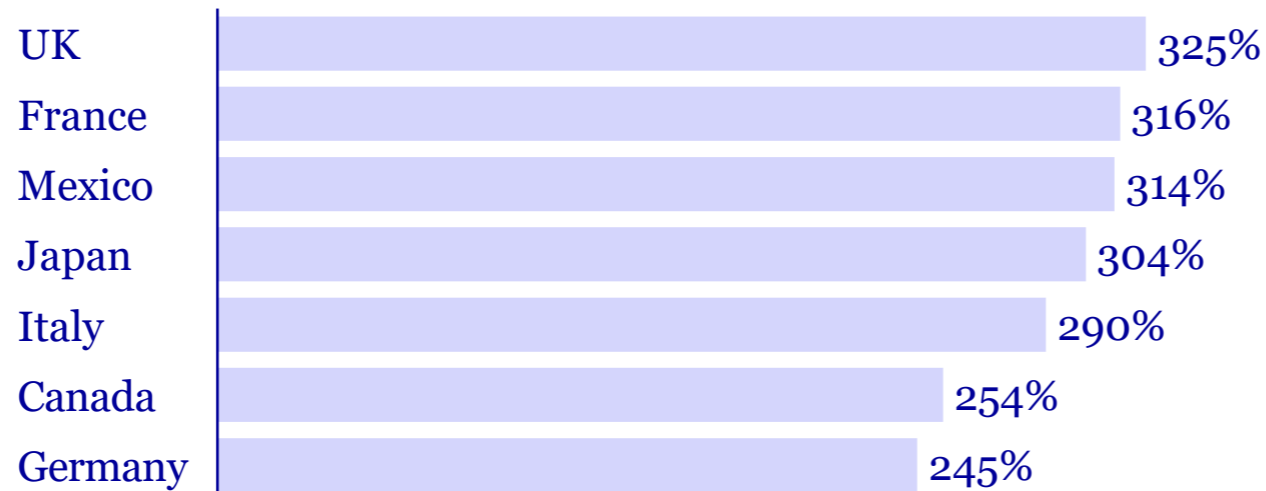


Case example for top-5 mAb therapy – Psoriatic Arthritis

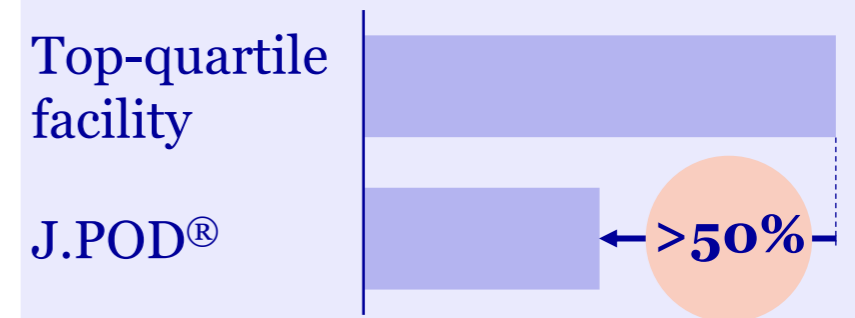
Comparison of annual treatment costs U.S., in USD (000s)¹



US Biologics prices as a % of other countries²



Lower COGs potential US\$/g



Proximity to key markets



J.POD[®] technology can be quickly established in other countries/regions



With the IRA, a first domino piece fell over with regard to drug pricing

Illustrative scenario for end-of-lifecycle biologics and biosimilars



Managed Healthcare
EXECUTIVE

NEWS MEDIA ▾ CONFERENCES PUBLICATIONS ▾ EVENTS ▾ CME/CE RESOURCES

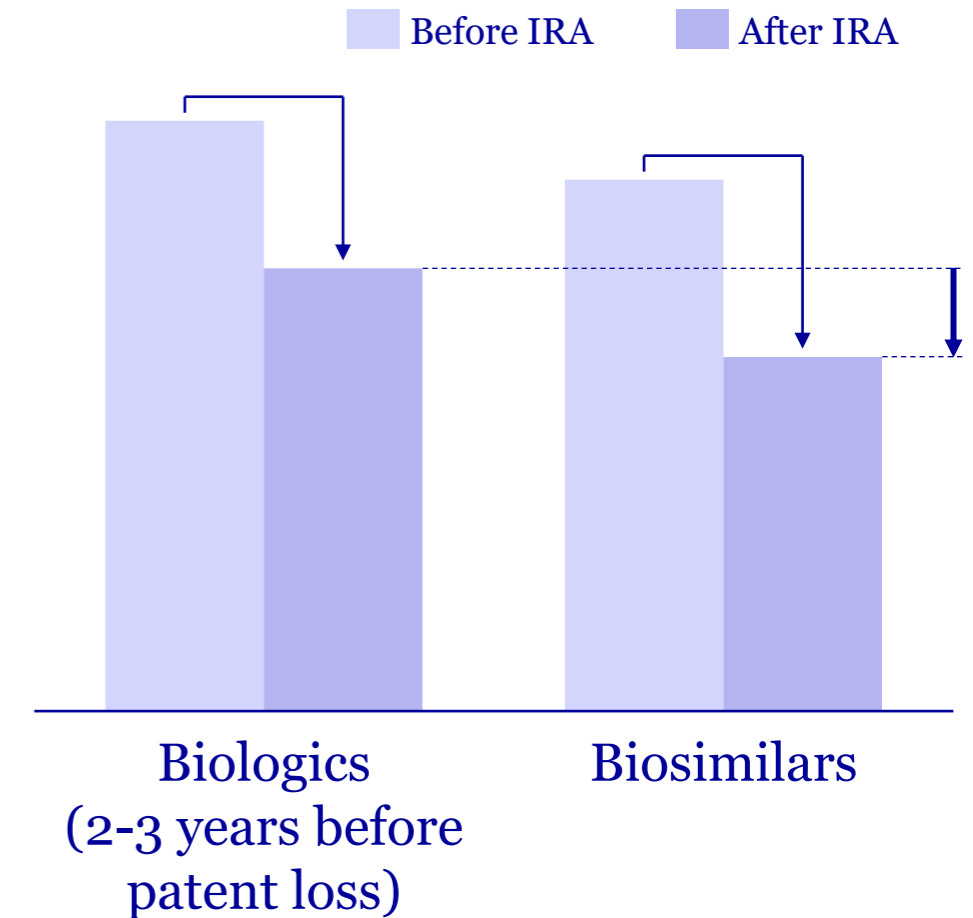
☰ How the Inflation Reduction Act May Affect Biosimilars

September 13, 2022
Tony Hagen

✓ The Inflation Reduction Act

A scenario for pricing impact?

Conceptual view on future price levels



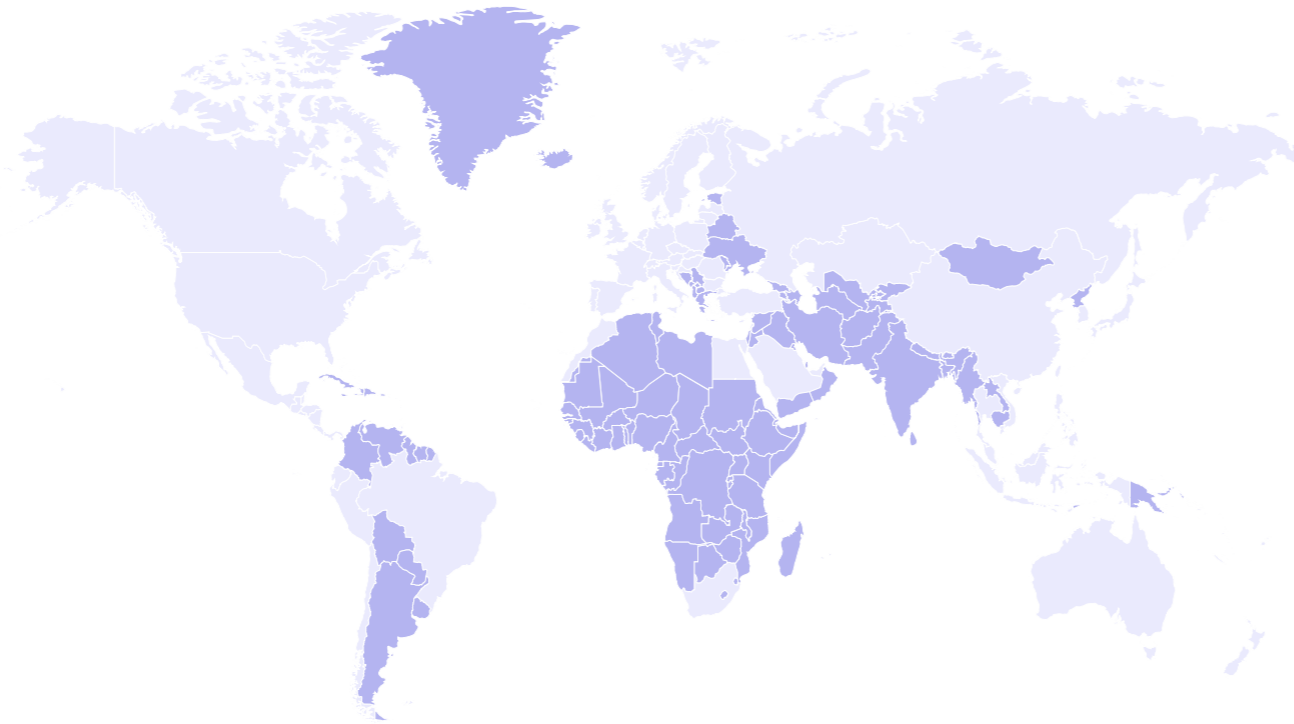


Solving one access challenge at a time: underserved regions

Illustration of challenge and solution elements



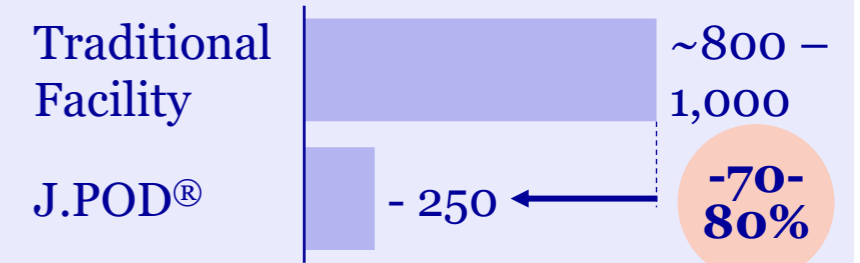
Case study – Countries where key PD-1 antibodies are currently not available



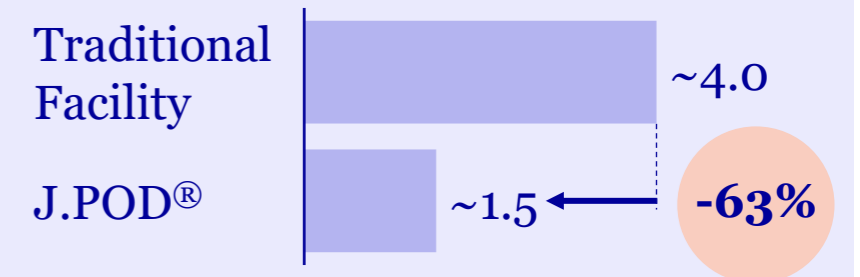
Enabling new business models



Facility building costs, US\$m



Time to set up facility, years





Solving one access challenge at a time: global health & pandemics

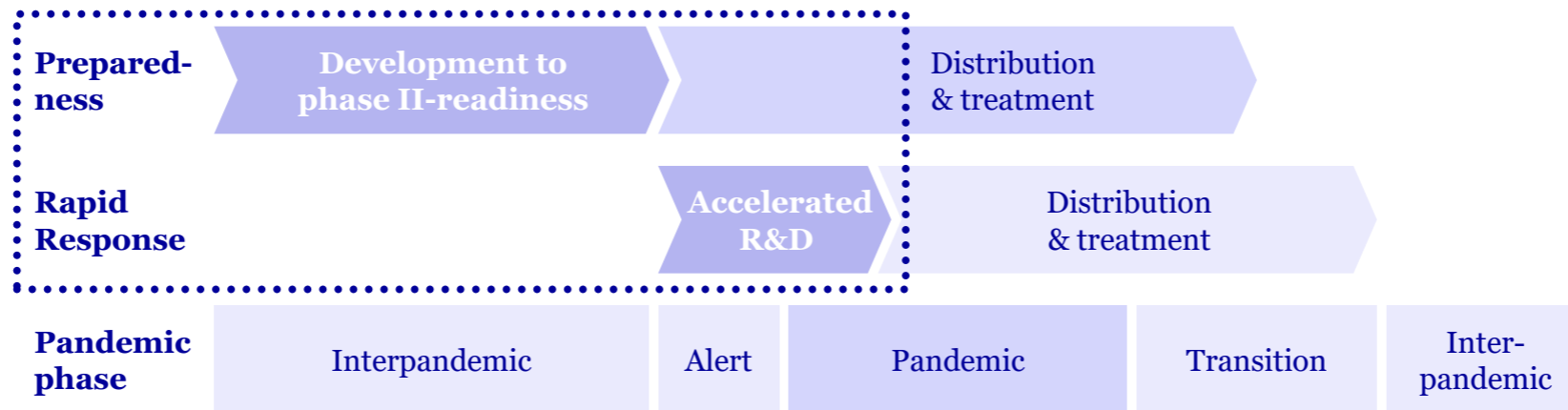
Illustration of challenge and solution elements



U.S. Department of Defense



Preparedness & Rapid Response activities during pandemic phases



Just
EVO TEC BIOLOGICS

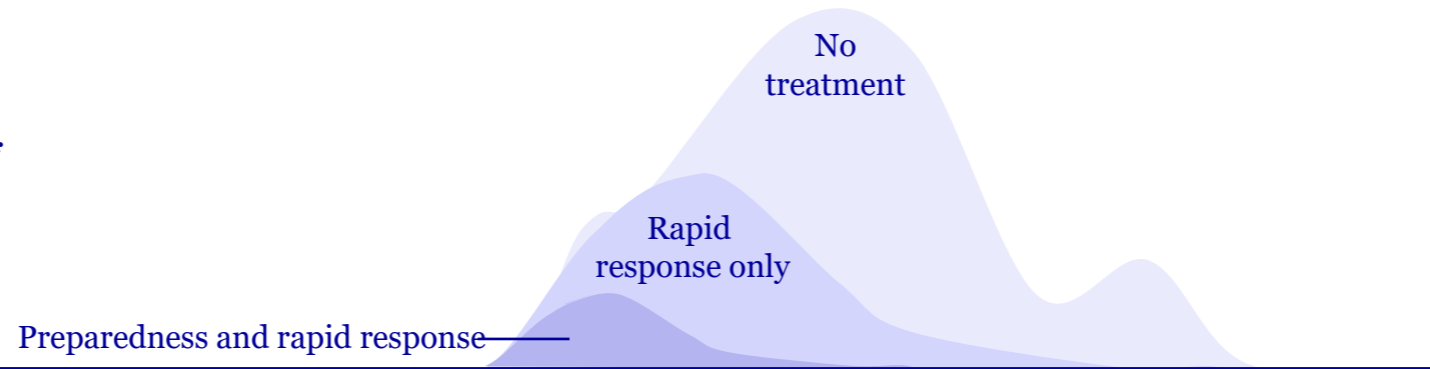
✓ **Low cost enabling preparedness**

✓ **Speed**

✓ **Flexibility**

✓ **Rapid Scale-up**

Number of infected patients





TOGETHER with our partners for access

Our mission, realized through partnerships



Design and apply innovative technologies to dramatically expand global access to biotherapeutics

Access to innovative molecules

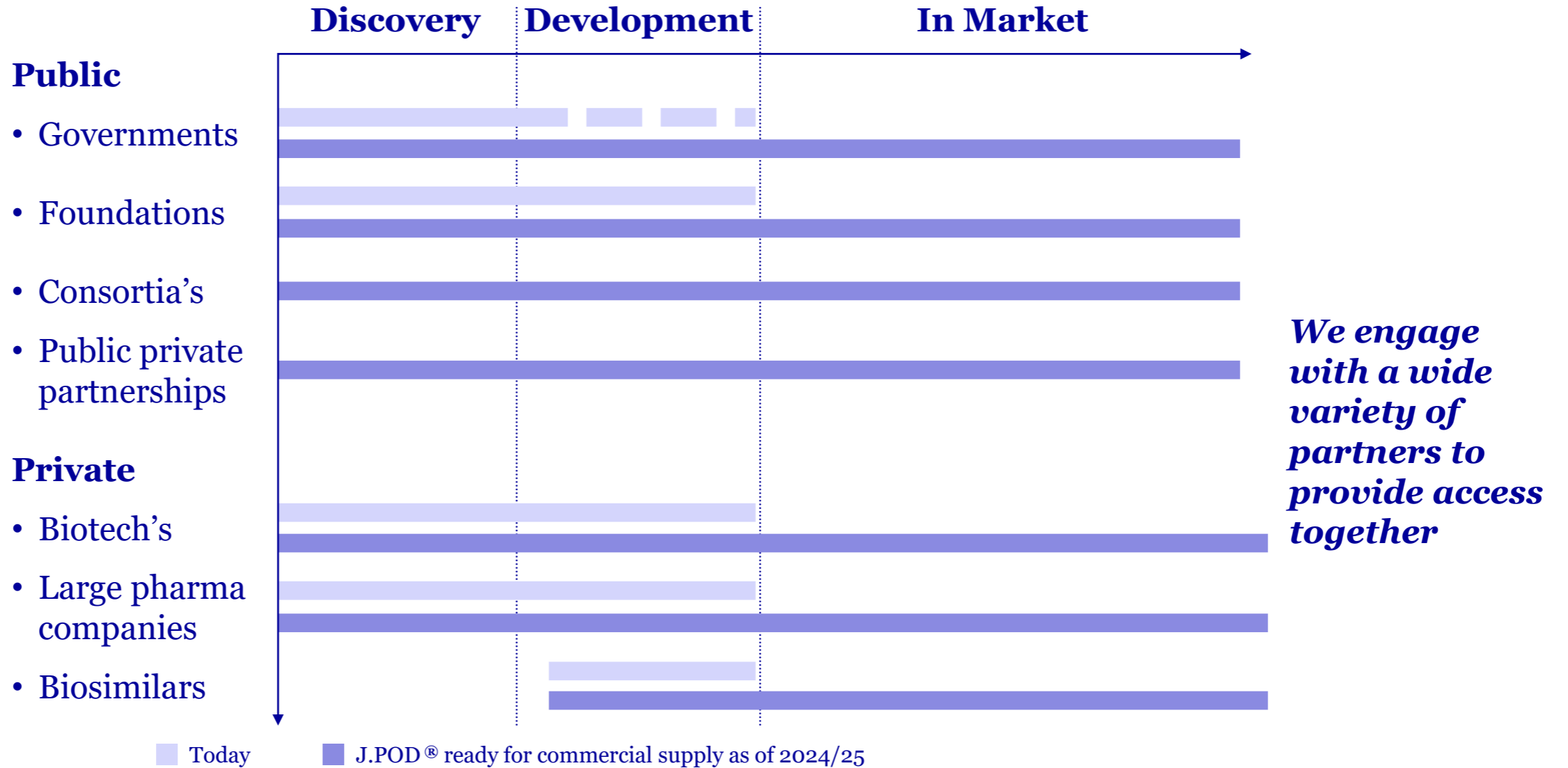
Access to biosimilars

Access to pandemic preparedness



We aim to tackle this challenge TOGETHER

Our key partnering archetypes





We are expanding across disease areas

Just - Evotec Biologics partnering programs

Disease area	No. of programs	Discovery	J.MD™ optimization	Pre-clinical development	Clinical manufacturing	Commercial manufacturing
Oncology	1	▶				
	4	▶▶▶▶				
Autoimmune	2	▶▶▶▶▶				
	1	▶▶▶▶▶▶				
Cardiovascular	2	▶▶▶▶				
CNS	1	▶▶▶▶▶				
Infectious diseases	1	▶▶▶				
	3	▶▶▶▶				
	3	▶▶▶▶▶				
Other / undisclosed	ND ¹⁾	▶▶▶▶				
	ND	▶▶▶▶▶▶				

Broad basis for sustained growth

- > 15 partners / 20 programs
- Continued emphasis on optimal value mix of
 - Fee for service
 - **EVO**royalty
 - **EVO**equity
- Better access to affordable medicine for all
 - >50% of programs addressing targets set to reach UN SDG 3²⁾

¹ Not Disclosed

² United Nations Sustainable Development Goal 3: Ensure healthy lives and promote well-being for all at all ages



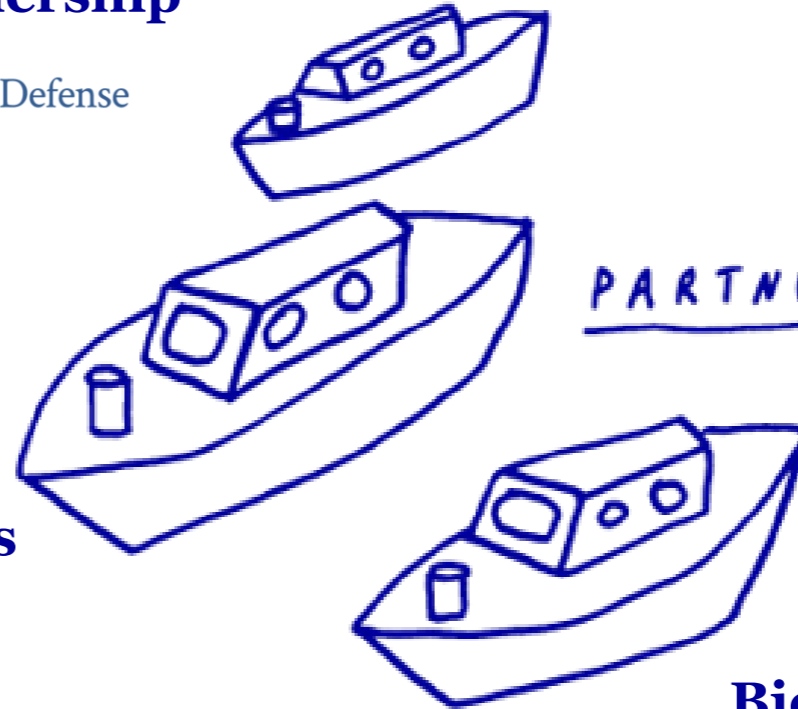
Case examples to illustrate our growing impact

Recent case examples and ongoing discussions

Government Partnership



U.S. Department of Defense



PARTNERSHIPS

Biotech Partnerships
Various partners

Biosimilar Partnership
Undisclosed partner



Partnership with U.S. Department of Defense (DOD)

Discovery to Phase I partnership example to ensure pandemic preparedness



U.S. Department of Defense

Important catalyst for future acceleration of expansion

- Repeated awards signal full validation of our technology platform
- As a member of the DOD network, we are identified as “preferred partner” for future programs
- Improved competitive position in light of the Executive Order of Biden Administration

2020

US\$ 18.2 m
Selection of anti-SARS-CoV-2 mAbs

2021

US\$ 28.6 m – Extension
COVID-19 prophylaxis

2022

Joining DOD’s advanced development and manufacturing network of facilities
Up to US\$ 49.9 m –
Development of mAbs against plague

2020

2021

2022

New

Q4 2022

selected for a 2nd award under the Accelerating Antibodies Program



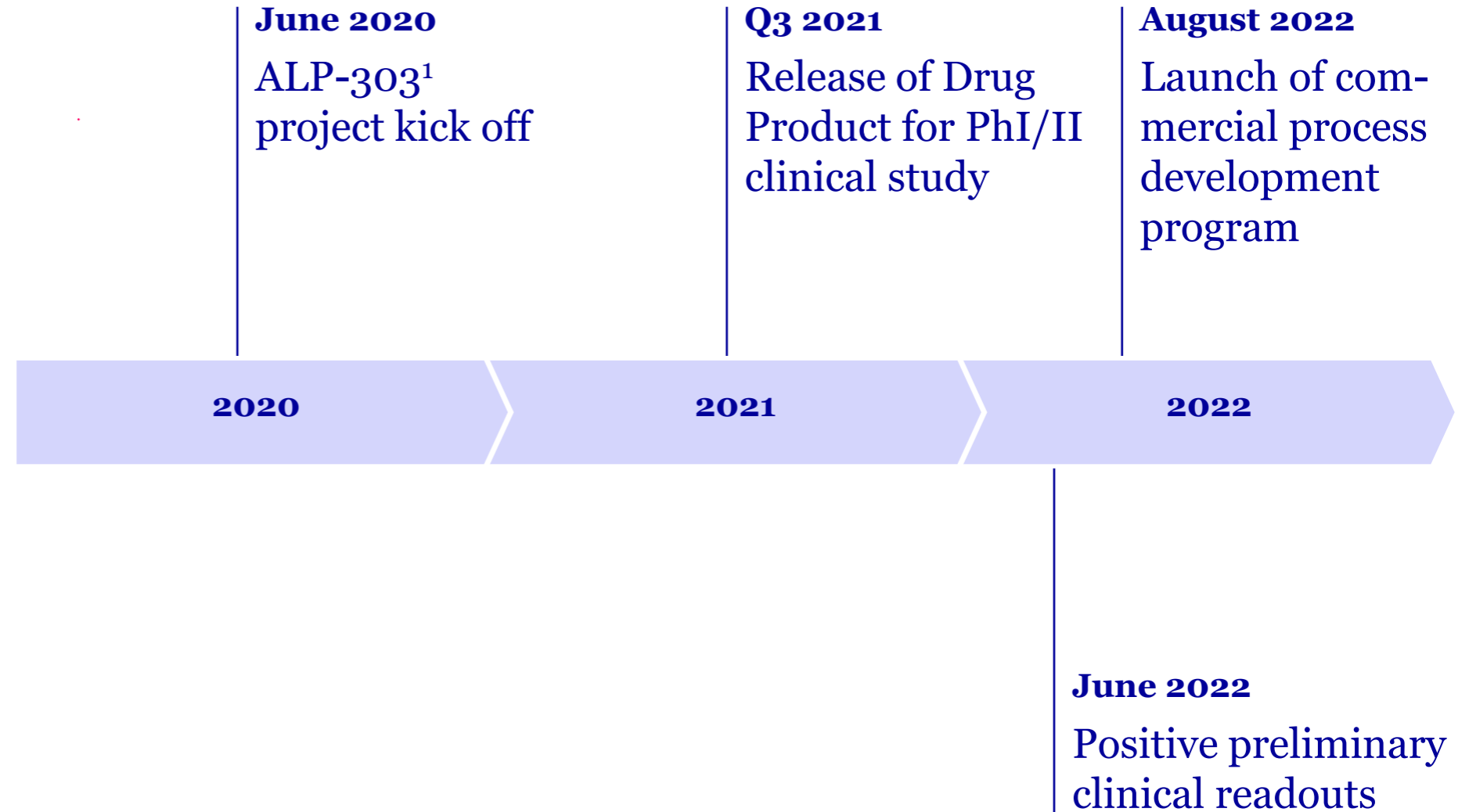
Partnership with Alpine Immune Sciences

From clinical to commercial partnership for novel biologics



Demonstration of Just – Evotec Biologics platform benefits to Biotech programs

- Rapid development from lead candidate to supply of Phase I/II material
- De-risking clinical development for non-standard antibody formats
- Securing transition from clinical to commercial stage

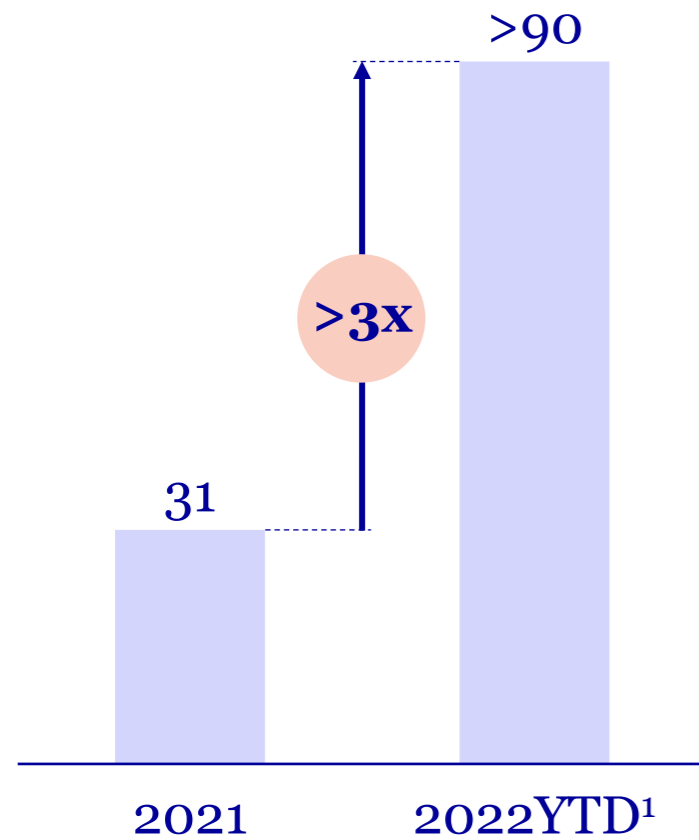




We are making progress in expanding the partnering pipeline

Summary of commercial progress 2022

Just – Evotec Biologics Closed Sales Sales in € m



Key progress since half year results



Secured and initiated new anti-Plague mAb development program in Q3 (up to US\$ 49.9 m over 5 years)



Launched commercial process development activities in Q3

Undisclosed biosimilar partner

Kicked off

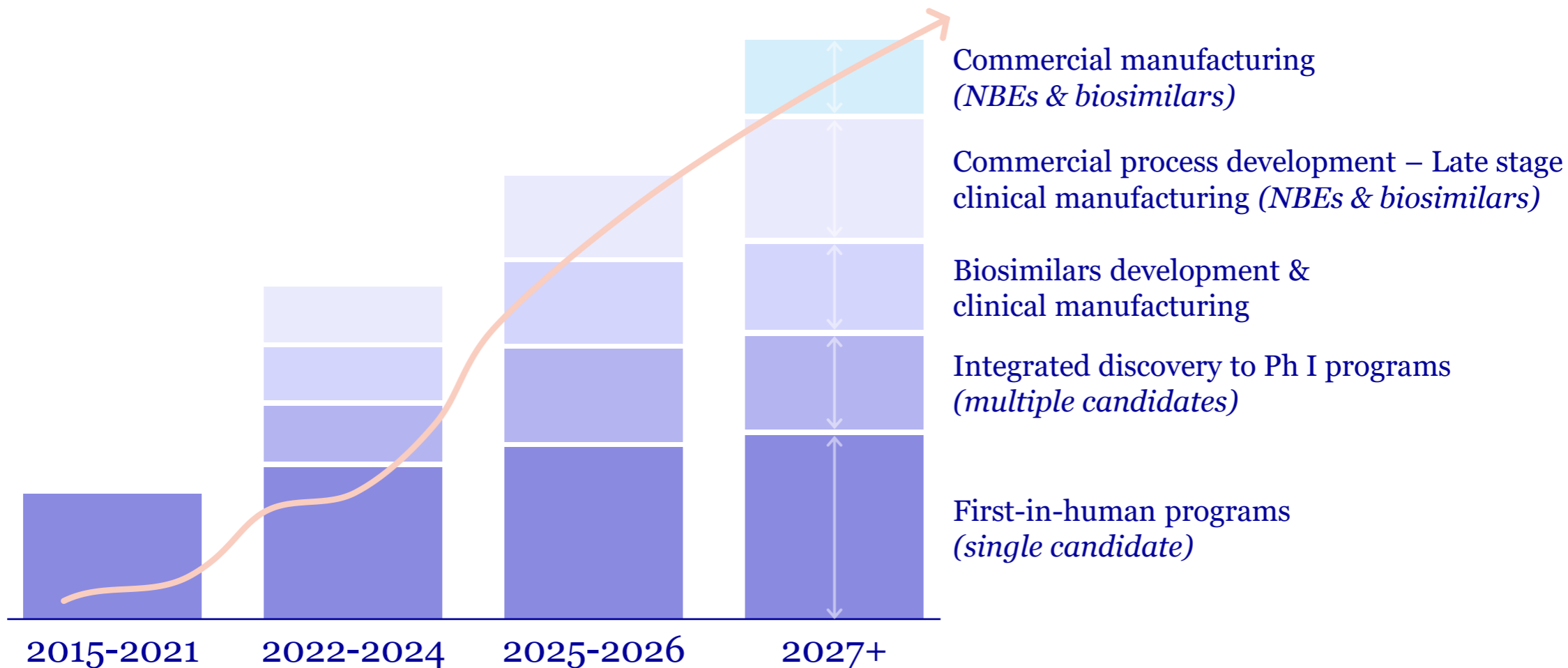
- Closed Sales is leading indicator of future 2023 and 2024 revenues
- Close Sales 2022 show strong growth – indicates market entry progressing and future potential
- Business Development is ramping up further to maximize partnering opportunities, particularly in U.S. and Europe



How we expect to evolve and accelerate the partnering portfolio

Just - Evotec Biologics – Revenues and composition of underlying project portfolio

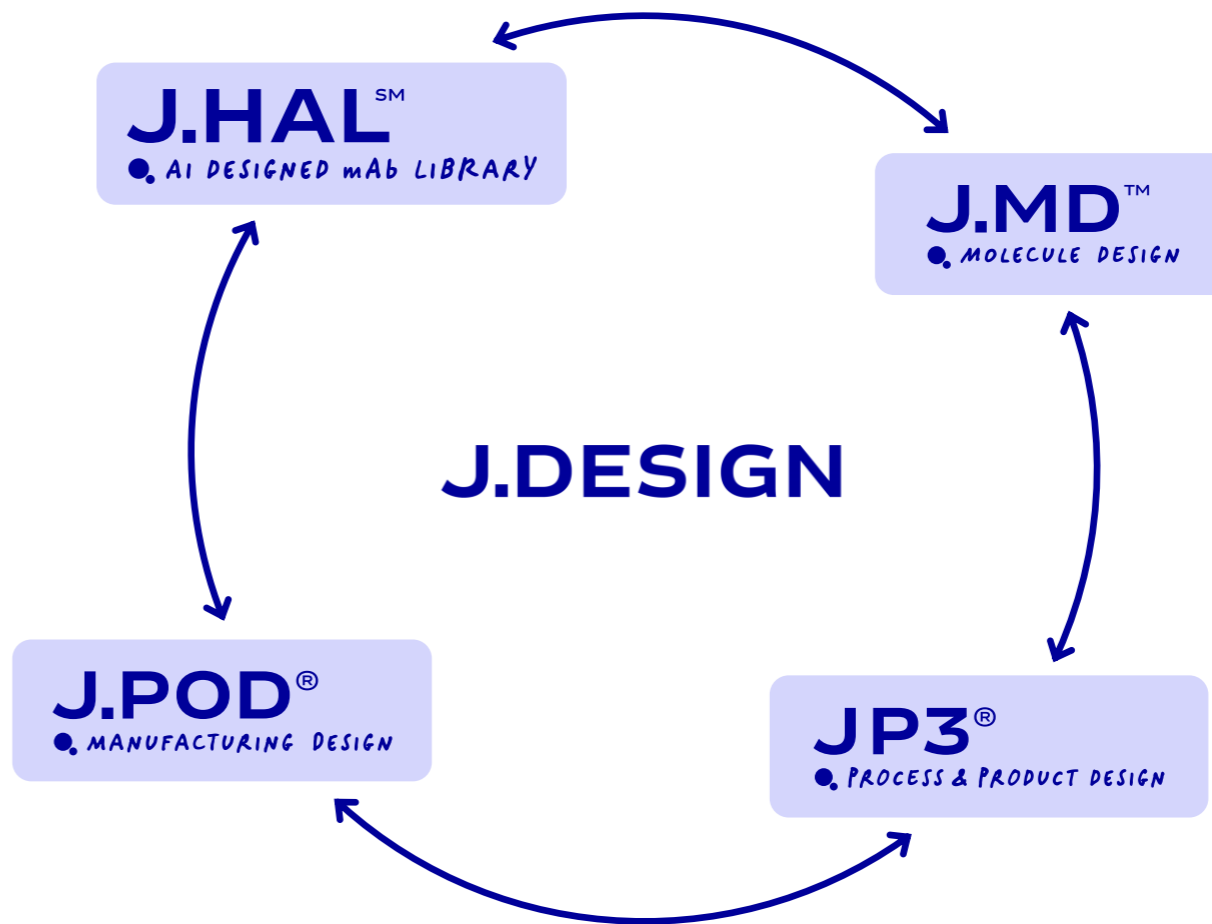
Revenues, US\$ m



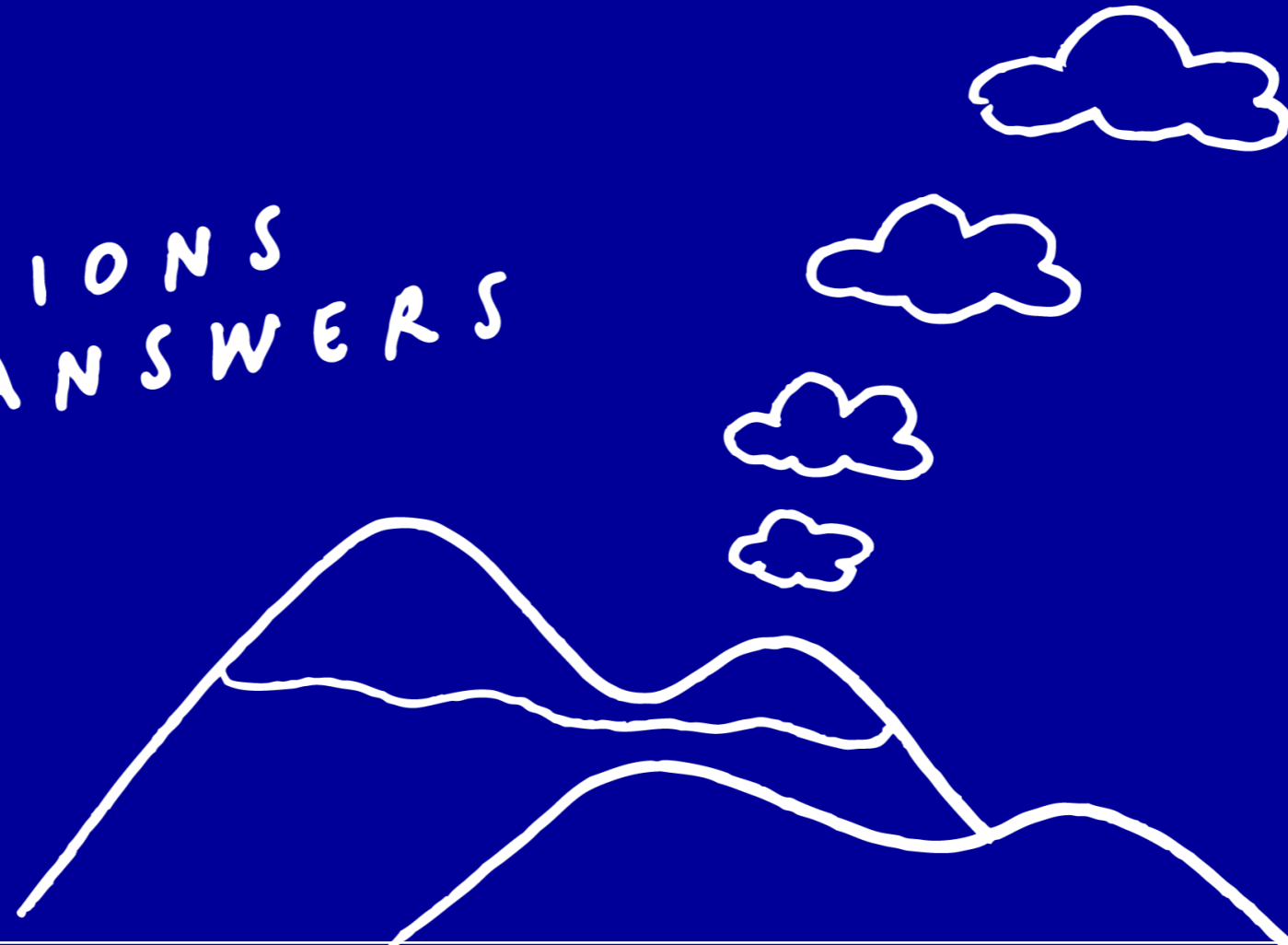


We are ready to tackle the global access challenge

Just - Evotec Biologics combines unique tools from discovery through manufacturing



QUESTIONS
AND ANSWERS





#RESEARCHNEVERSTOPS

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