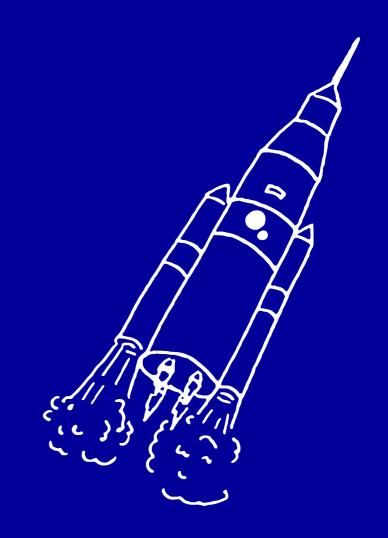
#RESEARCHNEVERSTOPS

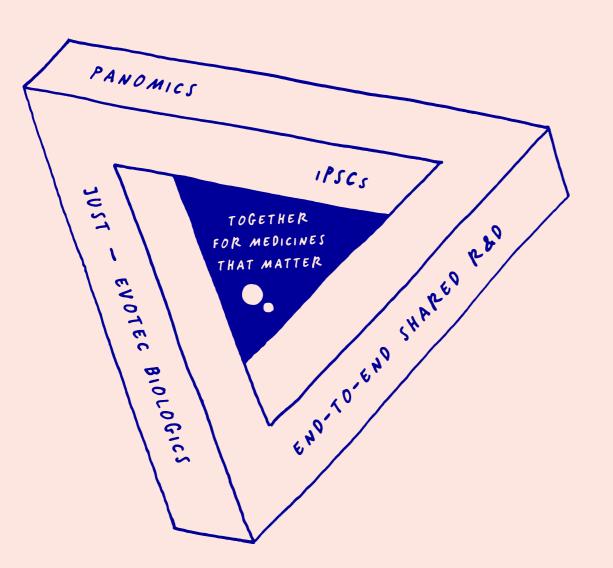


Just – Evotec Biologics

Introducing a paradigm shift in biologics



Together for Medicines that Matter



We aspire to impact patients' lives by

- **PanOmics**-driven drug discovery for deep disease understanding and effective therapies
- **IPSCs** "off-the-shelf" cell therapy based on induced-pluripotent stem cells

Just – Evotec Biologics

Artificial Intelligence and continuous manufacturing for better access to biologics

End-to-End Shared R&D

Integrated business-to-business platform for increased probability of success from target to the clinic



Together for medicines that matter

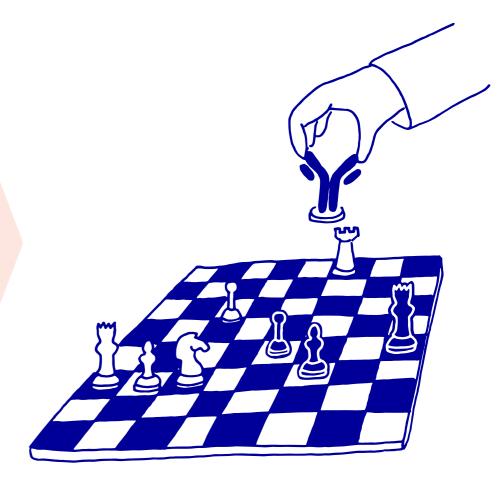
Game changers within business to business / partnered R&D

More precise medicine PanOmics databases, multi-modality End-to-End Shared R&D

A.I./M.L. & technology convergence Latest technologies coming together with drug discovery, development, safety prediction and molecular diagnostics

Right business model & best talents

Collaboration – from fixed to variable costs, with efficient access to best know-how





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

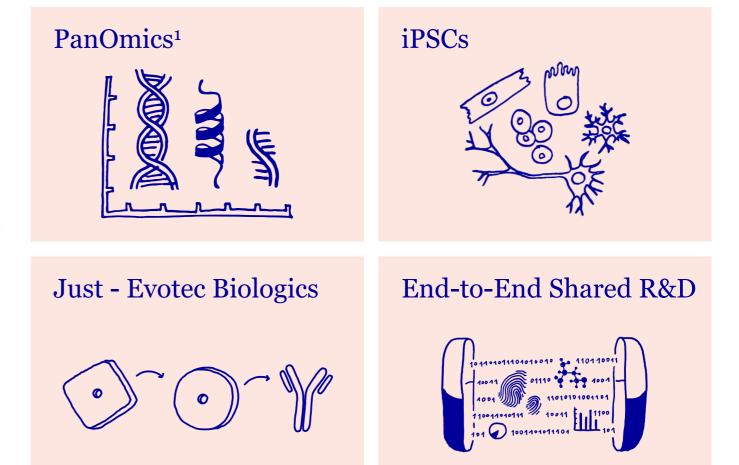
Lifetime risk for cancer e.g., 44% in men & 38% in women

Need for wider access

Less than 20% of world's population have access to life changing biotherapeutics

Need for better safety earlier 60% of all drugs still do not pass Phase I

Our focus areas



Sources: Schuhmacher A, et al. R&D efficiency of leading pharmaceutical companies - A 20-year analysis. Drug Discov Today. 2021 Aug;26(8):1784-1789. doi: 10.1016/j.drudis.2021.05.005. BIO, QLS Advisors, Informa UK Ltd: Clinical Development Success Rates and Contributing Factors 2011–2020, February 2021. Hingorani, A.D., Kuan, V., Finan, C. et al. Improving the odds of drug development success through human genomics: modelling study. Sci Rep 9, 18911 (2019). <u>https://doi.org/10.1038/s41598-019-54849-w</u>: Ageing and Health, WHO, October 2021; Evotec estimates 1 Includes PanOmics-enabled drug discovery, iPSC drug discovery platforms as well as molecular patient databases and clinical stratification



TOGETHER with our partners for a paradigm shift

Creating a massive impact on our industry





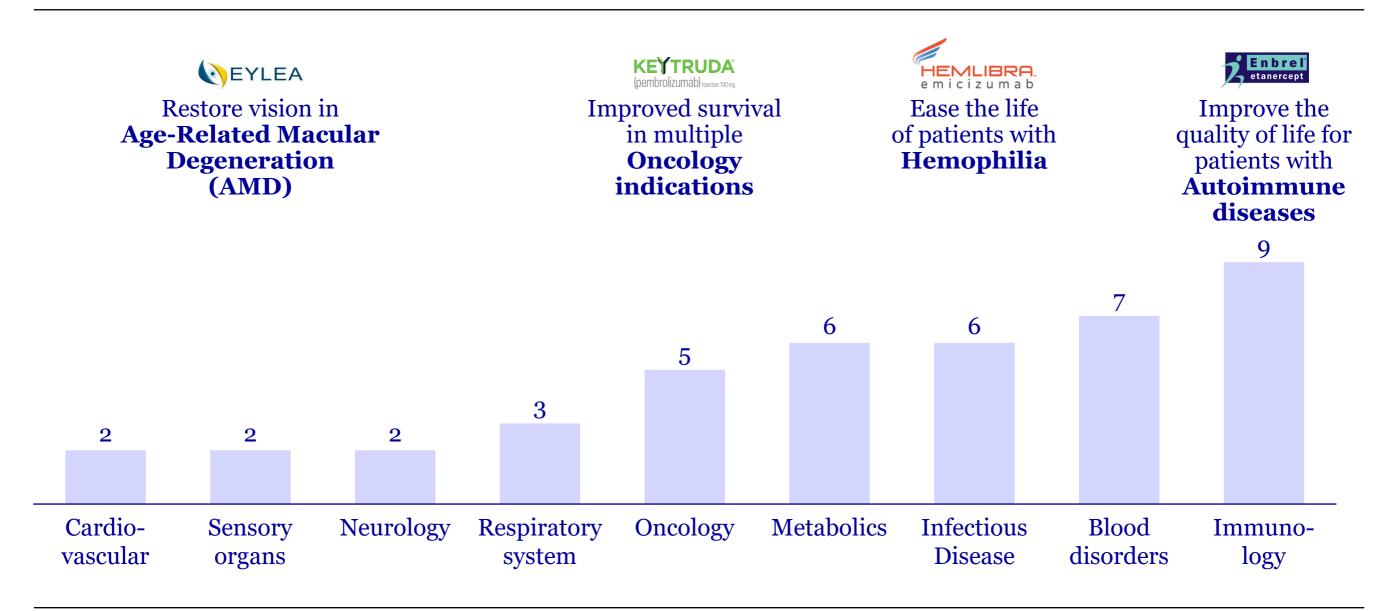
Our mission is to design and apply innovative technologies to dramatically expand global access to biotherapeutics

Together we will create a massive impact by providing access to critical biotherapeutics



Biologics have become foundational therapies ...

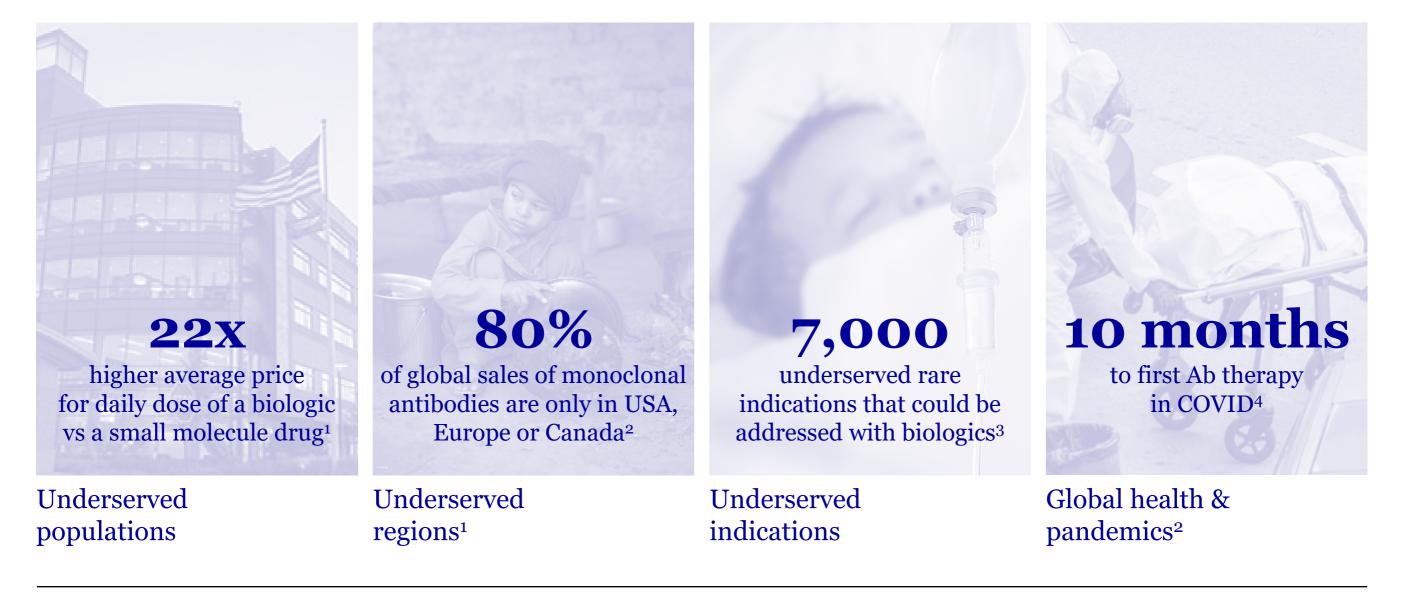
Antibody-based therapies within top-10 drugs in disease by value, number / selected examples





... but do these important therapies reach everyone?

Limited access to biologics exists today in many patient segments



1 Makurvet FD. Medicine in Drug Discovery; 2021;9:10075.

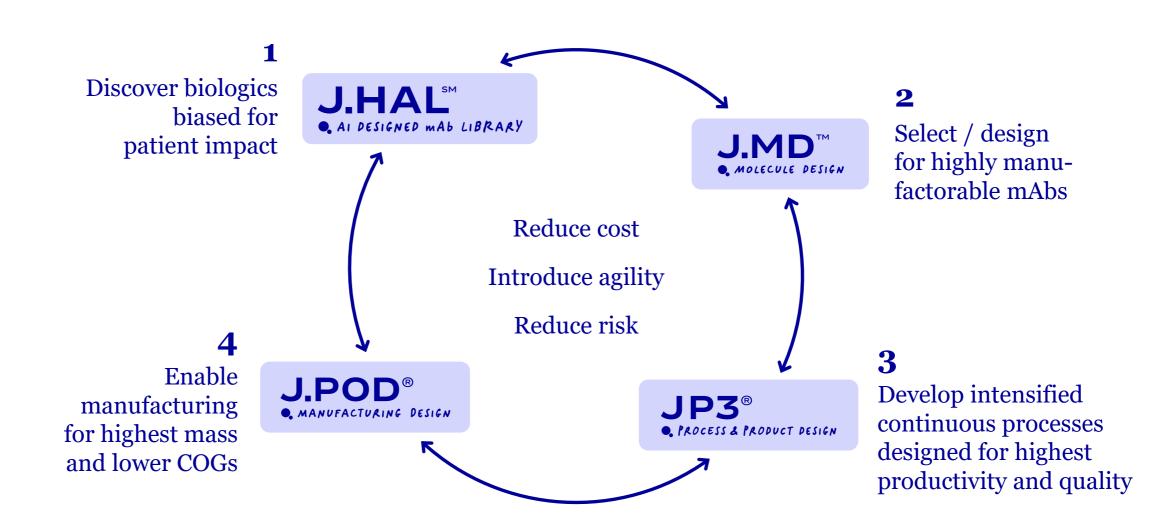
2 Morin S, et al. Lancet Glob Health 2023;11:e145-54.

A Photo by Muhammad Muzamil on Unsplash; B Photo by Isaac Quesada on Unsplash

3 Chediak L. I have a rare disease. This is my hope for the future of medicine. World Economic Forum. Available at: https://www.weforum.org/agenda/2019/05/rare-diseases-arent-rare-but-treatments-for-them-are-its-time-to-change-that/. Accessed October 24, 2023. 4 Toussi, S.S., Hammond, J.L., Gerstenberger, B.S. et al. Therapeutics for COVID-19. Nat Microbiol 8, 771–786 (2023). https://doi.org/10.1038/s41564-023-01356.

We aim to address low accessibility with J.DESIGN

Agility, reduced costs and risk for biotherapeutics



1. A complete offering to solve even the hardest discovery campaign

Generation of fully human antibodies: from traditional platforms to A.I.-driven approaches

Exploration of natural immune repertoire using phage display



Key distinguishing features

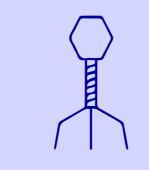
- Immune library generation upon immunization or natural infection
- *In vitro* selection of rare yeasts

Cost

• No species restriction

Risk

J.HAL[®], A.I.designed phage and yeast libraries



Key distinguishing features

- Highly diverse A.I. designed human library
- Time + cost savings for therapeutic development

B cell technology



Key distinguishing features

- Direct screening of millions of B cells upon immunization or natural infection
- No species restriction

In silico mAB design (coming soon)



Key distinguishing features

- State-of-the-art platform to identify optimal binders *in silico*
- Fastest way to generate binders
- Initial client projects started

Just – Evotec Biologics (J.DiscoveryTM)

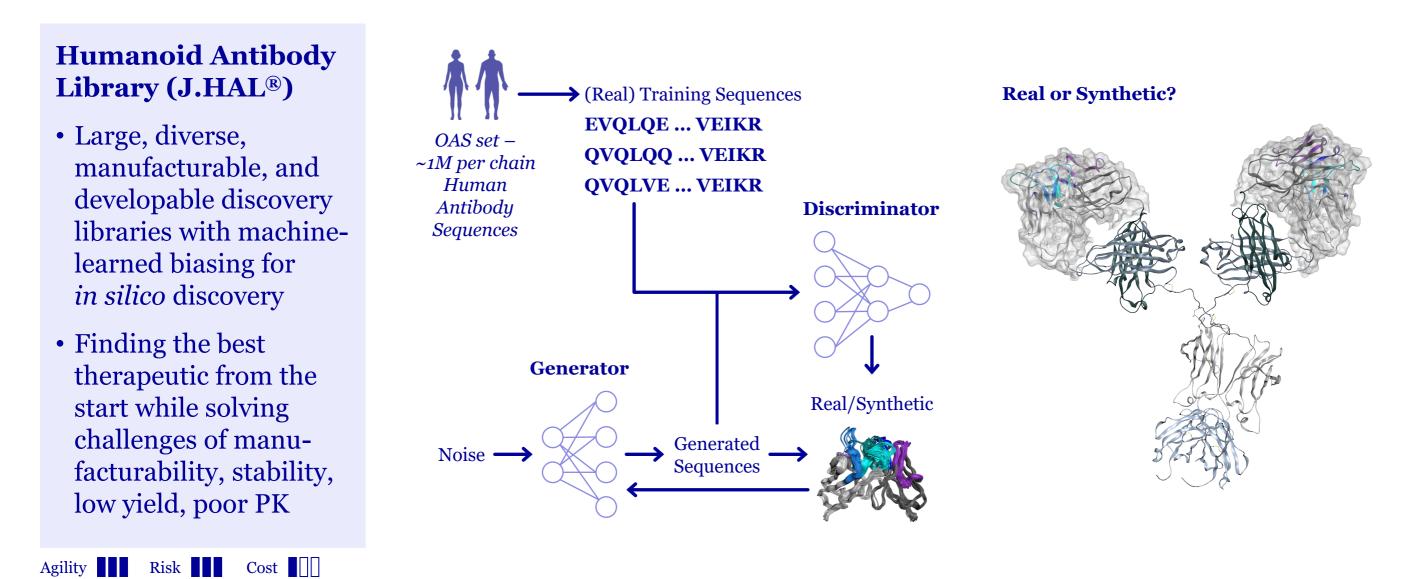
Evotec Hamburg/Toulouse

Agility



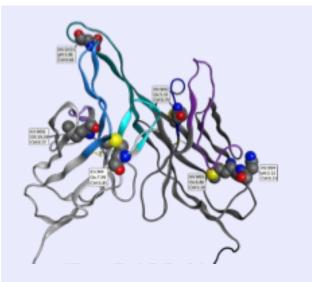
1. J.HAL[®]: Biased libraries to find the best therapeutic

The right pharmacodynamic properties combined improved stability, titer, attributes ...



2. Selection and design of best antibody enables highest productivity

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



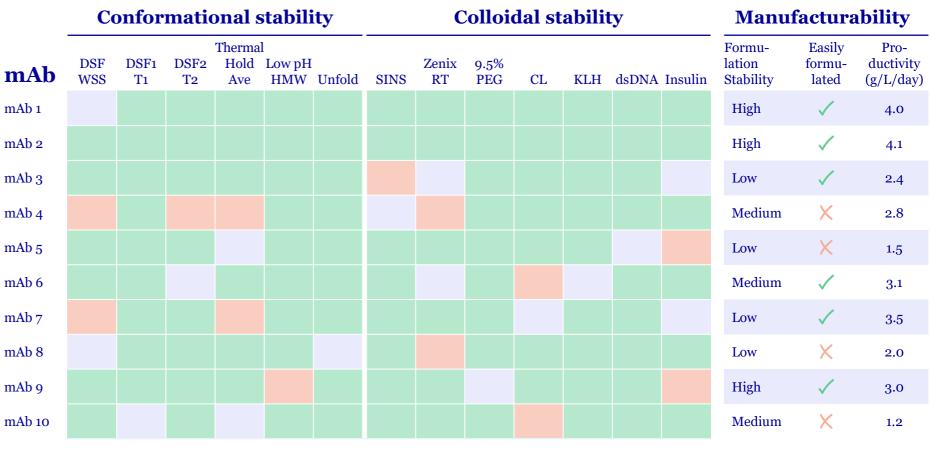
- *In silico* validation: Identify manufacturability of Ab by its sequence
- Selection for biophysical characterization
- Conformational stability

Risk

Cost

No violation

• Colloidal stability



High throughput biophysical characterization of mAbs

mAb 1 and 2 had best profile \rightarrow chosen for cocktail

Violation Undefined

Agility



2. Publication in Nature Medicine journal validates Molecular Design suite

A candidate antibody drug for prevention of malaria | Nature Medicine

nature medicine	Ø
Article	https://doi.org/10.1038/s41591-023-02659-z
A candidate of malaria	antibody drug for prevention
Received: 10 March 2023	Katherine L. Williams O ¹ ☉, Steve Guerrero O ¹ , Yevel Flores-Garcia ² ,
Accepted: 20 October 2023	Dongkyoon Kim ¹³ , Kevin S. Williamson ¹ , Christine Siska ⁴ , Pauline Smidt ⁴ ,
	Sofia Z. Jepson ⁽³⁾ ⁴ , Kan Li ⁵ , S. Moses Dennison ⁽³⁾ ⁵ , Shamika Mathis-Torres ² , Xiaomu Chen ¹ , Ulrike Wille-Reece ⁴⁷ , Randall S. MacGill ⁽³⁾ , Michael Walker ⁸ ,
	Erik Jongert ⁹ , C. Richter King ⁷ , Christian Ockenhouse ⁷ , Jacob Glanville ¹⁰ ,
Check for updates	James E. Moon ¹¹ , Jason A. Regules ¹² , Yann Chong Tan ¹²³ , Guy Cavet ¹³⁴ ,
	Shaun M. Lippow ³ , William H. Robinson @ ¹⁵ , Sheetij Dutta ¹² , Georgia D. Tomaras @ ¹⁵⁸ , Fidel Zavala @ ² , Randal R. Ketchem @ ⁴
	& Daniel E. Emerling @ ¹
	Over 75% of malaria-attributable deaths occur in children under the age
	of 5 years. However, the first malaria vaccine recommended by the World
	Health Organization (WHO) for pediatric use, RTS, S/AS01 (Mosquirix),
	has modest efficacy. Complementary strategies, including monoclonal
	antibodies, will be important in efforts to eradicate malaria. Here we
	characterize the circulating B cell repertoires of 45 RTS,S/ASO1 vaccinees
	and discover monoclonal antibodies for development as potential
	therapeutics. We generated >28,000 antibody sequences and tested 481 antibodies for binding activity and 125 antibodies for antimalaria
	activity in vivo. Through these analyses we identified correlations
	suggesting that sequences in Plasmodium falciparum circumsporozoite
	protein, the target antigen in RTS, S/ASO1, may induce immunodominant antibody responses that limit more protective, but subdominant,
	responses. Using binding studies, mouse malaria models, biomanufacturing
	assessments and protein stability assays, we selected AB-000224 and
	AB-007088 for advancement as a clinical lead and backup. We engineered the variable domains (Fv) of both antibodies to enable low-cost
	the variable domains (Fv) of both antibodies to enable low-cost manufacturing at scale for distribution to pediatric populations, in
	alignment with WHO's preferred product guidelines. The engineered clone
	with the optimal manufacturing and drug property profile, MAMOI, was
	advanced into clinical development.
Malaria is a mosquito-borne, parasit	
impacting over 1.5 billion people Middle East and Africa. More than 2	
619,000 malaria-related deaths were	e reported in 2021 (ref. 1), with a key tool in control and eradication of other infectious diseases, the
76.8% of these deaths occurring in ch	ildren under the age of 5 years. development of a vaccine for malaria has been a 50-year challenge'.

Molecular Design (J.MDTM)

- Team supported lead candidate selection of anti-malaria antibodies by ranking a panel of candidates for developability using our proprietary Abacus tool
- Designed optimized variants of lead candidates for improved developability properties informed by stability violations found with Abacus
- Created stable pools to generate material for biophysical characterization and activity assays
- Identified best-producing clonal cell line, expressing the candidate in continuous-perfusion bioreactors at twice the original titer
- Advanced candidate into GMP production to support early phase clinical studies use in pediatric populations living in Low to Middle Income Countries

Link: A candidate antibody drug for prevention of malaria | Nature Medicine



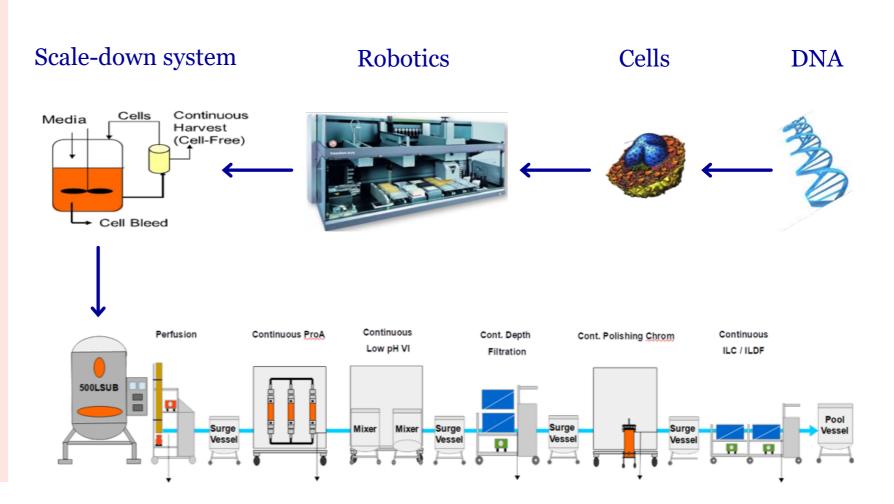
3. JP3[®]: Continuous process development based on robotics and M.L.

Intensified processes can be rapidly developed using high-throughput technologies and M.L.

Cutting edge high throughput process development

- Just Evotec Biologic's optimized proprietary cell lines and vectors or partner cell lines and vectors
- Accommodates an array of molecules and process formats: intensified fed batch, continuous perfusion
- Custom media tuned for productivity
- High density perfused culture conditions
- Connected downstream processing
- High resolution analytical methods
- Highly stable drug product formulation conditions
- Perfusion platform yields are generally 2-4+ grams/L/day

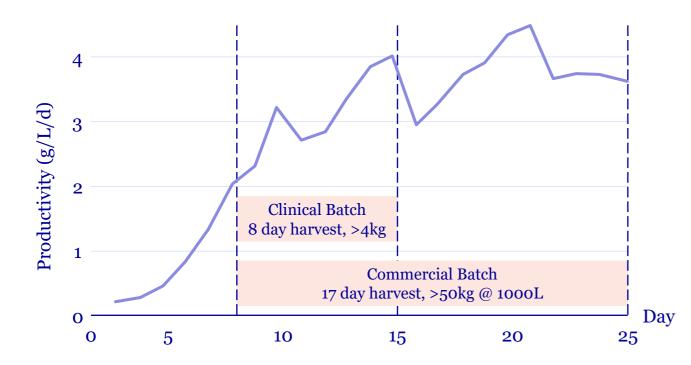
Agility Risk Cost



4. Continuous harvest outperforms fed batch by 10x

Example: Perfusion and continuous manufacturing compared to traditional fed batch

Productivity vs. Day

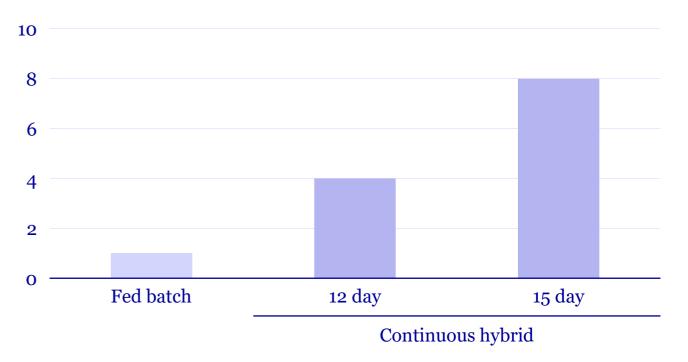


- 3L model system gives high confidence in scale-up
- High productivity: 3-4 grams product / L / day

Agility Risk Cost

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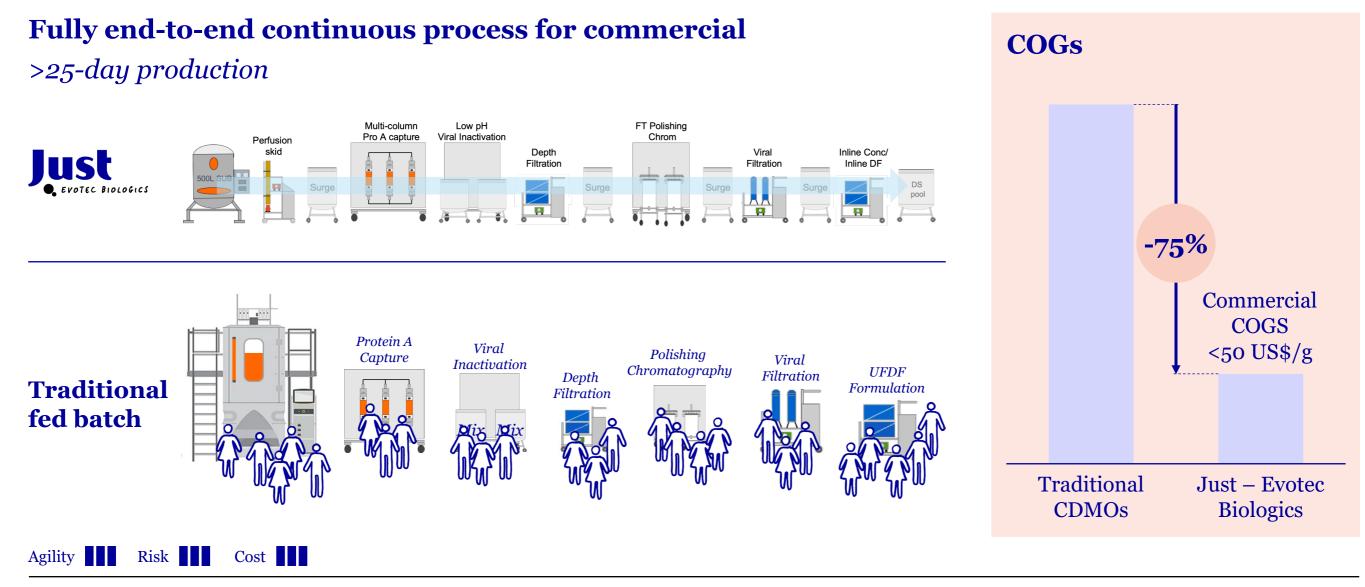
Comparison of 1 x 500L Run *in kg DS per 500L Bioreactor*



- Total of 18kg and 18.3kg to date (5 x 500L runs)
- Extending culture duration to 15 day increases mass produced

4. Highly intensified processing yields lowest possible COGs

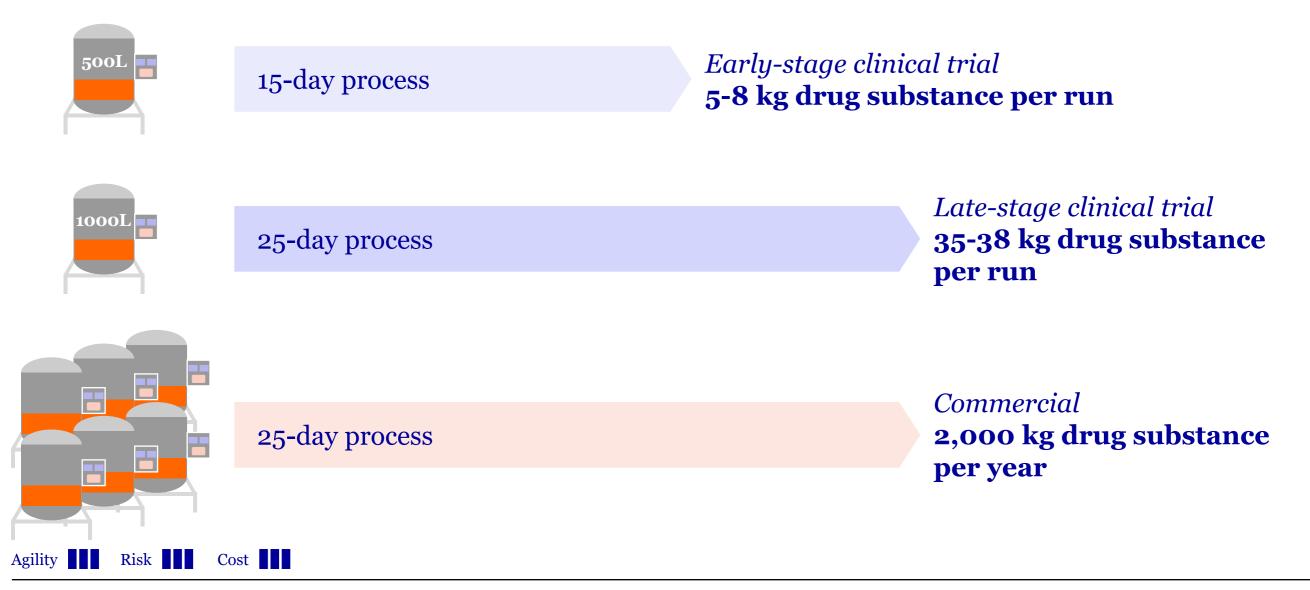
The key to start the paradigm shift/leaving rudimental ways to become more efficient



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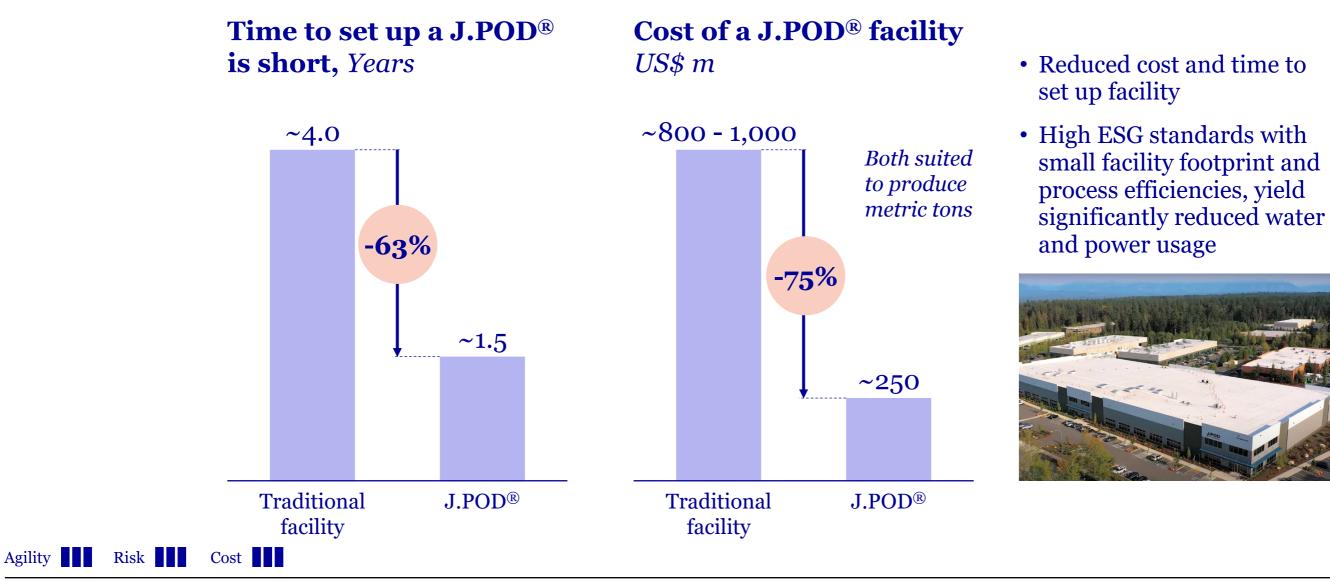
4. No need to scale up from clinical to commercial

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



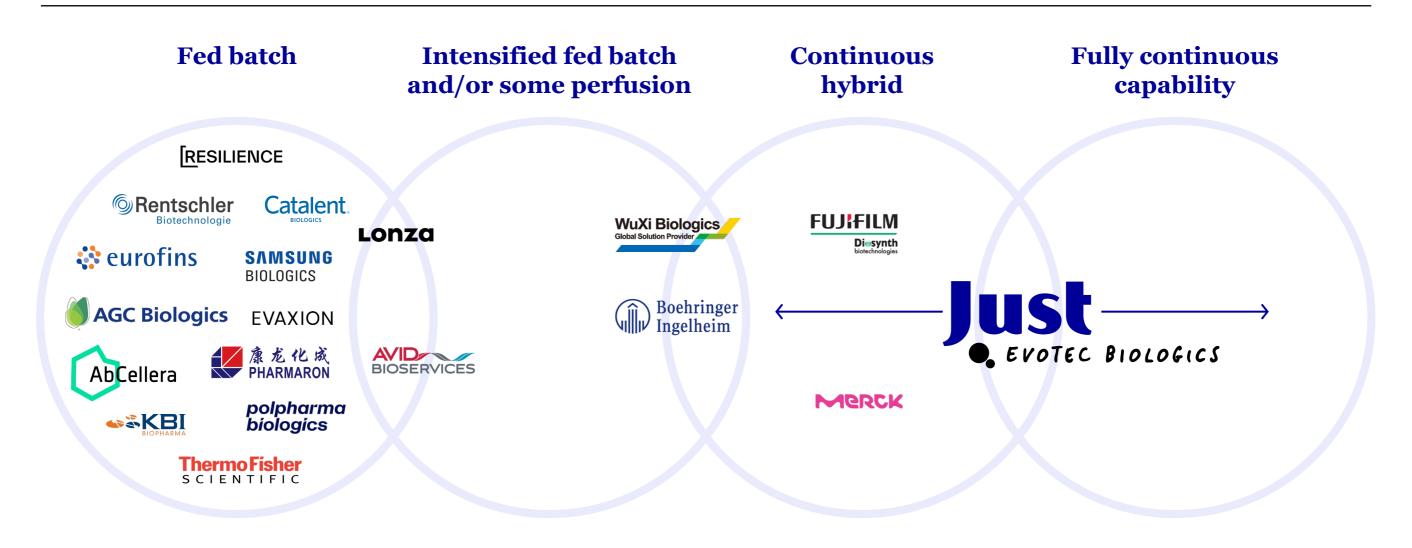
4. J.POD[®]: Introducing continuous manufacturing to mAb production

Disrupting the industry by introducing continuous manufacturing plus environmental benefits





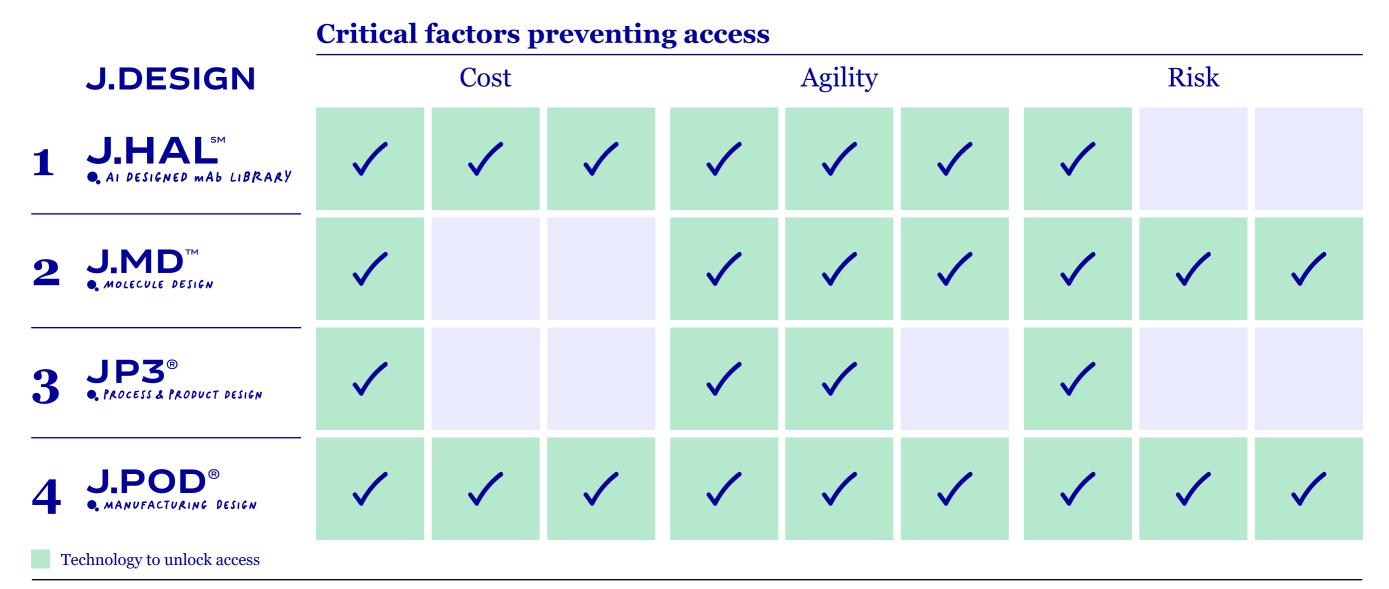
We were working on continuous manufacturing from early on





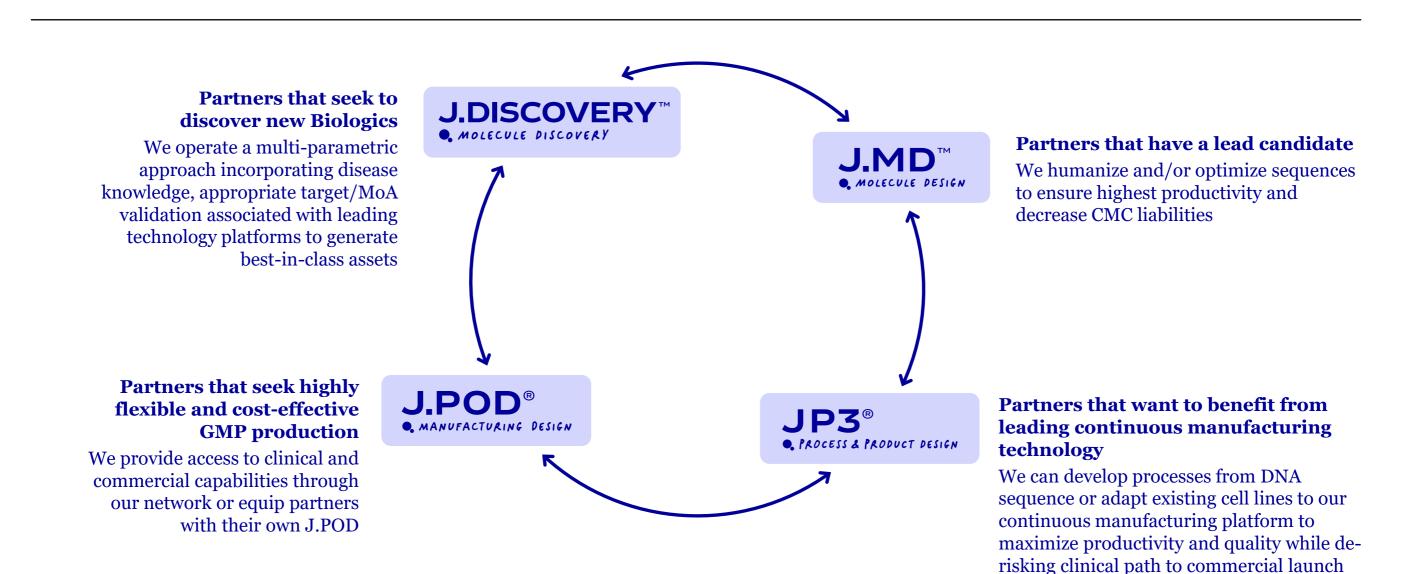
J.DESIGN enables accessibility

Key hurdles are overcome by all four aspects of J.DESIGN



Our partnering landscape and access points

From preclinical to commercial – many ways to drive the paradigm shift together





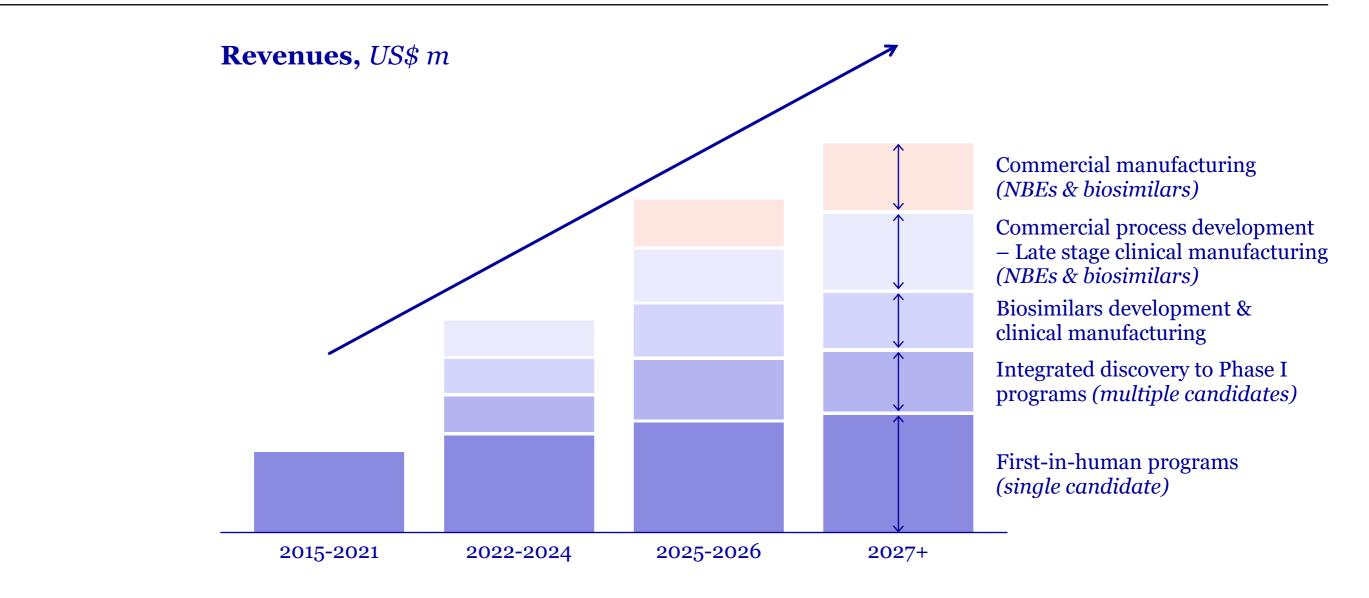
We are driving the paradigm shift with a distinct value proposition

Accelerating the paradigm shift in biologics day-by-day

From		То	Just EVOTEC BIOLOGICS	Others
Large	e stainless steel bioreactors	Flexible & agile capacity		
Facil	ty cost >US\$ 500 m	Facility cost << US\$ 500 m		\bigcirc
	oatch process operated in rate upstream & downstream	Fully automated and integrated platform operating continuous proces	SS	
Fixed	l cost focus	Variable cost focused		\bigcirc
	S > 150 US\$/g in median s industry	Targeted COGS <50 US\$/g¹ at Just – Evotec Biologics		\bigcirc

How we expect to evolve and accelerate our partnering portfolio

Where we stand today and where we want to go with our partners





An expanding J.POD[®] manufacturing network to meet global needs

Present state



J.PLANT Seattle, Washington, US -

- Discovery and Process Development
- 500L SUB
- Phase I Clinical
- Over 34 runs
- 100% success



J.POD[®] Redmond, Washington, US

- Process Development
- 500L & 1,000L SUB
- Phase I Commercial
- First cGMP run Oct 2021
- Capacity: 2,5 t/yr



J.POD® Toulouse, France, EU

- Process Development
- 500L & 1,000L SUB
- Phase I Commercial
- Groundbreaking 2022, Expected CQV 2024
- Capacity: 2,5 t/yr

Cloning of J.POD[®] facilities (option)

Just-Evotec Biologics "enables" from facility design to technology

Proximity to key markets



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



Experienced leadership team dared to dream

>500 combined years of expertise





#RESEARCHNEVERSTOPS

Philip Boehme, MD, PhD, MBA EVP, Head of Partnering and Transformation Just – Evotec Biologics

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