Antibodies to Watch in 2021

Nick Hutchinson, EngD

Mammalian Cell Culture Business Steering Group Lead

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FUJIFILM Diosynth biotechnologies

Lessons learned from SARS-CoV-2 antibody development

Programme Parameter	Pandemic	Non-Pandemic
Speed of Development	Rapid development needed. Prepared to take additional risk.	Many firms actively looking to reduce timelines, reach milestones sooner or fail fast
Meeting Commercial Demand	Large doses and global patient population requires production at an enormous scale	Timing of investments in large-scale facilities and associated risks given market uncertainties

Companies can relate challenges associated with development and commercialization of anti-SARS-CoV-2 antibodies to non-COVID-19 pipeline

Speed of therapeutic antibody development

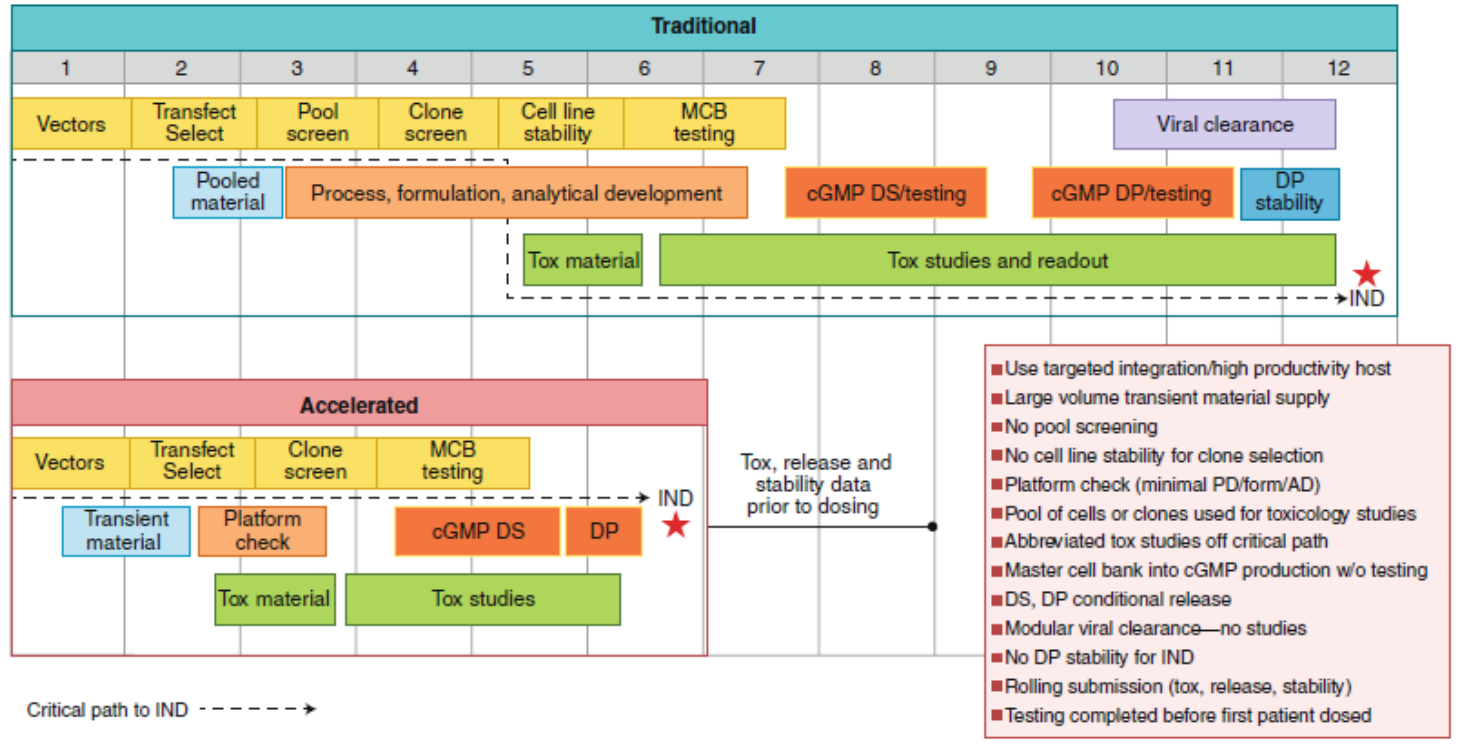

Fig. 1 | **Accelerated phase 1 CMC mAb timeline for a pandemic.** The timeline to phase 1 clinical studies using mAb therapeutics for pandemic outbreaks can be substantially accelerated without heightened product safety risks as compared with current practice. Tox, toxicology; MCB, master cell bank; DS, drug substance; DP, drug product; PD, process development; form, formulation; AD, analytical development.

Developing therapeutic monoclonal antibodies at pandemic pace. *Brian Kelley*.
Nature Biotechnology (April 2020)
https://doi.org/10.1038/s41587-020-0512-5

Robust, scalable platform processes shorten development timelines

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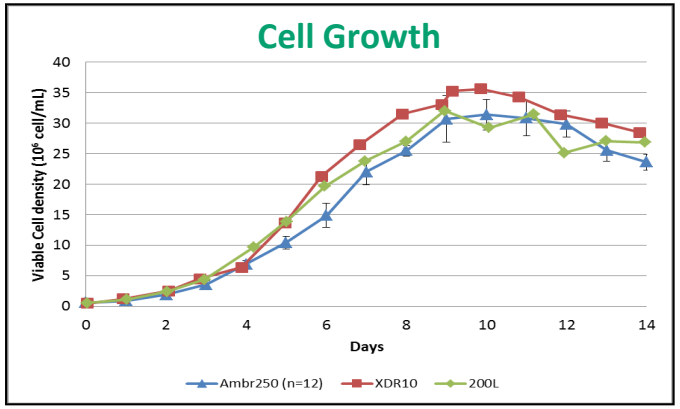
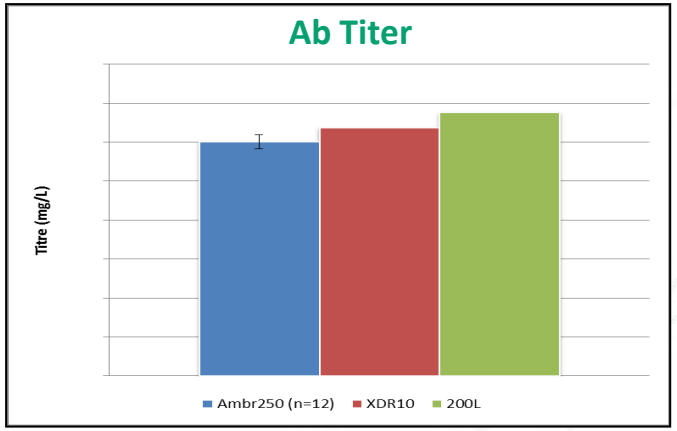
Cell Culture

- Vial Thaw
- Seed Shake Flasks
- Seed Bioreactors
- Production Bioreactor
- Feed Strategies
- Harvest

Purification

- Harvest
- Affinity Chromatography
- Viral Inactivation
- Cation Exchange Chromatography
- Anion Exchange Chromatography
- Viral Filtration
- UF/DF
- Bulk Fill





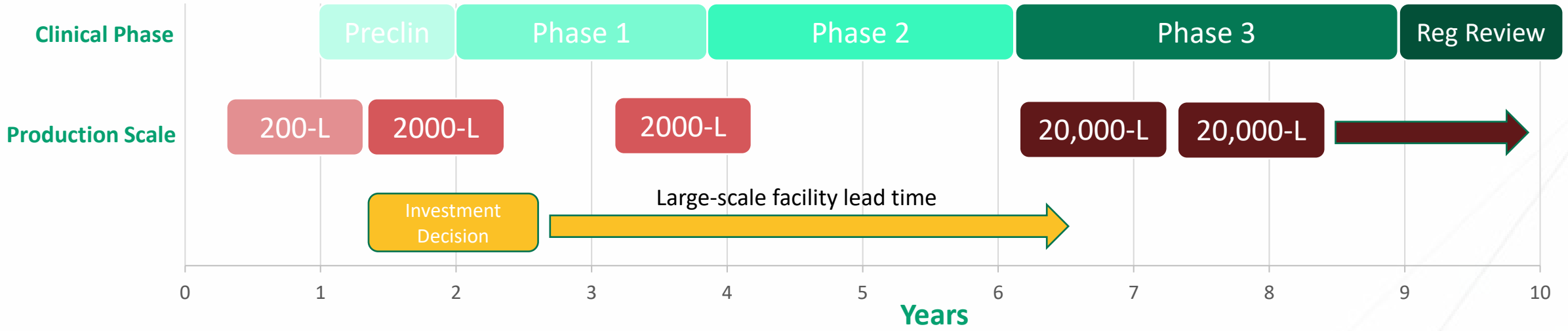
An antibody production platform scalable from microbioreactor through 10-L benchtop, 200-L process demonstration and 2,000-L GMP

Accelerated timelines for antibody development

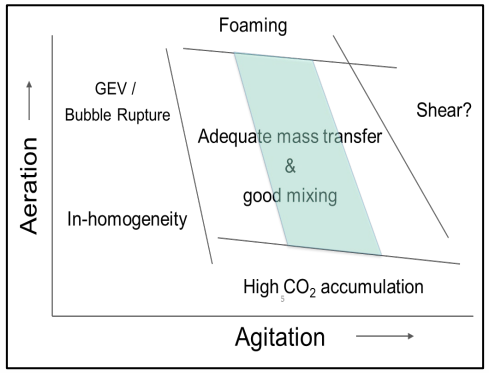
Traditional	Accelerated	Potential Risks
Full process development specific and fully optimized for the candidate antibody	Platform check with minimal process or analytical development	Less fully optimized process for early phase clinical trials
Process and formulation development with lead clonal cell line	Use of transfectant pools or pools of clones for formulation development, tox material and even GMP material	Lack of comparability during development leading to delays, rework and bridging studies
Comprehensive Formulation Development for IND	Leveraging historical data and generic conditions	Poor stability and delayed regulatory submissions
Creation of new supply chains for manufacturing materials	Standardized materials and consumables	Lack of flexibility
Separate Drug Substance and Drug Product manufacture	Co-location within a single facility or site	Loss of flexibility within production processes

Adapted from "Developing therapeutic monoclonal antibodies at pandemic pace. *Brian Kelley*. Nature Biotechnology (April 2020)"

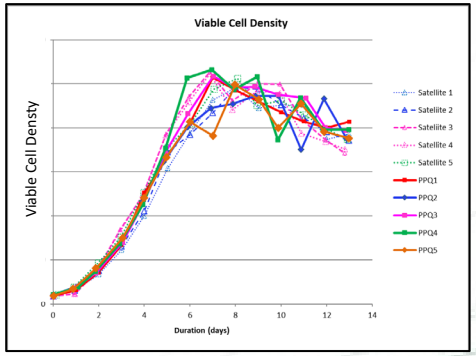
Traditional scale-up strategy



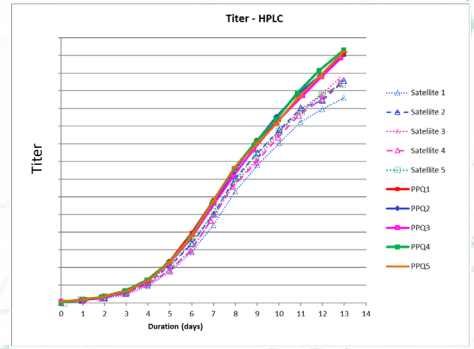
Pandemic-pace scale-up to large-scale facilities is possible with the right models and know-how if the capacity is available



Cell Growth



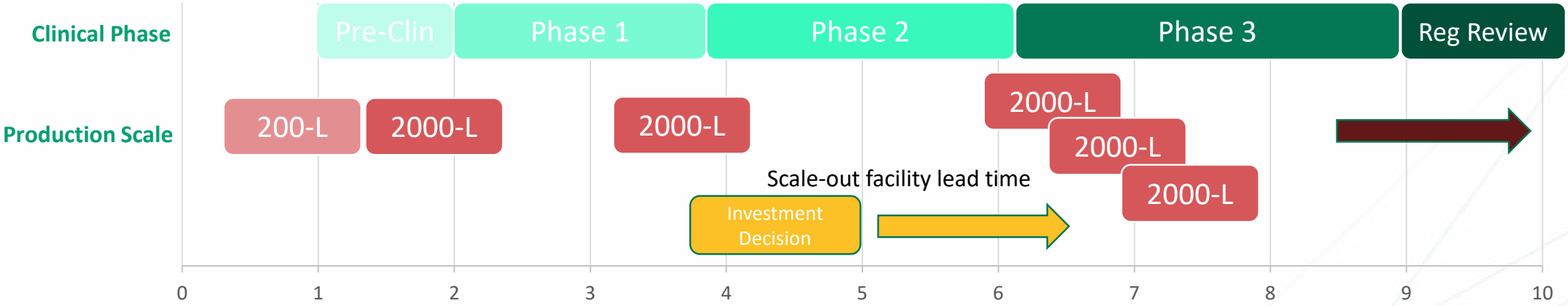
Ab Titer



Process performance: 5-L Satellite bioreactor model versus 20,000-L

Data from FDB Denmark Facility

Scale-out strategy



High-throughput facilities with 9-12 x 2,000-L single-use bioreactors reduce risk and costs associated with scale-up.

Investment decision can be later and based on more data.

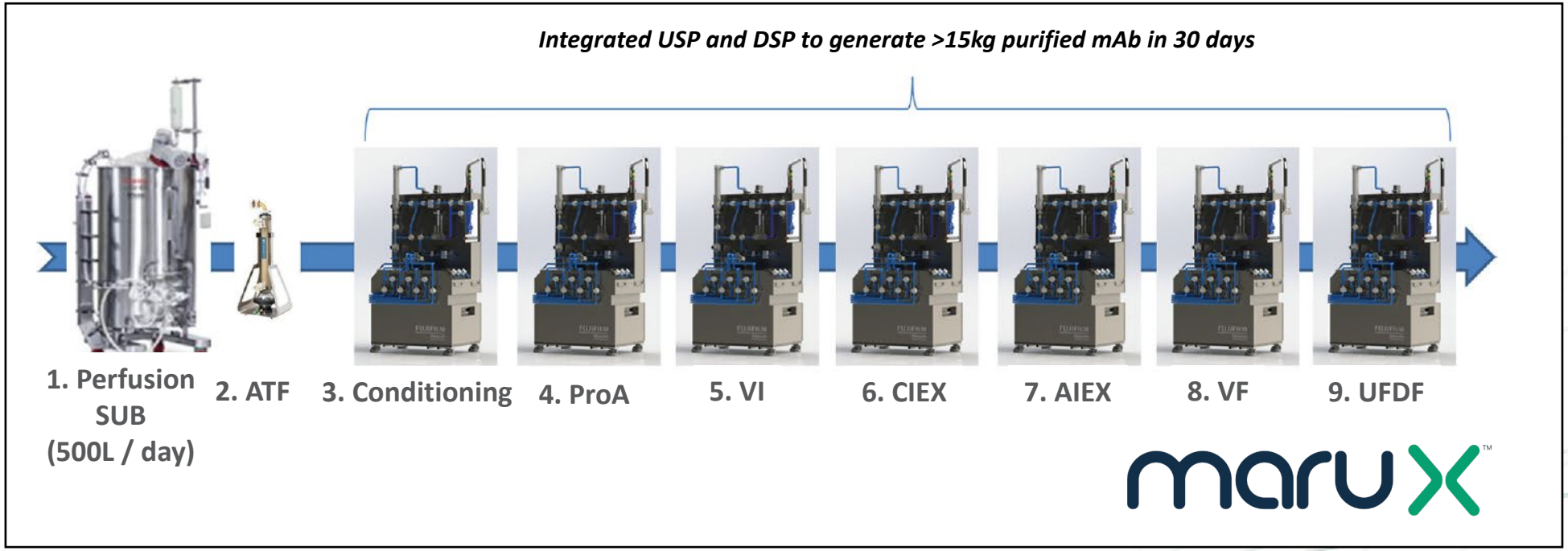
Dedicated, high-throughput mAb manufacturing

- Improvements in productivity of our Apollo™ X cell lines and platform processes mean a 2000-L bioreactor can deliver the same amount of antibody as a 5-6000-L bioreactor could only a few years ago.
- Advancements in single-use bioreactor technology that allows them to be installed and reliably operated in large numbers in open plan facilities.
- The adoption of the ballroom concept of facility design that allows multiple batches to be manufactured simultaneously in closed processes without risk of batch-to-batch product contaminations.
- A very flexible approach to help manage uncertainty in demand forecasts.
- Supports a decentralized strategy with regionally localized manufacturing facilities.

FDB Texas: Production bioreactor suite can run up to 10 x 2,000-L single-use bioreactors.

Continuous processing for intensified mAb production

- Connected and integrated bioprocess batch strategy developed
- 5 to 10-fold increase in antibody output from a 500-L bioreactor
- Utilizes the same mAb purification platform as fed-batch process
- Allows demand for antibody to be met with a significantly smaller, more agile facility



Strategies of meeting market demand

Scale-Up

Multiple 20,000-L bioreactors

25-30 runs to provide 2 tons of Ab

Scale-Out

Multiple 2,000-L bioreactors

160-170 runs at high titer to provide 2 tons of Ab

Continuous

4 x 500-L or 1 x 2000-L bioreactors

Operated continuously to give 2 tons of Ab

Summary

- Therapeutic antibody pipelines are very robust.
- The COVID-19 pandemic has increased demand for short development timelines and significant manufacturing capacity.
- Innovative approaches to development and manufacturing will support the industry, now and in the future to help avoid capacity crunches.

Contact: nick.hutchinson@fujifilm.com

https://www.linkedin.com/in/drnickhutchinson/

www.fujifilmdiosynth.com