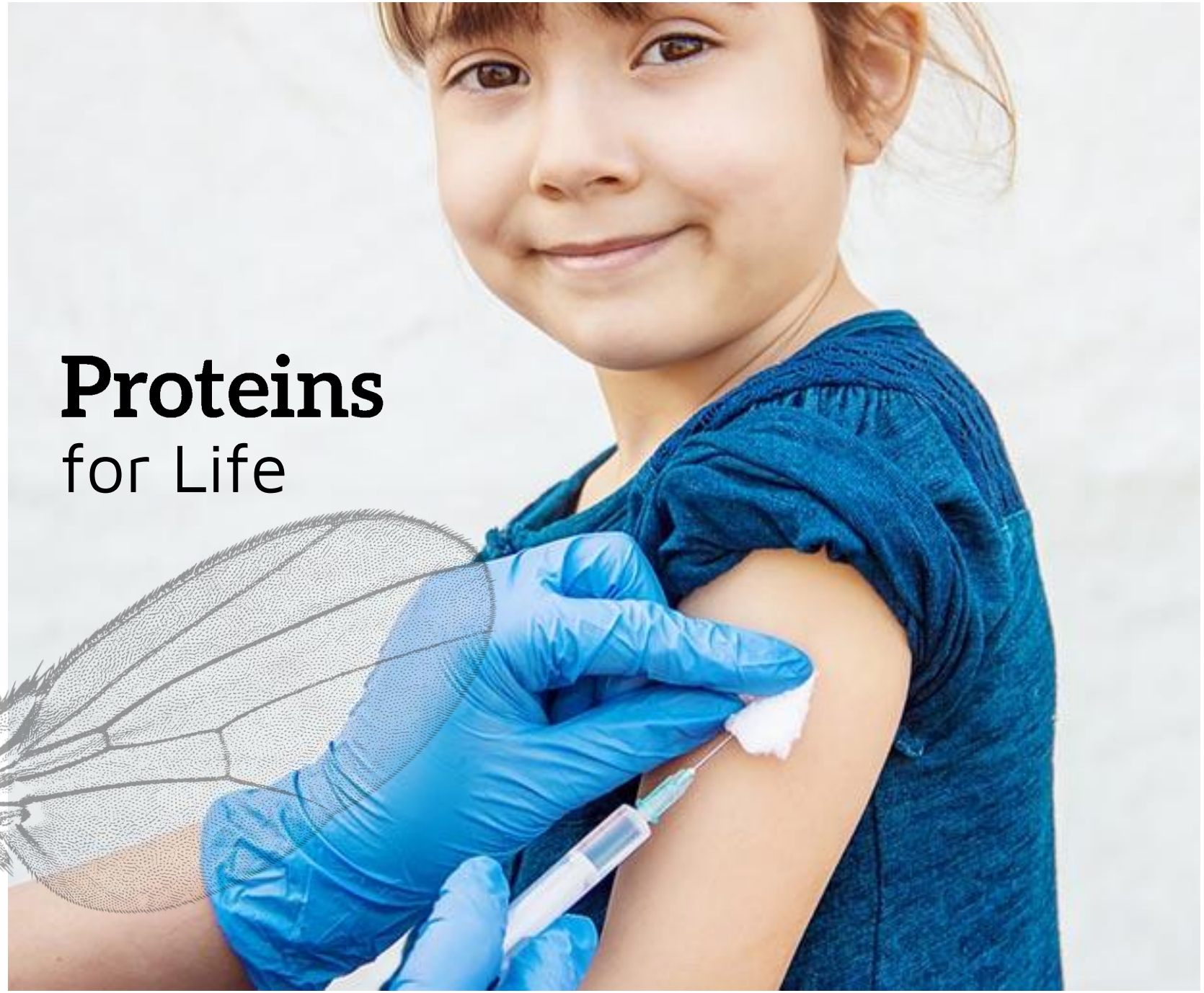


Fast-track Development of SARS-CoV-2 Subunit Vaccine

–

Synergy of Platform Technologies

Max Søgaard PhD, VP R&D and technology

EXPRES^{2}ION
BIOTECHNOLOGIES

Summary

- A virus-like-particle platform was developed over 5 years in the Sander group at Københavns Universitet (KU)
- The technology resides in the company **AdaptVac** and was used to create a COVID-19 subunit vaccine in 2020
- The company **ExpreS2ion Biotechnologies** makes SARS-CoV2 antigens using a insect cell based production platform and develops and transfers production processes to CMO

- Preclinical data indicates some of the highest levels of SARS-CoV2 neutralising antibodies in Immunised animals
- Headed by Adaptvac, a **Prevent-CoV consortium** carried development of a SARS-CoV2 vaccine from construct to First-In-Human Phase I/II trials in one year

- The ABNCoV2 vaccine First entered humans on the 15 March 2021 in a phase I clinical trial in the Netherlands (https://www.radboudumc.nl/en/trials/coronavirus-vaccine-research/timelines)

- The company **Bavarian Nordic** licensed the vaccine for further phases and commercialisation (July 2020)

Prevent-nCoV Consortium

Funding total ~ 8 million USD

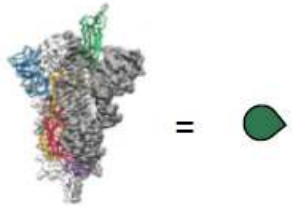
Horizon 2020

CARLSBERG FOUNDATION

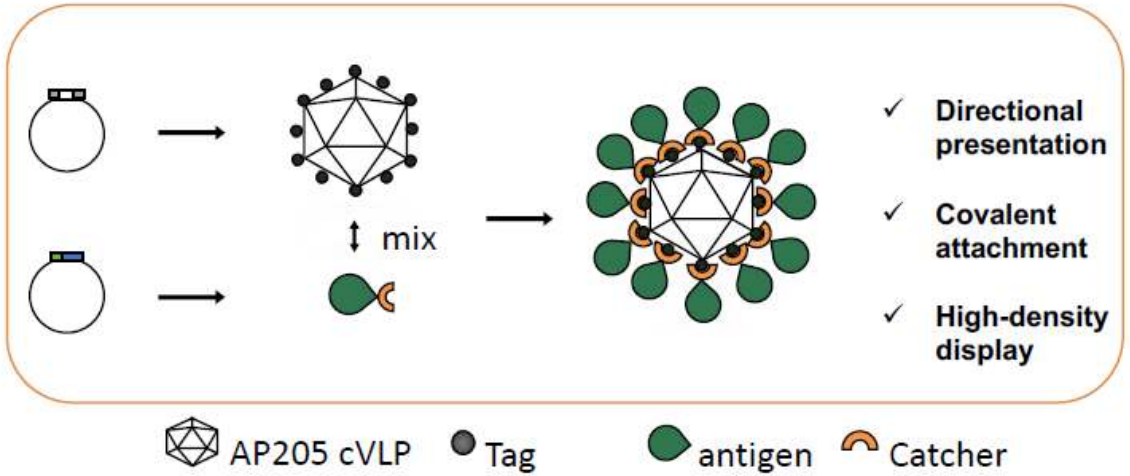
GUDBJØRG & EJNAR HONORES FOND

Adaptvac's Unique and Versatile Technology Platform – VLP made in E.Coli, Antigens can be made in any system

Simple *E.coli* based VLP production



Antigen (Spike RBD) can be made in S2 cells



Key benefits

- Increased immunogenicity
- Faster immune response
- Focus immune response
- Longevity of response

Receptor binding domain (RBD) is a hot-spot for SARS-CoV2 neutralizing epitopes.
Non-neutralizing epitopes are expected to be rare

Scalable process: VLP can be produced at concentrations of >1 g/l

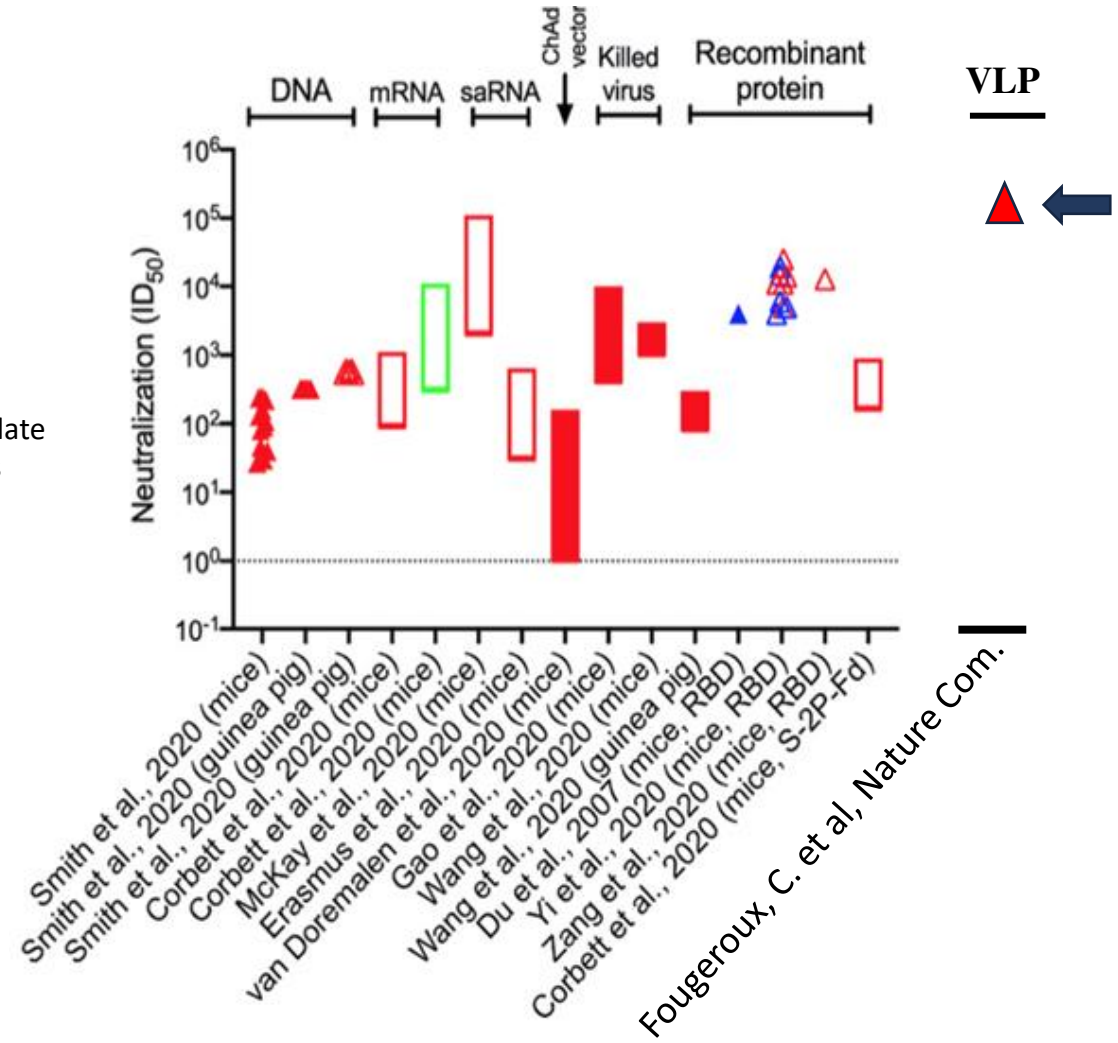
Protein production by ExpreS^2

- **Non-viral, non-lytic**, expression system based on stably transfected *Drosophila melanogaster* (fruit fly) S2 cell lines
- **Constitiutive, non-induced expression** from proprietary vectors to ensure highly homogeneous product
- **Transient transfection** enables fast screening of candidate target proteins or constructs
- **Stable transfection** provides a non-exhaustible source of homogeneous protein from polyclonal or monoclonal cell banks
- **Templated antigen purification procedure** based on clinically accepted four amino acid C-terminal affinity tag (Capture Select C-tag, Thermo Fisher)

COMPARISON TO PUBLISHED DATA

Virus-strain:
- Red: SARS-2
- Blue: SARS-1
- Green: MERS

Neutralization assay:
- Filled: Live virus isolate
- Open: Pseudo-virus

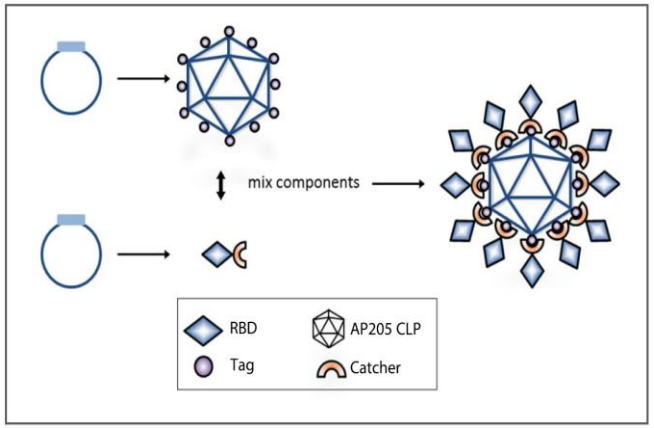


..óne dose RBD-VLP gives similar or higher neutralization titers as two doses of Oxford/Astrazeneca's adeno-based vaccine.

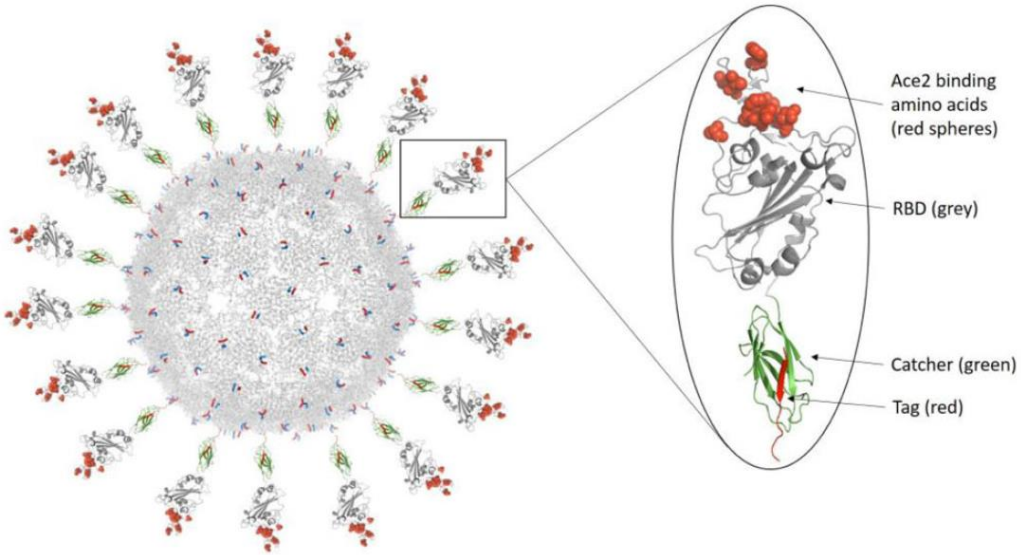
UNIVERSITY OF COPENHAGEN

Reference: John P. Moore, P. J. Review. Journal of Virology. 2020. DOI: 10.1128/JVI.01083-20

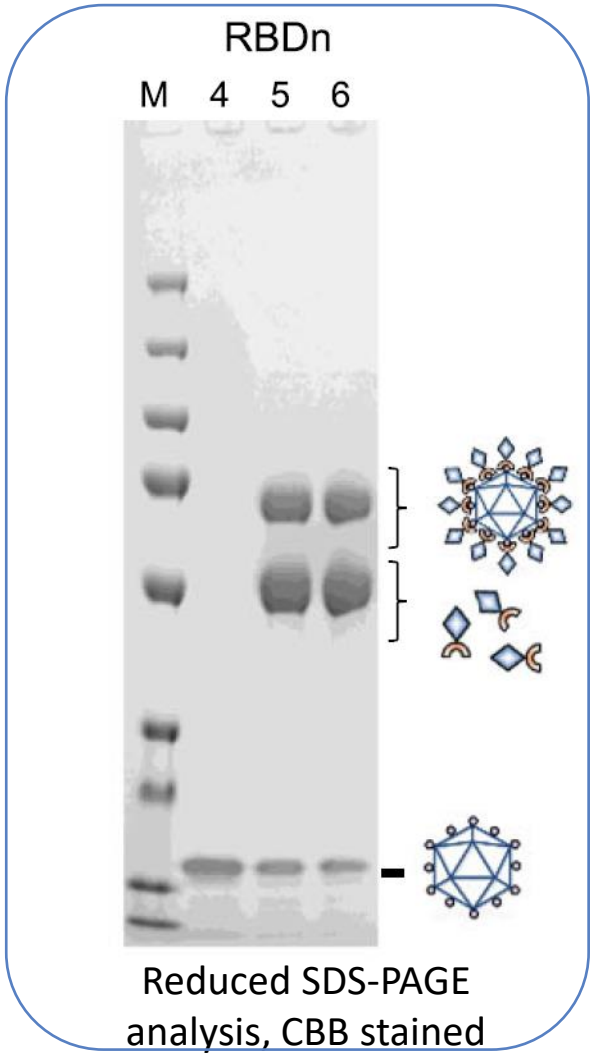
Vaccine components



Note: cVLP assembly occurs independent of antigen
Any RBD variant can be coupled to the AdaptVac cVLP



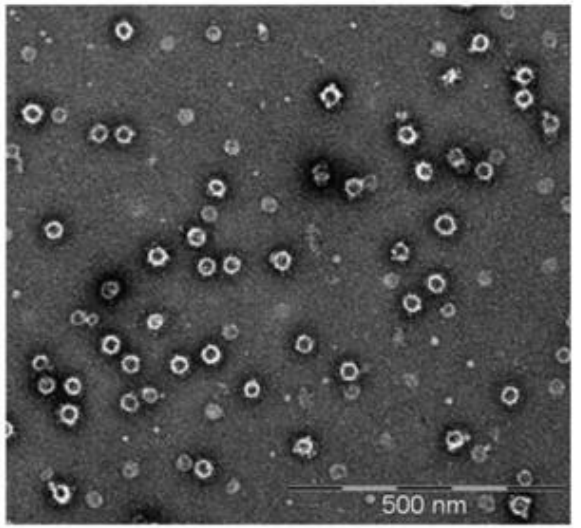
RBD presents receptor binding surface to immune system



Reduced SDS-PAGE analysis, CBB stained

The coupling reaction components

RBDn

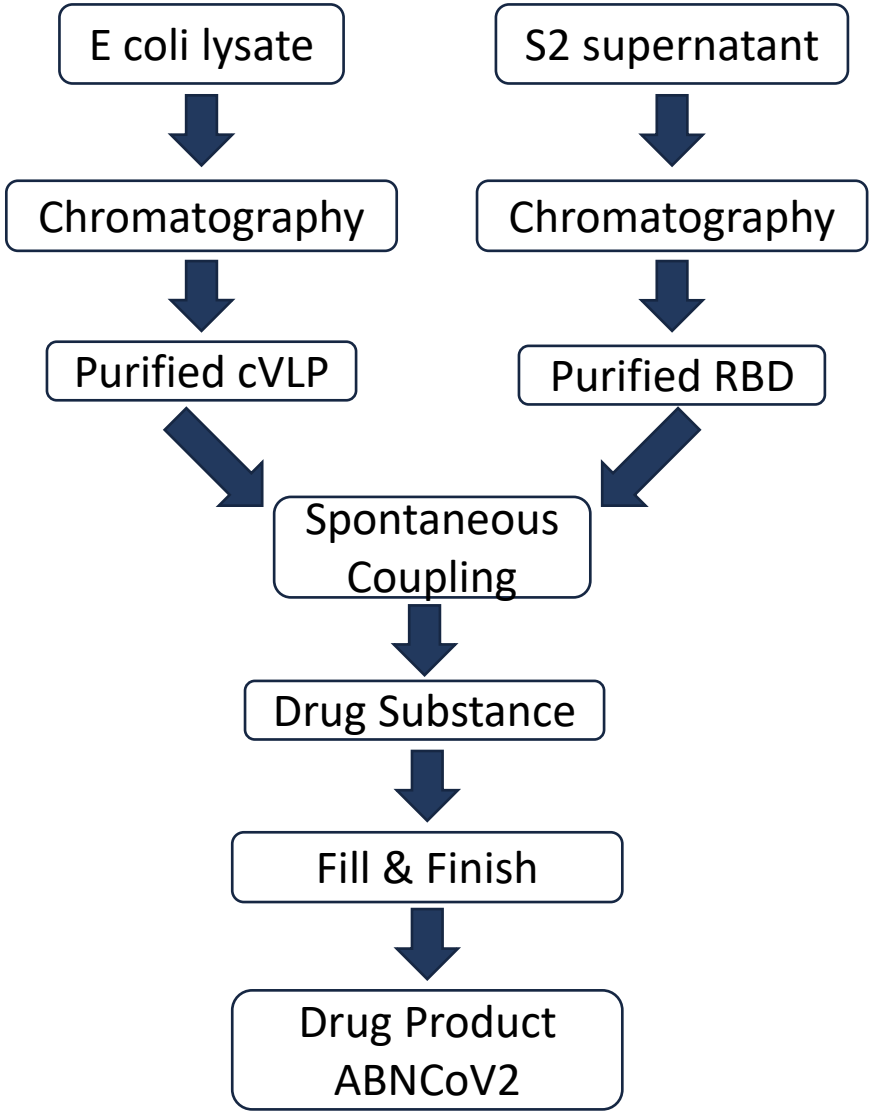


Transmission electron microscopy analysis of the cVLP-based Vaccine ABNCoV2

Process Development

Specific challenges:

- A process using both prokaryote and eukaryote production lines
- Purification at scale, host cell protein profile
- Removal of LPS (endotoxin) originating from E coli cell walls
- Optimization of coupling process
- Scaled removal of uncoupled RBD after coupling step



Construct to First-In-Human in 2020

According to a CEPI report* the cost of developing a vaccine from pre-clinical to clinical Phase I/IIa is a minimum of 31 million USD

**Gouglas, D., et al The Lancet Global Health, 6(12), e1386–e1396. 2018*

Bolstered by a total of 8 mill USD the Off for the F.I.H race goes in early March 2020

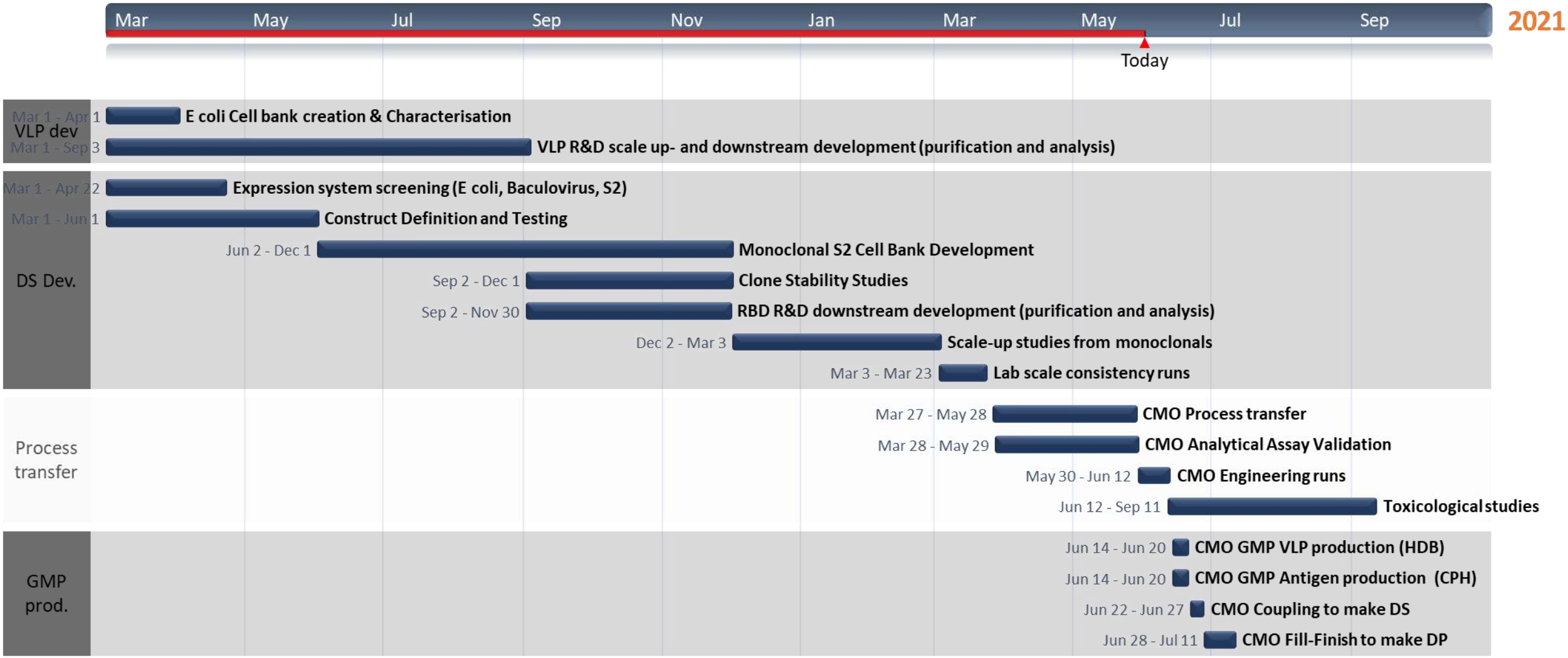
General challenges

- Grant funding introduced tight budgetary constraints:
  - No room for engineering run at CMO's (a "first-take" scenario)
  - Dependency on limited GMP production slot opportunities at CMO (AGC Biologics)
  - Distributed CMO production at facilities in GER and DK and logistics in a COVID-19 situation
- Process Development and scaling timeline
  - Scaling chromatography both up- and downstream (timelines: how fast does a cell double to enable bank creation and development batches?/ how to purify a 3 MDa multiprotein complex to homogeneity at scale?)
- Limited process scale required the CMO's to be creative (within the bounds of GMP)
- Generally, COVID-19 related timeline disruptions (nobody catch COVID-19, please!)

The production challenge

EXPRES²ION BIOTECHNOLOGIES

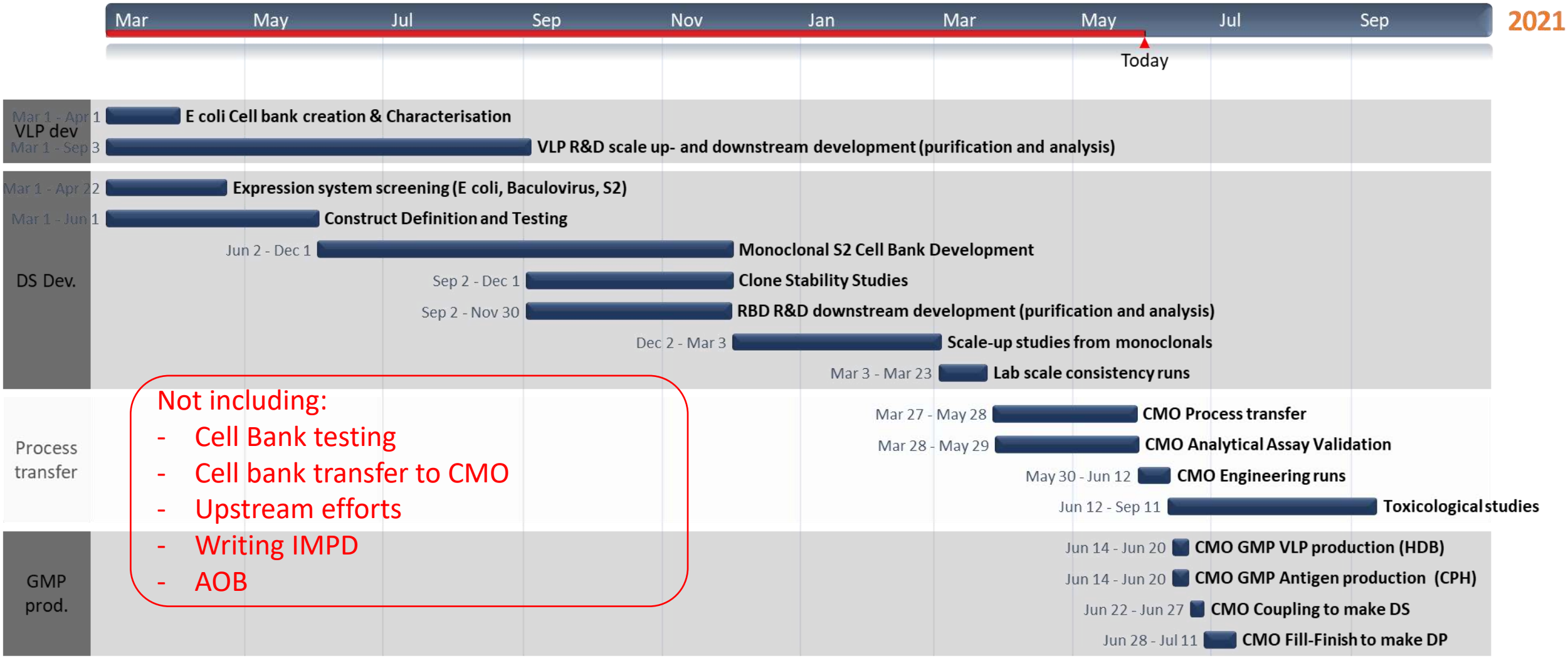
- Accelerated sequential timeline to DP (hypothetical and non-comprehensive)



The production challenge

EXPRES²ION BIOTECHNOLOGIES

- Accelerated sequential timeline to DP (hypothetical and non-comprehensive)



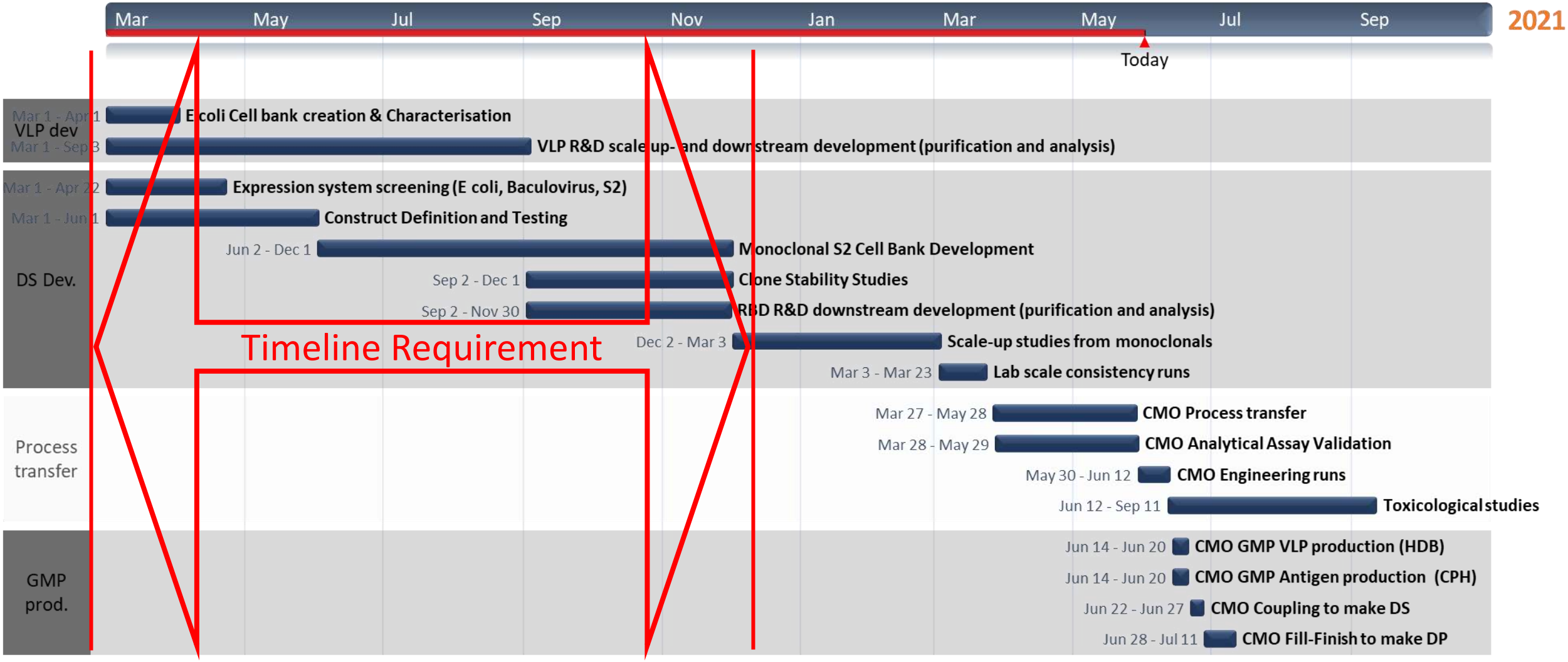
Not including:

- Cell Bank testing
- Cell bank transfer to CMO
- Upstream efforts
- Writing IMPD
- AOB

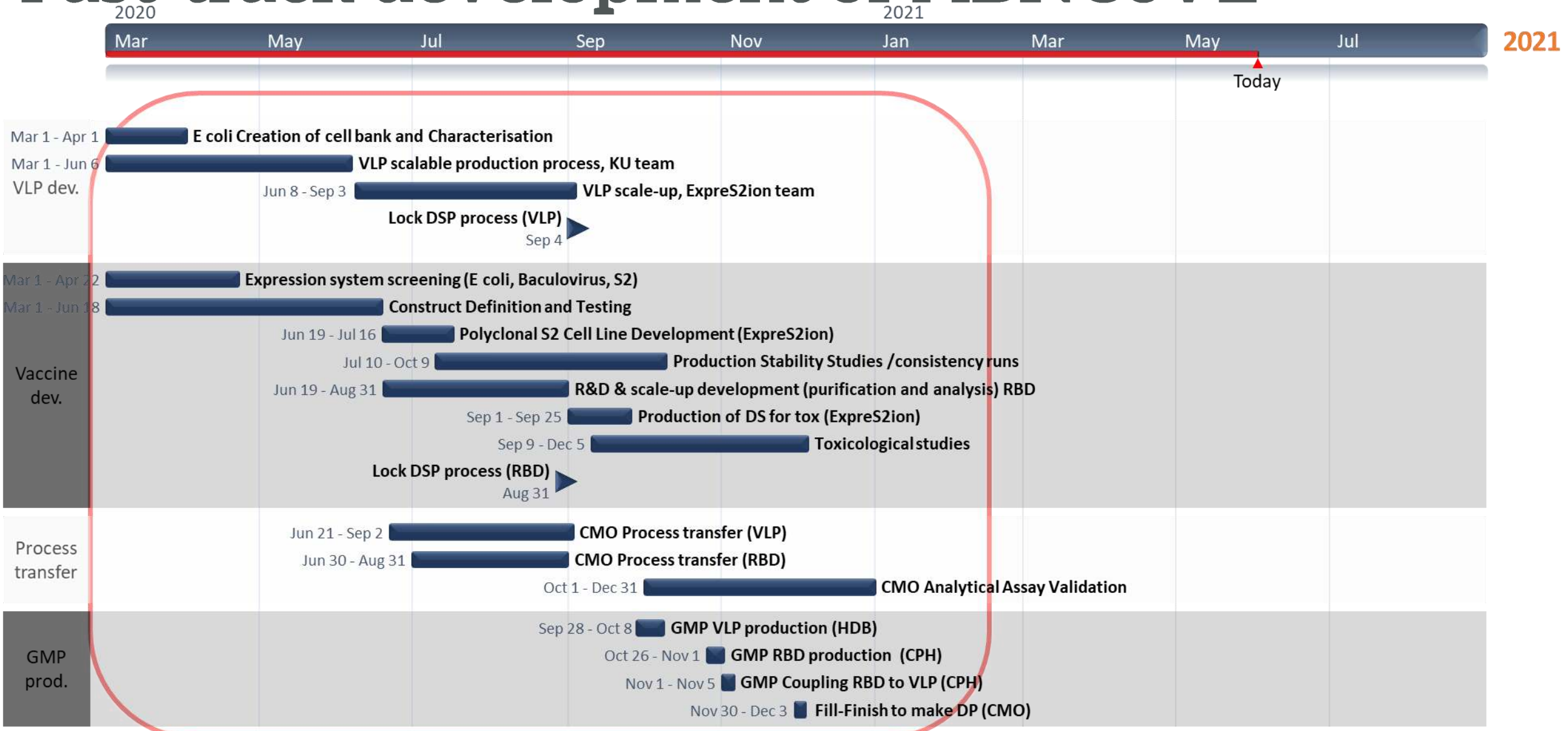
The production challenge

EXPRES²ION BIOTECHNOLOGIES

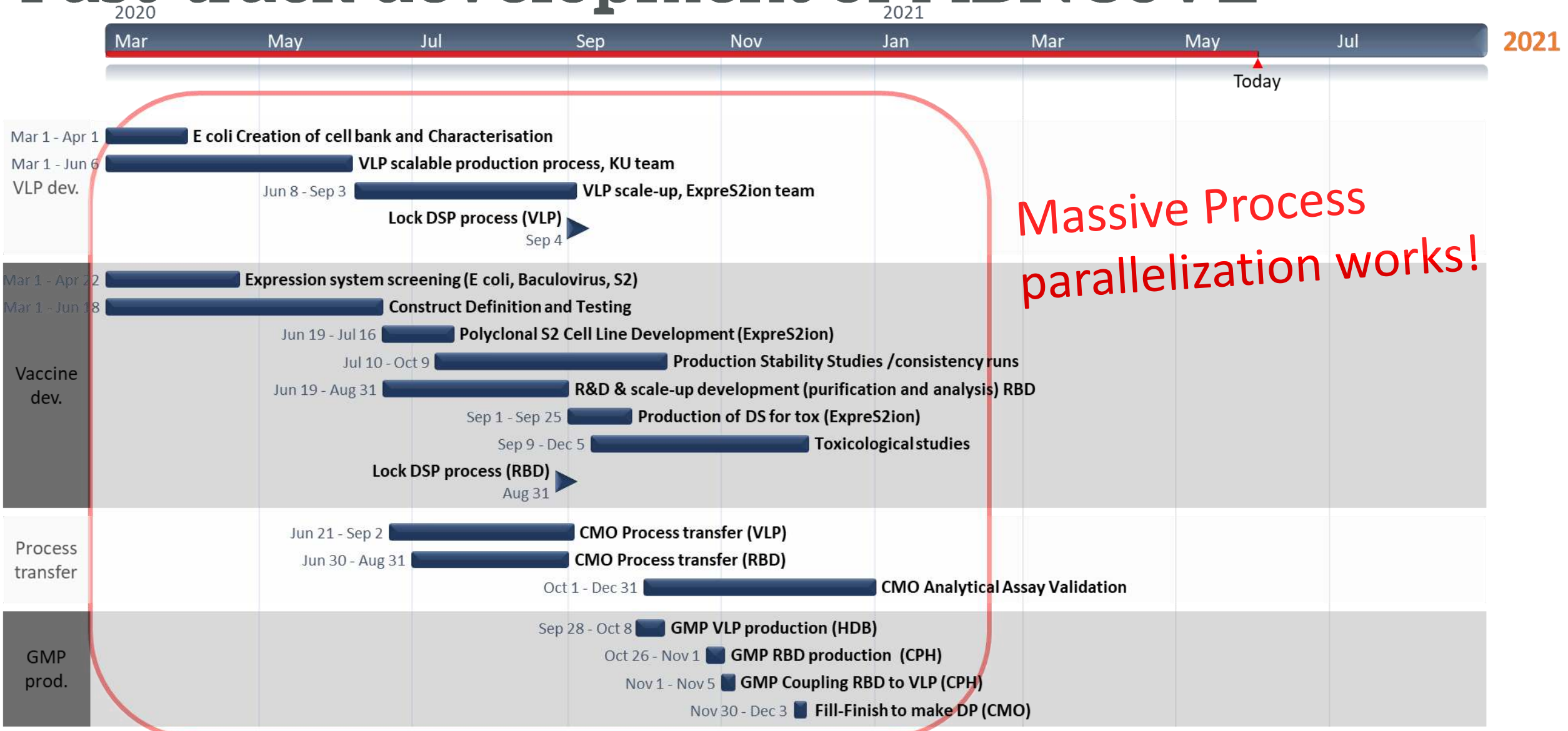
- Accelerated sequential timeline to DP (theoretical)



Fast-track development of ABNCoV2



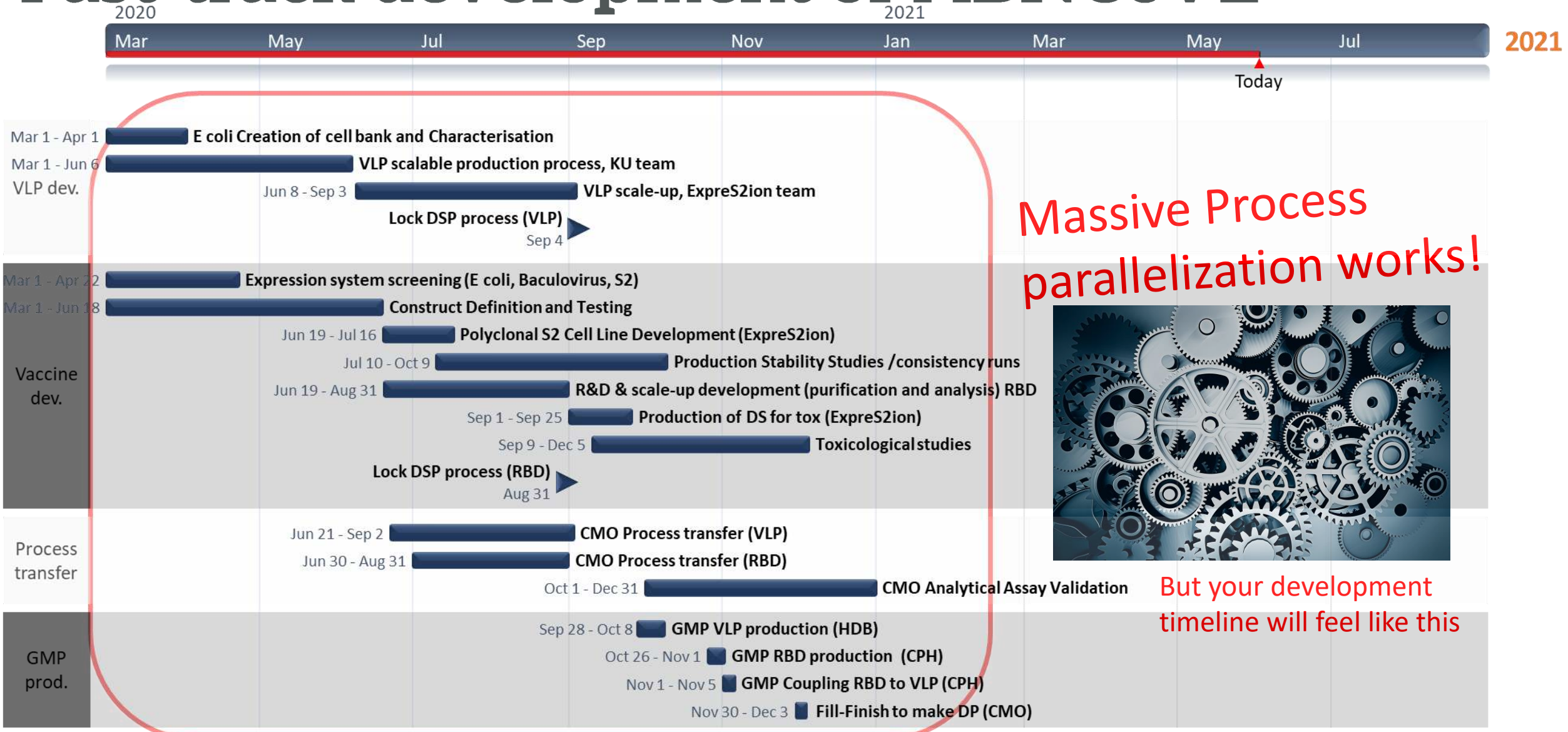
Fast-track development of ABNCoV2



Massive Process parallelization works!

Fast-track development of ABNCoV2

EXPRES²ION BIOTECHNOLOGIES



Massive Process parallelization works!

But your development timeline will feel like this

Take-home notes

We are all in a new setting:

- A single virus can force a connected world to its knees
- A few good ideas can bring the world back on its feet
- Massively increasing support for innovation is key to solve our future challenges.

- It is not essential to be large pharma corporation to develop a good idea, but development will be comparatively delayed and at high-risk. The project may fail on a pure technicality or unforeseen circumstance.

- Managing the economic risk when developing vaccines on a tight-rope budget is extremely challenging - especially in grant funded projects

- Small companies can make the difference, but a economic foundation needs to be put in place to avoid loss of essential great ideas

Thank you for your attention! Questions?

Acknowledgements

adaptVAC

Louise Goksøyr
Adam F. Sander
Willem Adriaan de Jongh
Susan Thrane

KØBENHAVNS UNIVERSITET

Robert Dagil
Christoph M. Janitzek
Kara-Lee Aves
Emma W. Horsted
Sayit Mahmut Erdogan
Tobias Gustavsson
Laurits Fredsgaard
Elena E. Vidal-Calvo
Thor G. Theander
Morten A. Nielsen
Ali Salanti
Paul Khalifé
Thomas M. Hulen
Swati Choudhary
Søren Buus
Anette Stryhn Buus
Jan Pravsgaard Christensen

EXPRES²ION BIOTECHNOLOGIES

Vladislav Soroka
Max Søgaard
Jerzy Dorosz
Stine Clemmensen
Bettina Hierzberger
Tanja Domeyer
Blanka W. Nalewajek
Anette Strøbæk
Magdalena Skrzypczak
Laura F. Andersson

Article | Open Access | Published: 12 January 2021

Capsid-like particles decorated with the SARS-CoV-2 receptor-binding domain elicit strong virus neutralization activity

Cyrielle Fougeroux, Louise Goksøyr, Manja Idorn, Vladislav Soroka, Sebenzile K. Myeni, Robert Dagil, Christoph M. Janitzek, Max Søgaard, Kara-Lee Aves, Emma W. Horsted, Sayit Mahmut Erdoğan, Tobias Gustavsson, Jerzy Dorosz, Stine Clemmensen, Laurits Fredsgaard, Susan Thrane, Elena E. Vidal-Calvo, Paul Khalifé, Thomas M. Hulen, Swati Choudhary, Michael Theisen, Susheel K. Singh, Asier Garcia-Senosiain, Linda Van Oosten, Gorben Pijlman, Bettina Hierzberger, Tanja Domeyer, Blanka W. Nalewajek, Anette Strøbæk, Magdalena Skrzypczak, Laura F. Andersson, Søren Buus, Anette Stryhn Buus, Jan Pravsgaard Christensen, Tim J. Dalebout, Kasper Iversen, Lene H. Harritshøj, Benjamin Mordmüller, Henrik Ullum, Line S. Reinert, Willem Adriaan de Jongh, Marjolein Kikkert, Søren R. Paludan, Thor G. Theander, Morten A. Nielsen ✉, Ali Salanti & Adam F. Sander ✉ -Show fewer authors

Nature Communications **12**, Article number: 324 (2021) | Cite this article

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