Leveraging mRNA Platform Technologies to Enable Pandemic Supply of COVID-19 Vx

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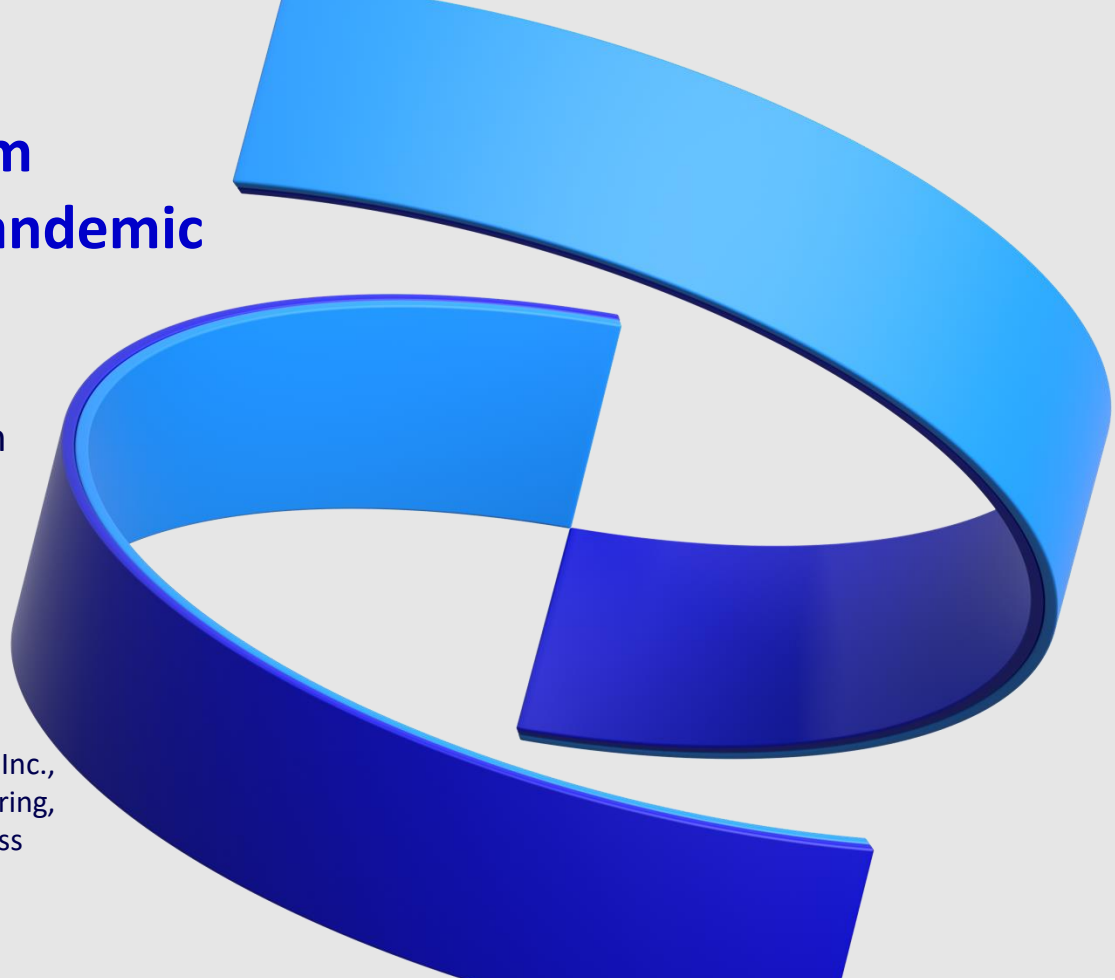


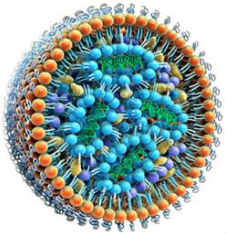
Outline of Presentation

- Background of collaboration between Pfizer and BioNTech
  - Multiple mRNA clinical lead candidates with acceleration of timelines
  - Multiple development activities done in parallel
  - Utilization of sites for pDNA/mRNA process development and manufacturing
- Platform technologies leveraged to accelerate development
  - pDNA manufacturing platform
    - Cell line screening/cell banking
    - pDNA manufacturing platform with linearization
  - mRNA platform used for influenza vaccine research by Pfizer and BioNTech and oncology programs at BNT
  - process development platforms
    - Automated Multiple Bioreactor (AMBR) platform
    - Commercial scale-up using disposable technology platforms
    - Computational fluid dynamic modeling
- Summary of project and team attributes critical for success

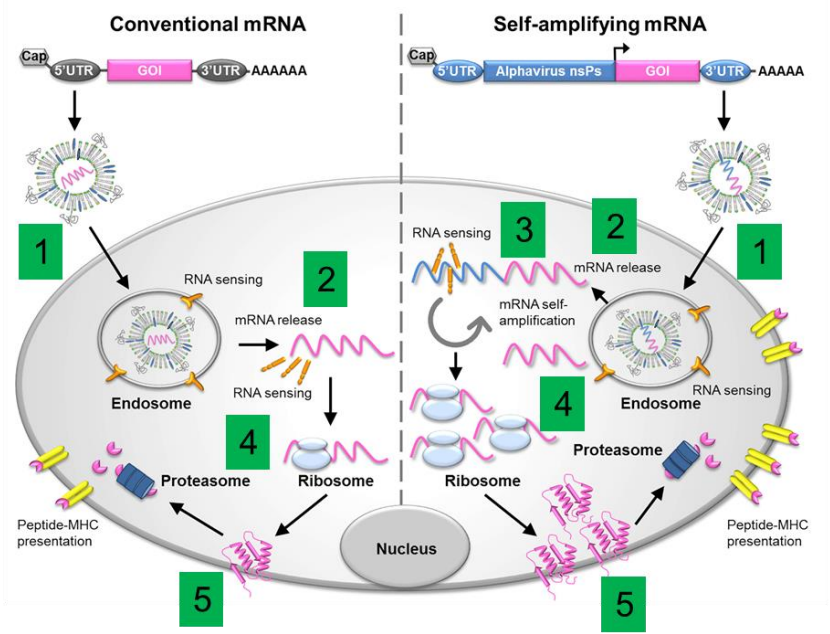
March 17, 2020: Pfizer and BioNTech announce collaboration for COVID-19 mRNA vaccine

- Collaboration aimed to accelerate BioNTech's mRNA-based vaccine program BNT162 to develop a vaccine to prevent COVID-19 disease
- Collaboration aimed to accelerate global development of BNT162 program, leveraging expertise and resources of both companies
- The rapid advancement of this collaboration builds on the R&D collaboration into which Pfizer and BioNTech entered in 2018 to develop mRNA-based vaccines for prevention of influenza
- The companies expect to utilize multiple R&D sites from both companies

COVID- 19 mRNA Vx Initial Clinical Leads Design & MOA



mRNA encapsulated within a nanoparticle comprised of cationic lipid, helper lipid, cholesterol, and PEG-lipid



Step	Description
1	LNP uptake
2	Endosome escape
3	Negative strand synthesis Positive strand synthesis Replicase expression
4	mRNA translation
5	Protein expression

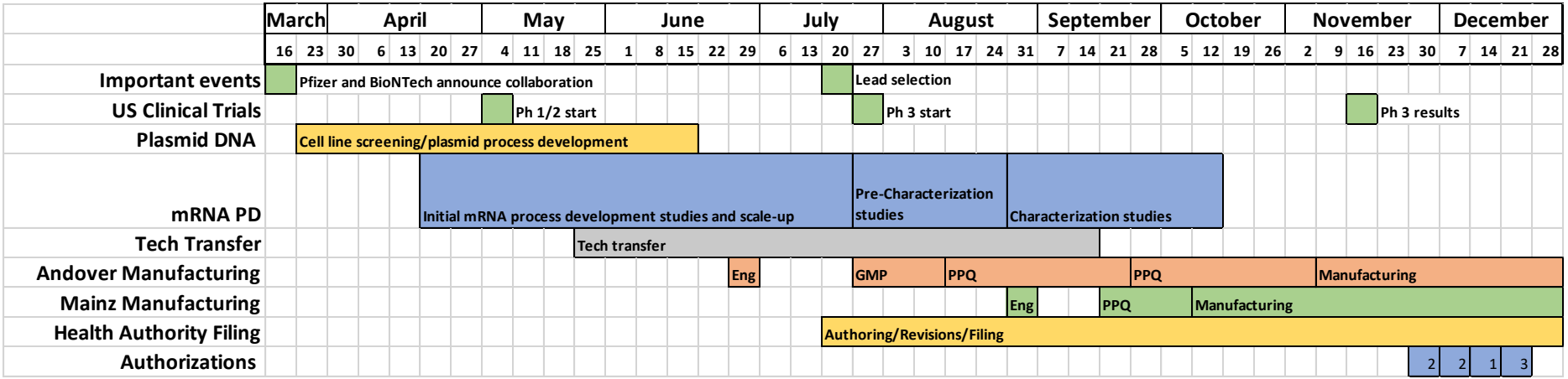
Hassett KJ; et al. *Mol Ther Nucleic Acids.* **2019** 15:1-11
Zhang, Y.; et al. *J Control Release*, **2014**, *174*, 7
Maruggi, G, et. al. *Molecular Therapy*, **2019**

BNT162 COVID-19 Lead mRNA Vx Candidates

Vaccine code	mRNA type	Vaccine encoded antigen
BNT162a1	uRNA	SARS-CoV-2 spike protein receptor binding domain
BNT162b1	modRNA	SARS-CoV-2 spike protein receptor binding domain
BNT162b2 ★	**modRNA**	**SARS-CoV-2 full spike protein S-P2 variant**
BNT162c2	saRNA	SARS-CoV-2 spike protein receptor binding domain

Accelerated Timeline for Covid-19 mRNA Vx Development

Required leveraging multiple platform knowledge and running multiple parallel activities



Authorizations week of:
11/30 – UK, Bahrain
12/7 – Canada, US EUA
12/14 – Switzerland
12/21 – EMA, Norway, Qatar

The Pfizer-BioNTech COVID-19 vaccine has not been approved or licensed by the U.S. Food and Drug Administration (FDA), but has been authorized for emergency use by FDA under an Emergency Use Authorization (EUA) to prevent Coronavirus Disease 2019 (COVID-19) for use in individuals 16 years of age and older. The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of the medical product under Section 564(b)(1) of the FD&C Act unless the declaration is terminated or authorization revoked sooner. Please see EUA Fact Sheet at www.cvdvaccine.com.

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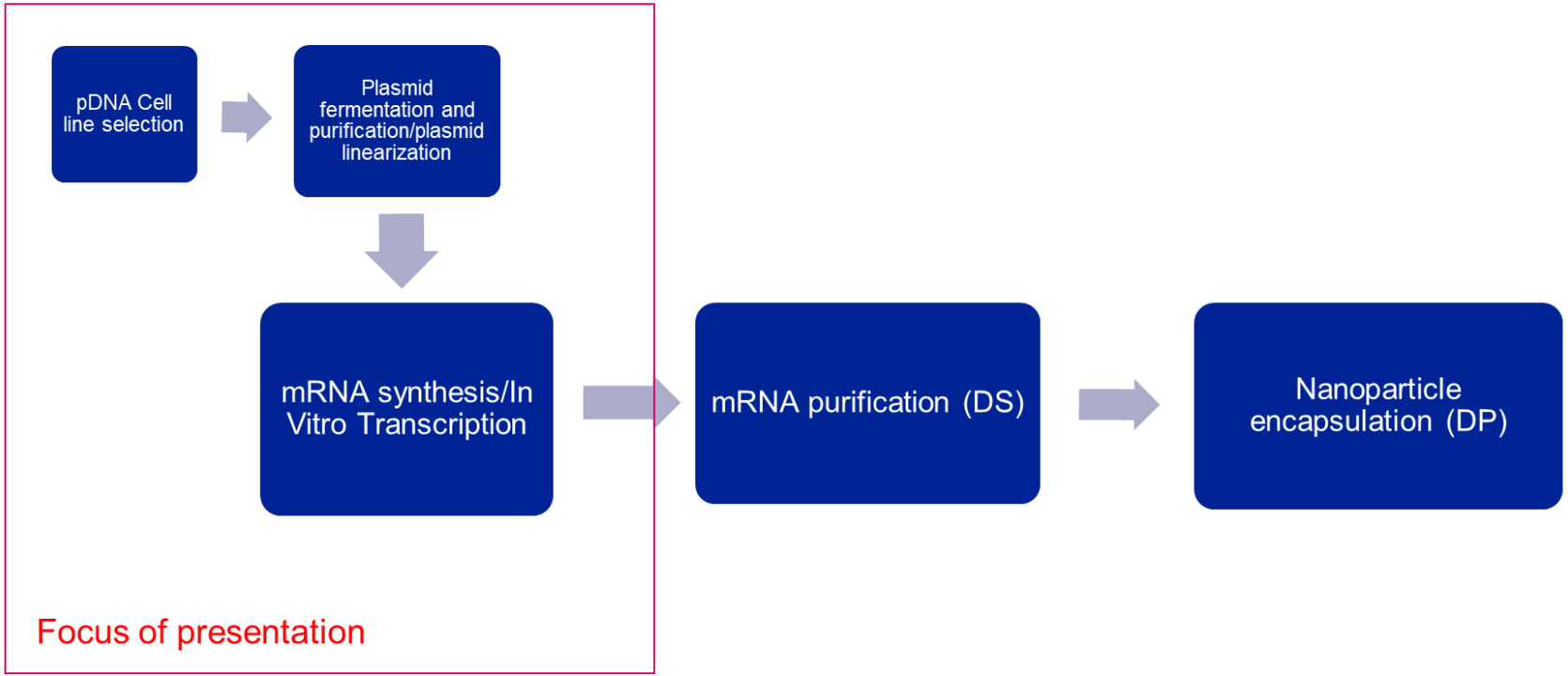
Delivering on accelerated timelines relied on leveraging existing platforms and implementing several novel manufacturing steps



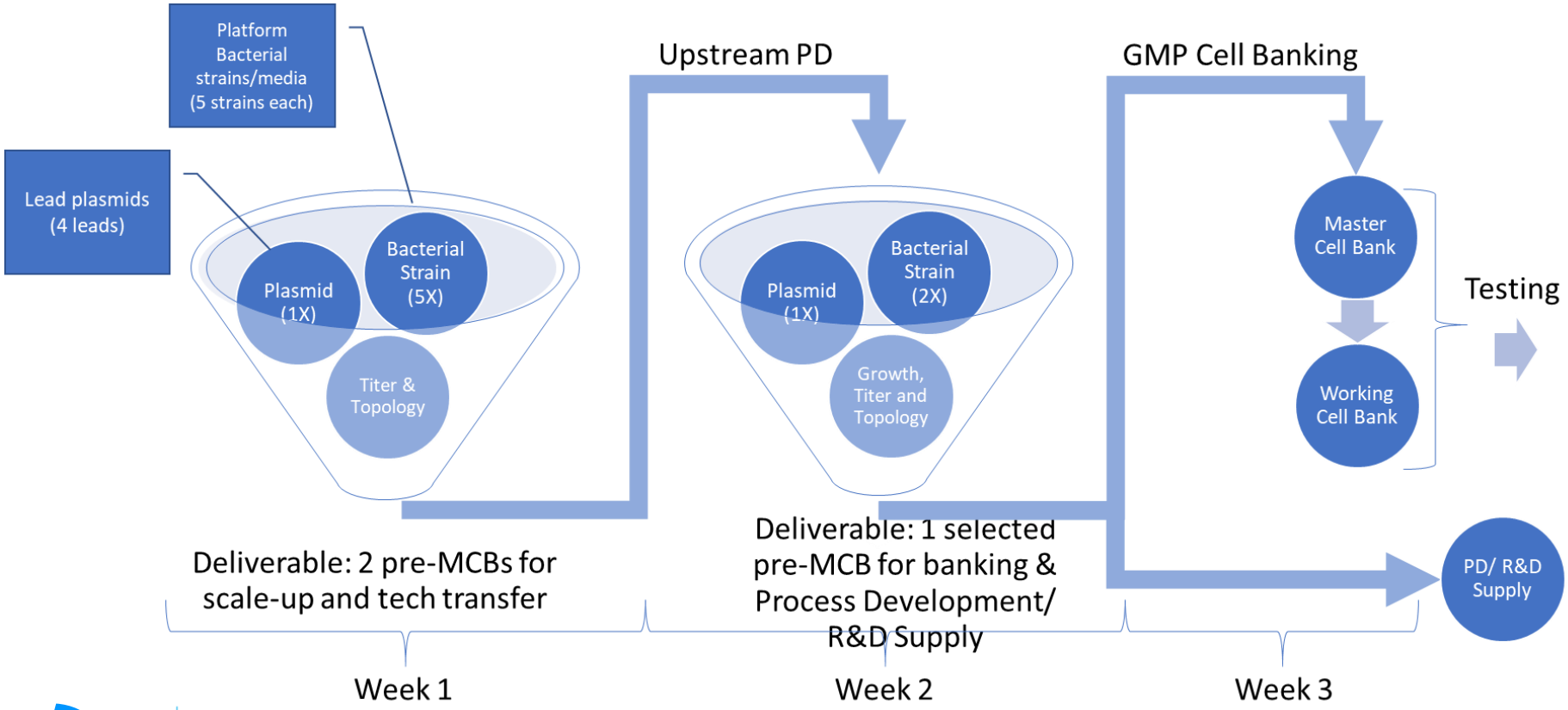
COVID-19 Vx pDNA and mRNA Manufacturing Strategy

Pfizer Chesterfield, MO
-pDNA Manufacturing
-pDNA PD/cell banking
-mRNA PD, characterization studies

GMP Manufacturing at Pfizer Andover, MA

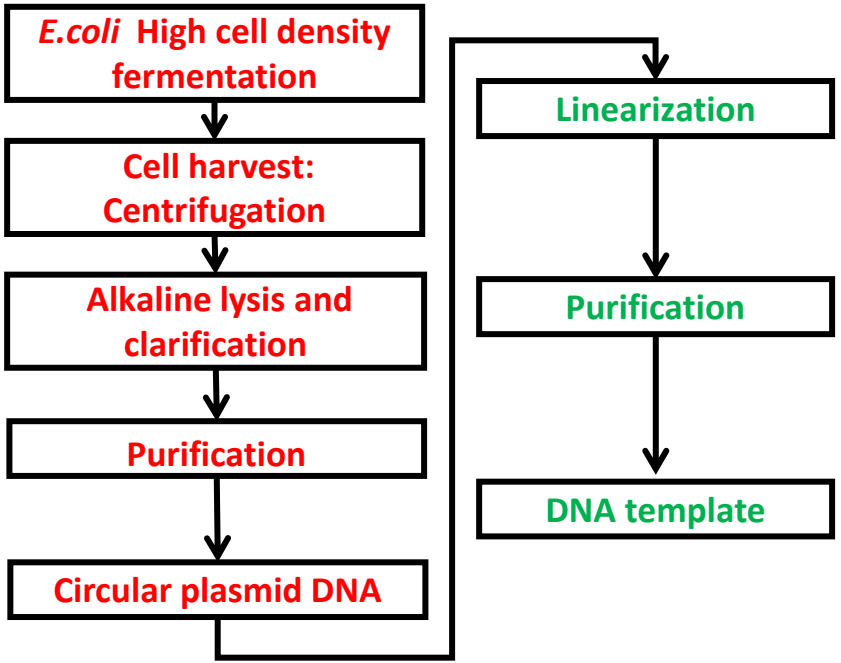
GMP Manufacturing at BioNTech Mainz, Germany

pDNA cell line platform accelerated screening timeline



pDNA manufacturing platform with linearization

- DNA template considered critical starting material and hence higher standard than other raw materials
- Build on Pfizer's internal pDNA platform manufacturing expertise built for gene therapy programs
- Utilize existing manufacturing infrastructure to generate DNA template

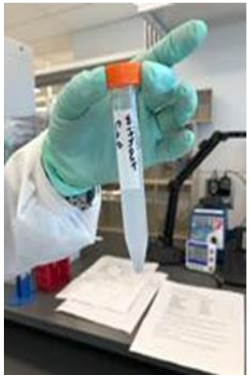


Leveraging of mRNA synthesis (IVT) platforms

- Leveraging of mRNA platform knowledge from influenza collaboration
  - In Vitro Transcription reaction (lab scale)
    - Prior platform knowledge leveraged from both BNT and Pfizer VRD (Pearl River, NY)
      - Raw materials (starting materials, enzymes, nucleotides, buffers, pyrophosphatase, DNAase I, etc)
        - Included vendors leveraging their existing manufacturing platforms for increasing needed capacity
      - Optimized IVT process parameters
- Leveraging of automated reactor systems for high throughput process development
  - Automated bioreactor system (AMBR)
  - Disposable bioreactor systems during scale-up
    - Included leveraging existing systems and use of computational fluid dynamics to assist scale-up

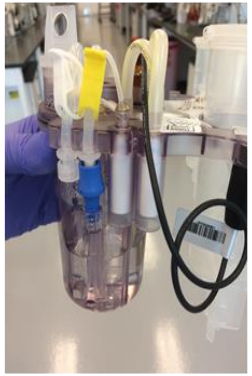
Scale down model platforms accelerated characterization and process understanding

5 ml



15 ml

250 ml



Scale down model benefits

- Disposable
- Scalable geometry and agitation
- Temperature controlled
- Automated additions

- Started at very small scale, qualified 2 scale down models
- Enabled process development, characterization, and satellite runs
- Performed over 350 reactions from April through December
- Completed process characterization studies in 6 weeks

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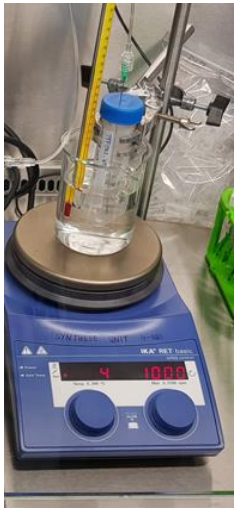
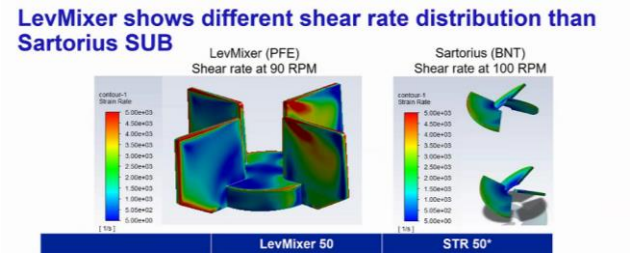
PD team scaled up IVT process over 200-fold; required leveraging existing disposable manufacturing platforms



Tech Transfer/Scale-up focus

- Agitation rates/mixing times
- Reagent additions
- Temp control
- Operations harmonization at both sites



Commercial Scale (June/July)

Mitigating Urgent Supply Chain Logistics:

Drug Substance from Andover, MA being loaded onto Pfizer Corporate jet to be delivered next day to Austria for DP formulation

Description of Covid-19 Vaccine Project

- Super Accelerated
- Highly Complex
- Constantly Changing Priorities
- Multi-Parallel Development/ Leveraged Platform Technologies
- Critical to Humanity

Attributes of the many Teams Working on the Project

- Highly Motivated / Committed
- Courageous
- Patience
- Great Teamwork / Leadership
- Purpose

The accomplishments to date, in such a short time have been simply amazing!!

A Special Thank You to:

- First responders/healthcare providers and caregivers performing heroic efforts during this pandemic
- Patients, physicians and nurses participating in our clinical trials
- Essential workers/teachers
- Pfizer and BioNTech Vendors/Suppliers who supported us along the way

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- BioNTech IMFS (Idar-Oberstein, Germany)

at Pfizer:

- Pfizer Vaccine Research Division (Pearl River, NY)
- Pfizer Pharmaceutical Sciences (Saint Louis, MO and Andover, MA)
  - Bioprocess Research & Development
  - Analytical Research & Development
- Pfizer Global Supply (Andover, MA)

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