mRNA Bio-CDMOs

A key catalyst for the evolution of mRNA therapeutics

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Advisors | MEHTA PARTNERS

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Executive Summary

Introduction to mRNA therapeutics

- mRNA-based agents use the body's own mechanism to deliver therapies
- They have a wide range of applications evaluated across 3 categories

Activities supporting the growth of mRNA space

- The space is gaining momentum with increasing funding, strategic initiatives, and clinical trials

Challenges related to the development of mRNA-based products

- Though mRNA technology offers a versatile platform for the development of multiple therapies, the space is still in its infancy
- Hurdles related to raw materials, process development, and manufacturing remain to be resolved

Bio-CDMOs are becoming an essential catalyst in the evolving field of mRNA-based therapeutics

- With few Bio-CDMOs offering end-to-end capabilities, the majority of the CDMOs specialize in custom services and process development
- An increasing shift is observed toward capacity and inorganic expansion by existing players
- Bio-CDMOs are building in-house expertise and co-developing technologies to address the growing demands
- Biopharma is cultivating strategic alliances with Bio-CDMOs due to their increasing technological expertise and know-how along the value chain

MP Group with >30 years of industry experience can help catalyze your journey to expand into the mRNA space

The mRNA toolkit: Teaching the body to make its own medicine

mRNA-based therapeutics are being broadly explored across 3 categories of applications

	Prophylactic vaccine	Therapeutic vaccine	Therapeutics
Mechanism of action	mRNA encodes antigens that stimulate the immune system	mRNA encodes antigens of the abnormal cells to stimulate the immune system against the abnormal cells	mRNA encodes missing/defective protein for therapeutic purposes
Therapeutic area	Infectious disease	Oncology	Rare genetic disease, oncology, respiratory, immunology, cardiovascular
Examples	○ COVID-19 ○ Influenza, HIV, Zika virus, RSV, HPV	○ Personalized cancer vaccines ○ KRAS-mutated lung/colorectal cancer	○ Cystic fibrosis ○ OX40L in ovarian cancer
Pipelines	○ Majority, 42% of all mRNA pipelines ○ Most mature with marketed COVID-19 products ○ 27 clinical-stage assets (Phase 1: 14, Phase II: 8 and Phase III: 5)	○ 18% of mRNA pipelines, but likely to boost upon clinical PoC ○ 21 clinical-stage assets (Phase I: 10, Phase II: 11)	○ 40% of all mRNA pipelines, spread across multiple therapeutic areas ○ 9 clinical-stage assets across multiple therapeutic areas (Phase I: 5; Phase II:4)

Source: Secondary Research, MP analysis

mRNA therapeutics space is gaining momentum

Investments into mRNA therapeutics have increased since 2020, from ~$5B between 2012-2016 to ~$20B in 2017-2021

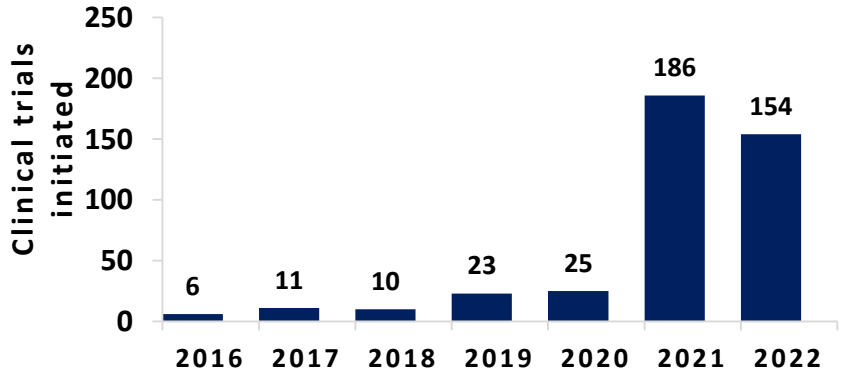
The global mRNA therapeutics market was estimated at ~$45B in 2021 and is projected to grow to ~$100B by 2028 at a CAGR of 13%

Significant influx of investments and partnerships observed, especially after the two 2 FDA approved products (Covid-19 vaccines)

Increase in the number of companies-from ~30 companies in 2021 to ~50 companies in 2023

Clinical trials have been trending upward, witnessing a ~6X increase, from 25 in 2020 to 186 trials in 2021, and 154 in 2022

- Infectious diseases comprise the majority of Phase 1 and Phase 3 assets whereas the majority of the Phase 2 assets are for oncology



Source: Company reports, Secondary Research, MP analysis

A few key milestones/partnerships in the last 4 years

2023

ReNAgade Therapeutics raised $300M in a Series A round to expand the application of its novel and robust LNP-based platform for RNA-based medicines

Orbital Therapeutics raised $270M in a Series A round to develop a novel RNA platform integrating all RNA technologies and delivery mechanisms except siRNA

Moderna acquired OriCiro for $85M for its cell-free synthesis and amplification of plasmid DNA technology

2022

Pfizer partnered with Beam Therapeutics paying $300M upfront and an additional $1B in milestones for its mRNA and lipid nanoparticle technologies to treat rare liver, muscular, and genetic diseases.

2021

Touchlight raised $125M in a Series B round to expand the manufacturing capacity of its synthetic DNA vector

Sanofi acquired Translate Bio for $3.2B for cystic fibrosis assets and vaccines for infectious diseases

2020

CureVac raised a total ~$640M in a private funding round

Significant challenges in mRNA product development

Despite mRNA technology offering a versatile platform for therapeutic innovation with a rapid development cycle, several challenges from raw materials to process development remain to be resolved

	Step	Challenge	Solutions
Raw materials	1 Plasmid	• Pressure on the supply chain as pDNA is also used for the production of gene therapies • Synthesis is labor-intensive and time-consuming • Template quality affects yield and mRNA integrity	• Cell-free technologies to generate pDNA • Optimization of chromatographic methods to increase yield
Raw materials	2 In-vitro transcription	• Complex steps requiring diverse, high-quality, and optimized enzymes, and reagents • Cost-effective and scalable capping method for mRNA stability • Currently, reactions are batch based increasing the inventory of expensive raw materials	• Developing capping enzyme that can work across a wide temperature range • Design of continuous reaction systems reducing the inventory of expensive raw materials
Process development	3 Purification	• Absence of a common purification platform due to the large size of the mRNA • Solvent extraction and precipitation steps are difficult to scale	• More adapted and mix-and-match purification methods (chromatography, filtration) would increase the yield and quality of mRNA
Process development	4 LNP encapsulation	• Absence of targeted, optimized reagent formulations • Need scalable instruments to create high-quality nanoparticles at increased volumes • Need ethanol (highly flammable) for dissolving the lipids prior to encapsulation	• Design of validated and scalable LNP formulations • Using flame-proof equipment
Process development	5 Storage	• Multiple types of storage capabilities, each with appropriate standard operating procedures is a significant cost driver	• Novel formulation approaches for the storage and transport of mRNA products at refrigerated or ideally room temperature

Bio-CDMOs are building the essential capabilities to mediate the challenges and address the growing mRNA market demands

Source: Literature, Company website, MP analysis;

Bio-CDMOs are expanding to support mRNA surge

The global mRNA Bio-CDMO space, estimated at ~$2.5B in 2020 is expected to reach ~$12B in 2030, growing at a CAGR of ~15%

The mRNA CDMO landscape comprises of ~70 companies
Limited companies offer end-to-end capabilities whereas the majority of them offer raw materials and process development services

Raw materials

Companies focusing on providing high-grade pDNA, enzymes, and reagents for efficient downstream processing

TOUCHLIGHT · NEW ENGLAND BioLabs Inc. · Jena Bioscience · ThermoFisher SCIENTIFIC

Process development

Companies building expertise catering to the various process steps such as purification, LNP encapsulation

cytiva · ACUITAS THERAPEUTICS · eTheRNA engineering RNA · PRECISION NANOSYSTEMS now part of Cytiva · Biologics

End-to-end services

Companies establishing core competencies to become a "one-stop-shop" solution offering services from raw materials to process development and manufacturing facilities

SAMSUNG BIOLOGICS · MERCK · curia · ReciBio Pharm

CDMOs are addressing the white space in mRNA technology through strategic initiatives

Expansion

- In Mar 2023 Samsung Biologics invested ~$1.5B expanding its capacity
- In Jan 2023 Catalent opened a commercial-scale plasmid DNA (pDNA) manufacturing facility in Belgium
- In Jan 2023 Kaneka invested $15M to scale up mRNA capacity in Belgium
- In June 2022 Vernal Biosciences raised $20M to expand to a commercial-scale GMP facility with plasmid, mRNA, LNP formulation, and fill/finish capabilities

M&A

- In Feb 2022 Recipharm acquired (undisclosed amount) Arranta Bio to expand into fermentation, purification, and mRNA clinical production capabilities establishing a US presence under its biologics vertical ReciBioPharm
- In Aug & Sep 2021 Curia acquired Integrity Bio and Lake Pharma respectively to offer comprehensive mRNA process development, formulation, and manufacturing services

Source: Company news, MP analysis;

Bio-CDMOs offer integrated capabilities through in-house expertise and strategic partnerships

Bio-CDMOs are becoming an essential catalyst through increasing technical expertise and know-how across the value chain

TOUCHLIGHT

Developed a novel, synthetic DNA vector called doggy bone DNA or dbDNA™ and enzymatic manufacturing platform enabling DNA production in weeks.

ACURABIO

cytiva

Co-developed a purification platform to deliver high-quality plasmid DNA.

1 Plasmid

3 Purification

Developed multiple platforms based on chromatographic and filtration methods for the capture of mRNA and removal of aberrant mRNA.

cytiva

Developed cellulose-based purification for removal of dsRNA at various scales and tangential flow filtration platforms for large-scale mRNA purification.

MERCK

NEW ENGLAND BioLabs Inc.

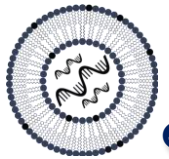
Designed a capping solution combining high activity and a broad temperature range for in-vitro transcription of mRNA.

GINKGO BIOWORKS

aldevron

Co-developed a platform to optimize the manufacturing yield of the capping enzyme, a key component required to produce mRNA therapies and vaccines.

2 In-vitro transcription



4 LNP encapsulation

Developed proprietary LNP formulations to facilitate targeted delivery of mRNA drug products.

eTheRNA engineering RNA

Aldevron will combine high-quality plasmid DNA, enzymes, and other key components with PNI's reproducible and scalable LNP manufacturing platform- NanoAssemblr® to develop and manufacture mRNA-based drugs.

PRECISION NANOSYSTEMS now part of Cytiva

aldevron

Source: Company news, MP analysis;

Bio-CDMOs are becoming key partners for biopharma companies

mRNA therapeutics biotechs are cultivating strategic alliances with Bio-CDMOs

Biotechs and pharma companies focusing on mRNA are turning to the bio-CDMOs to address the challenges related to plasmid DNA, LNP delivery technology, and manufacturing capabilities

Date	Biopharma/Biotech	Location	CDMO	Location	Deal type	Acquired/Partnership for
April 2023	**20Med Therapeutics**	Netherlands	**Touchlight**	UK	Partnership	doggybone DNA (dbDNA™)- alternative to plasmid DNA
February 2023	**RVAC Medicines**	Singapore	**GenScript ProBio**	US	Partnership	Plasmid DNA
August 2022	**GreenLight Biosciences**	US	**Samsung Biologics**	South Korea	Partnership	End-to-end capabilities for commercial scale manufacturing of mRNA vaccine
May 2022	**Sanofi**	France	**EUROAPI**	France	Partnership	LNP delivery system
January 2022	**Pfizer**	US	**Acuitas Therapeutics**	Canada	Partnership	LNP delivery system
January 2022	**Merck KGaA**	Germany	**Exelead**	US	Acquisition	Acquired for $780M for LNP formulation expertise to enhance Merck's mRNA and lipid manufacturing capabilities
May 2021	**Moderna**	US	**Aldevron**	US	Partnership	Plasmid DNA

Source: Company news, MP analysis;

MP Group can catalyze your initiative

With over 3 decades of diverse experience and integrated perspective in domestic and global BioPharma/CDMO space, and deep understanding of mRNA tx and the associated technologies, MP Group has the capabilities to help you

MP Team will be happy to be an extension of the management team and help with one or more of the below initiatives:

- Catalyze the growth and expansion strategy of the mRNA Bio-CDMOs for long term success
- Identify global opportunities with the key technologies in mRNA development and manufacturing
- Leverage MP's global network to identify potential below-the-radar opportunities for partnering or investment, unique to the vision of the company
- Develop a robust opportunity assessment framework with the desired criteria for bio-CDMO selection and evaluate the relevant opportunities against the framework
- Technical due diligence of mRNA CDMOs and/or the associated technologies to investigate the technologies best suited for the need

THANK YOU.

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