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# Genetics: Transforming medicine

Exciting, investible, now

Linden Thomson and Peter Hughes

September 2021

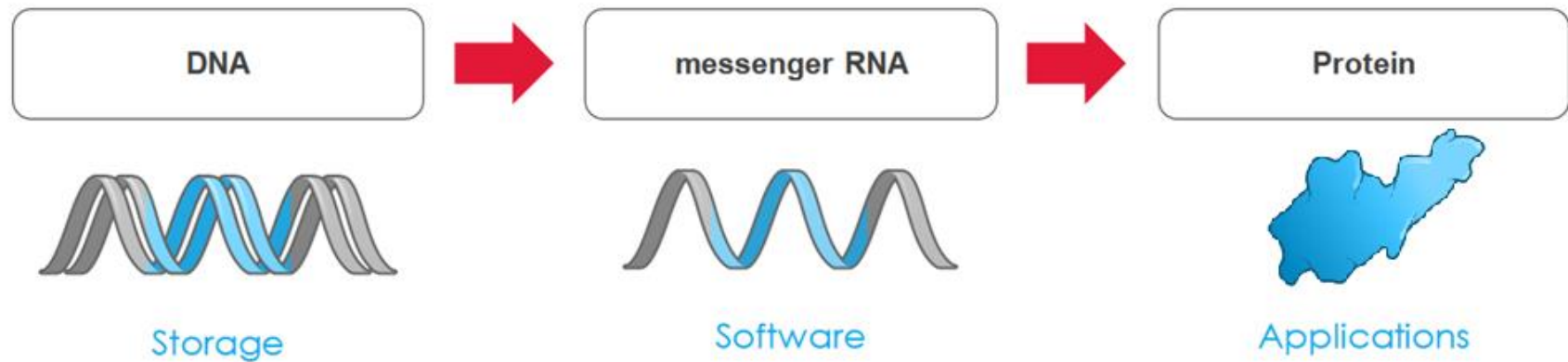
# Genetics a case study in accelerating innovation

## Tackling Spinal Muscular Atrophy (SMA)



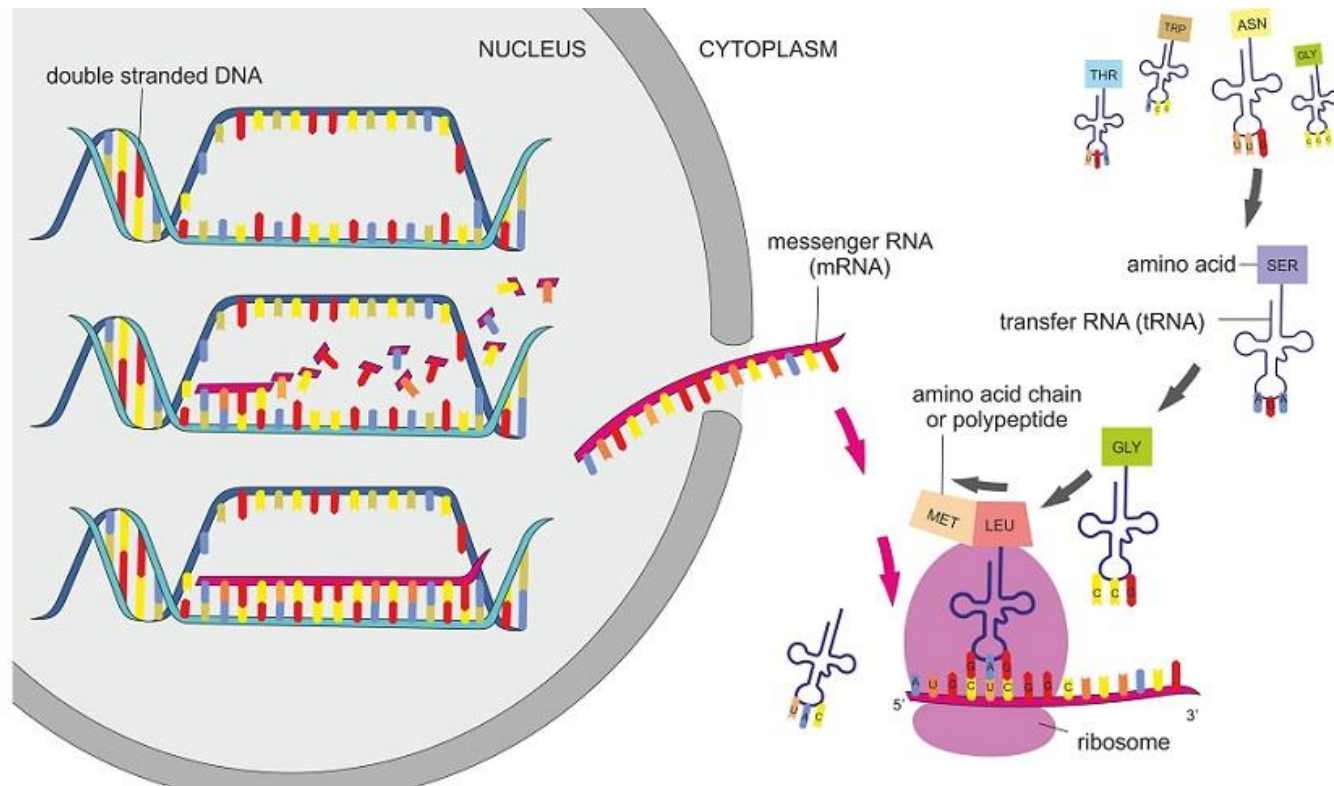
Source: SVB Leerink LLC Biotech Boom to Bust (and Back Again) October 2019. Reprinted with permission CR09911/07-19. Stocks are mentioned for illustrative purposes only and do not constitute investment advice or a recommendation.

# Genetics basics



Source: moderna

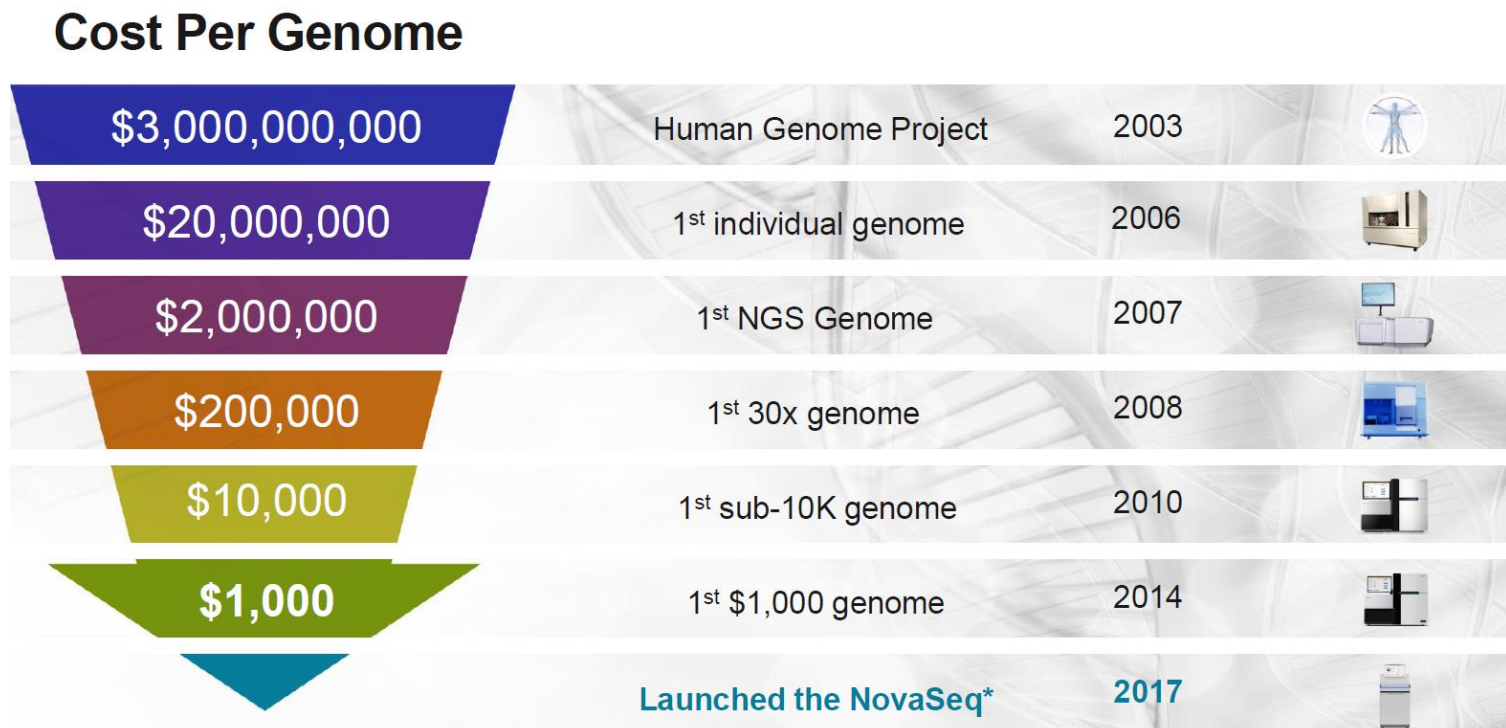
# Protein production



Source: biologydictionary.net/protein-synthesis/ accessed on 6/9/2021

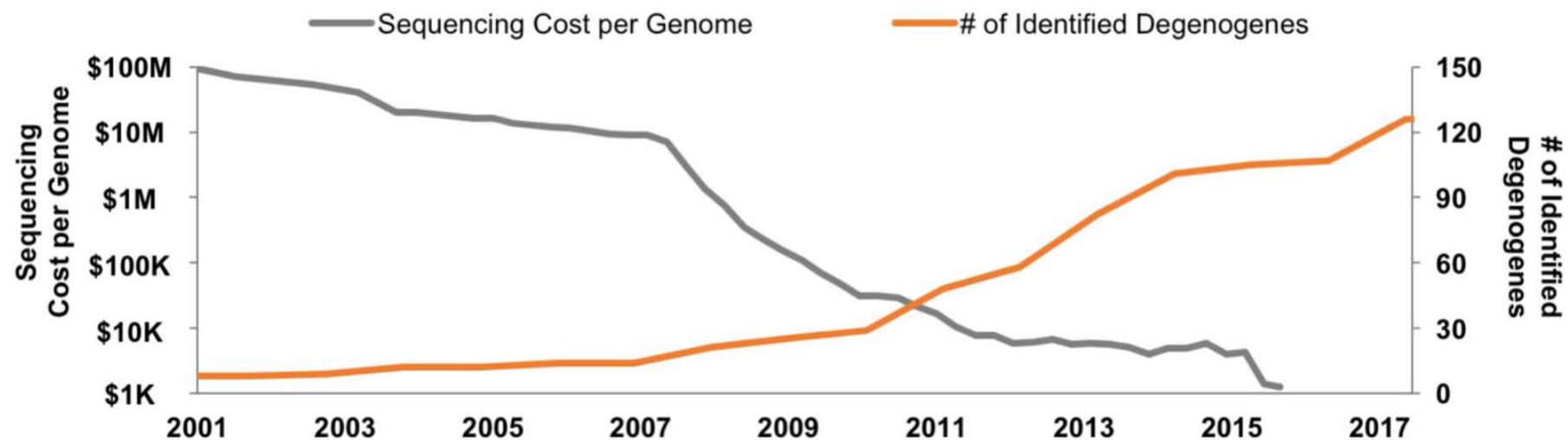
# Cheaper, Better, Faster, Stronger

Advances in genomics has led to the promise of curing (some) genetic diseases via gene therapy



Source: Illumina as at 13/07/2018. CR12178/08-19

## As cost has fallen, progress has advanced



Source: Denali Therapeutics Corporate Presentation, Dec 2018

# Miniaturisation facilitating access to the technology

From this...



Source: Project Management Institute

# Miniaturisation facilitating access to the technology

...to this



< 450 g

Sequence anywhere, pocket-sized devices

From \$1,000

Low-cost sequencing for every lab

Up to 50 Gb\*

Real-time sequencing data

\* Theoretical max output when system is run for 72 hours at 420 bases / second. Outputs may vary according to library type, run conditions, etc.

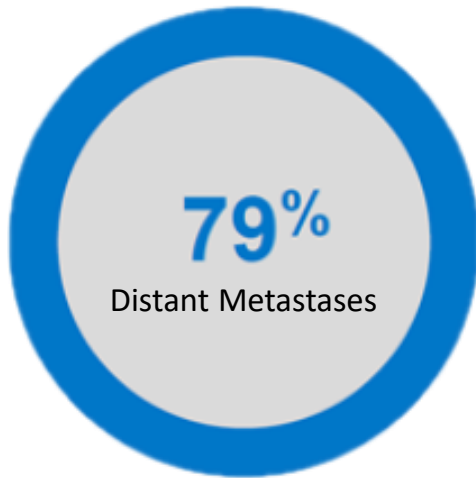
Source: Oxford Nanopore website August 2021: <https://nanoporetech.com/products/minion>



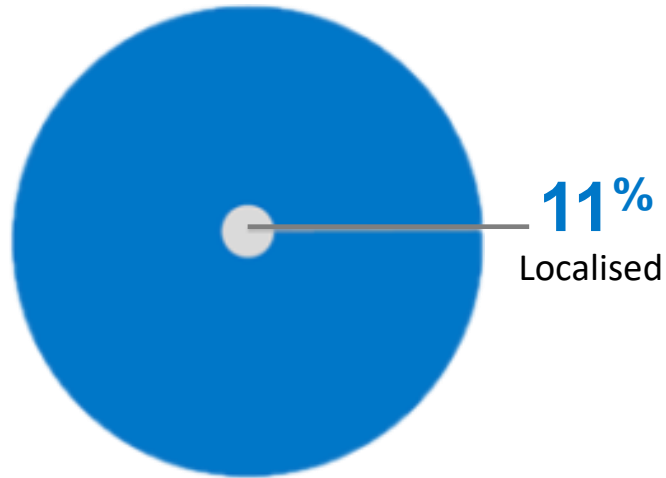
# Cancer diagnosis and screening

Detecting cancer early will save lives

High 5-year cancer death rate when diagnosed late



Low 5-year cancer death rate when diagnosed early



**71%**

of cancer-related deaths today are in cancers with no recommended screening

# Genetic screening case study

Improving cancer survival with genetic-based screening

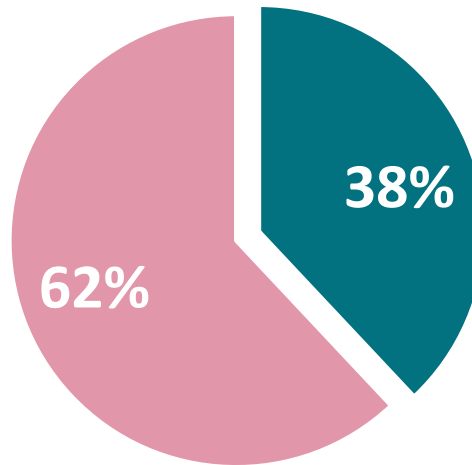
## EXACT SCIENCES

Colorectal cancer: second deadliest cancer in the US

53k Annual Deaths

90% Survival if caught early

Only 38% of colorectal cancer is diagnosed at early stage



Accurate screening test offers chance to increase early stage diagnosis

 cologuard<sup>®</sup>  
Rx only

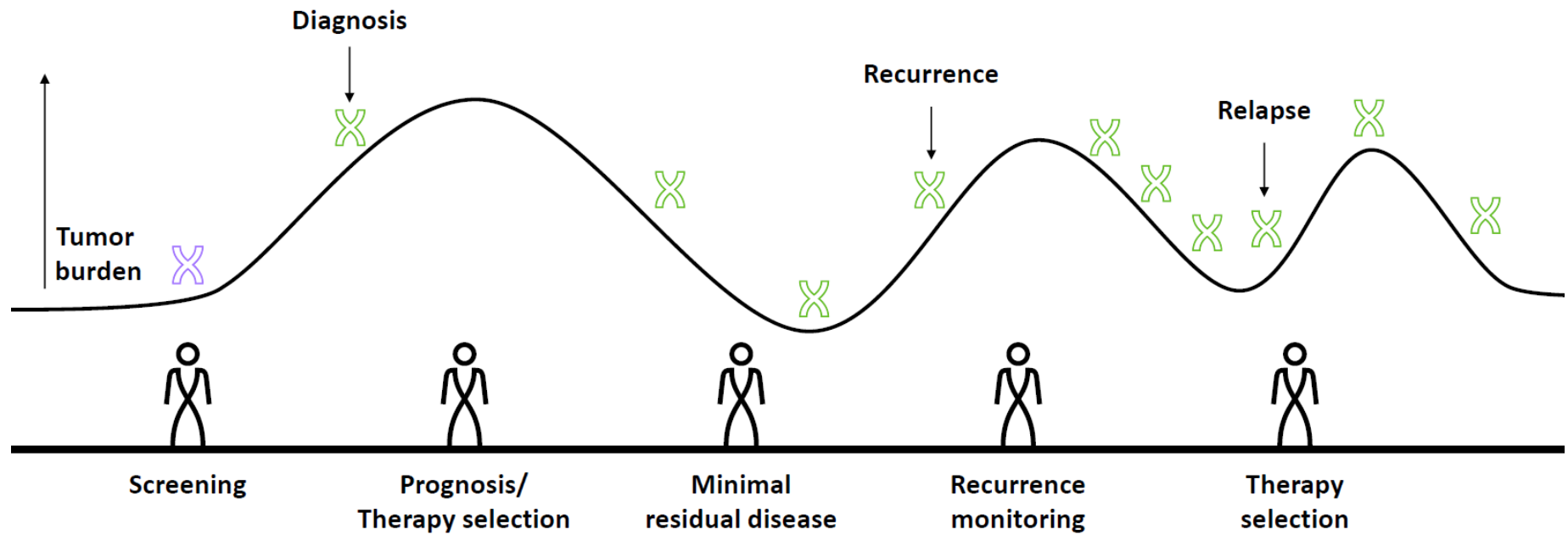
94%

Early-stage cancer sensitivity

Source: 1. Exact Sciences Corporate Presentation, Jan 2021  
2. <https://www.cancer.net/cancer-types/colorectal-cancer/statistics>, accessed on 1/9/2021  
3. <https://www.cologuard.com/faq/is-cologuard-fda-approved>, accessed on 1/9/2021

# Liquid biopsy

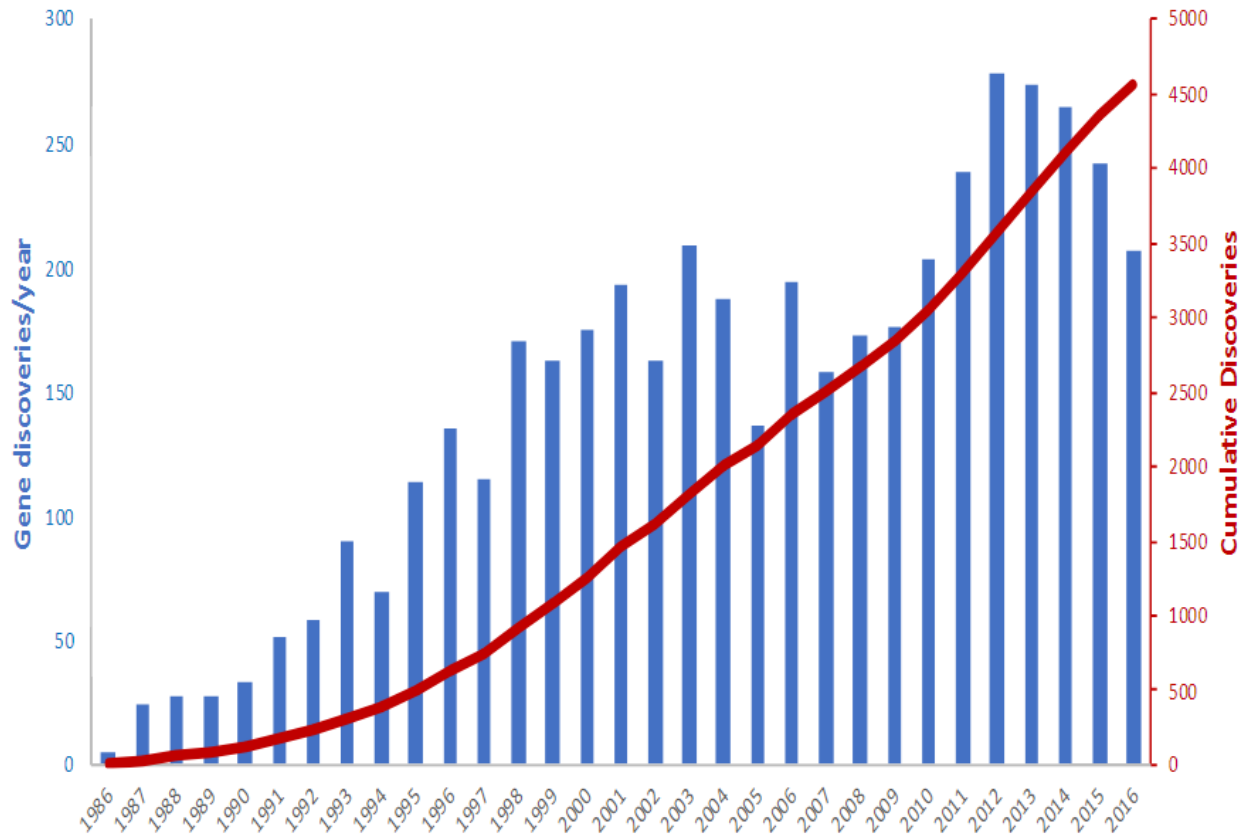
Investible now and a large potential total addressable market



Source: Exact Sciences Corporate Presentation, Jan 2021.

# Drug discovery

Gene mutations are important disease drug targets



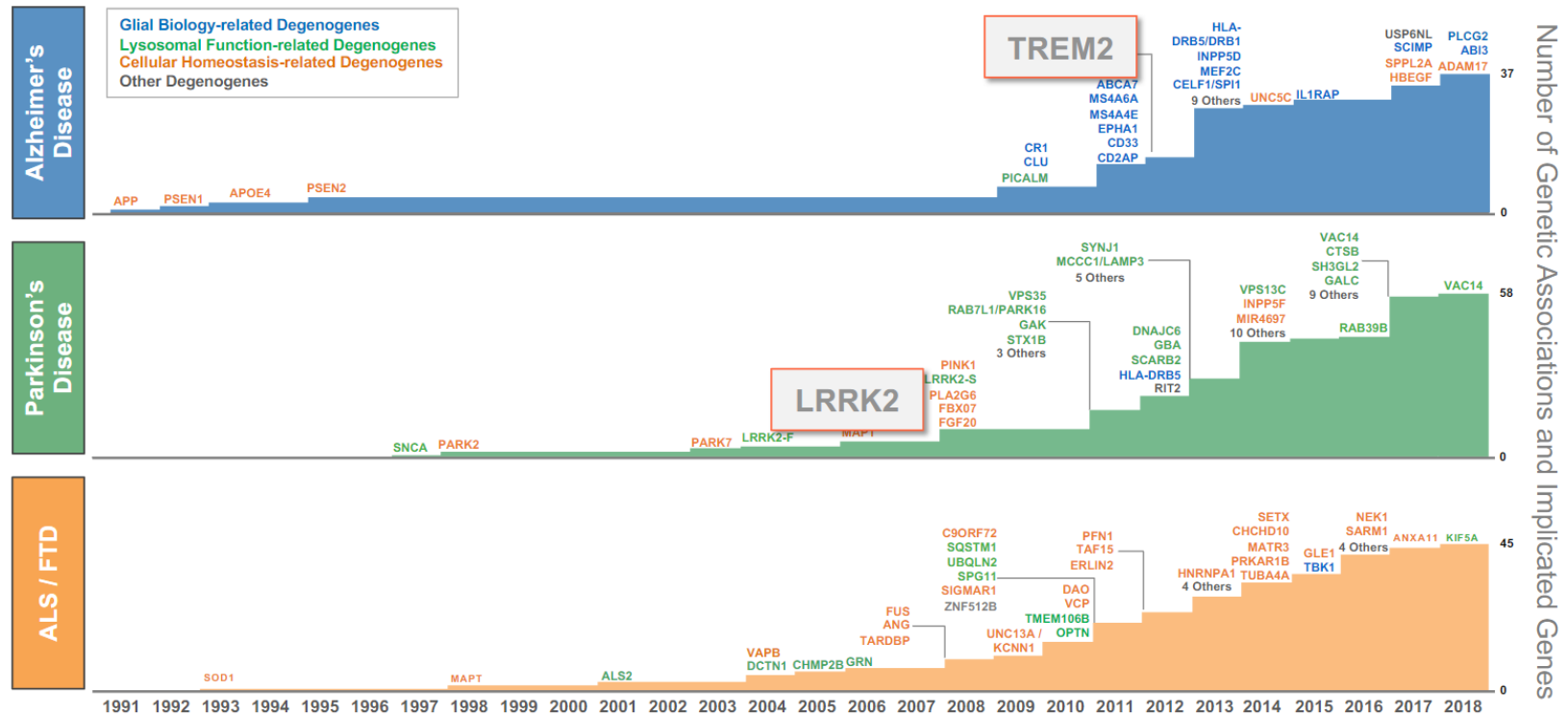
**Drug development programs with genetically validated targets are twice as likely to succeed**



Source: Biomarin R&D day 2018 presentation

# Genetically validated targets case study

## Understanding the link between genetics and disease

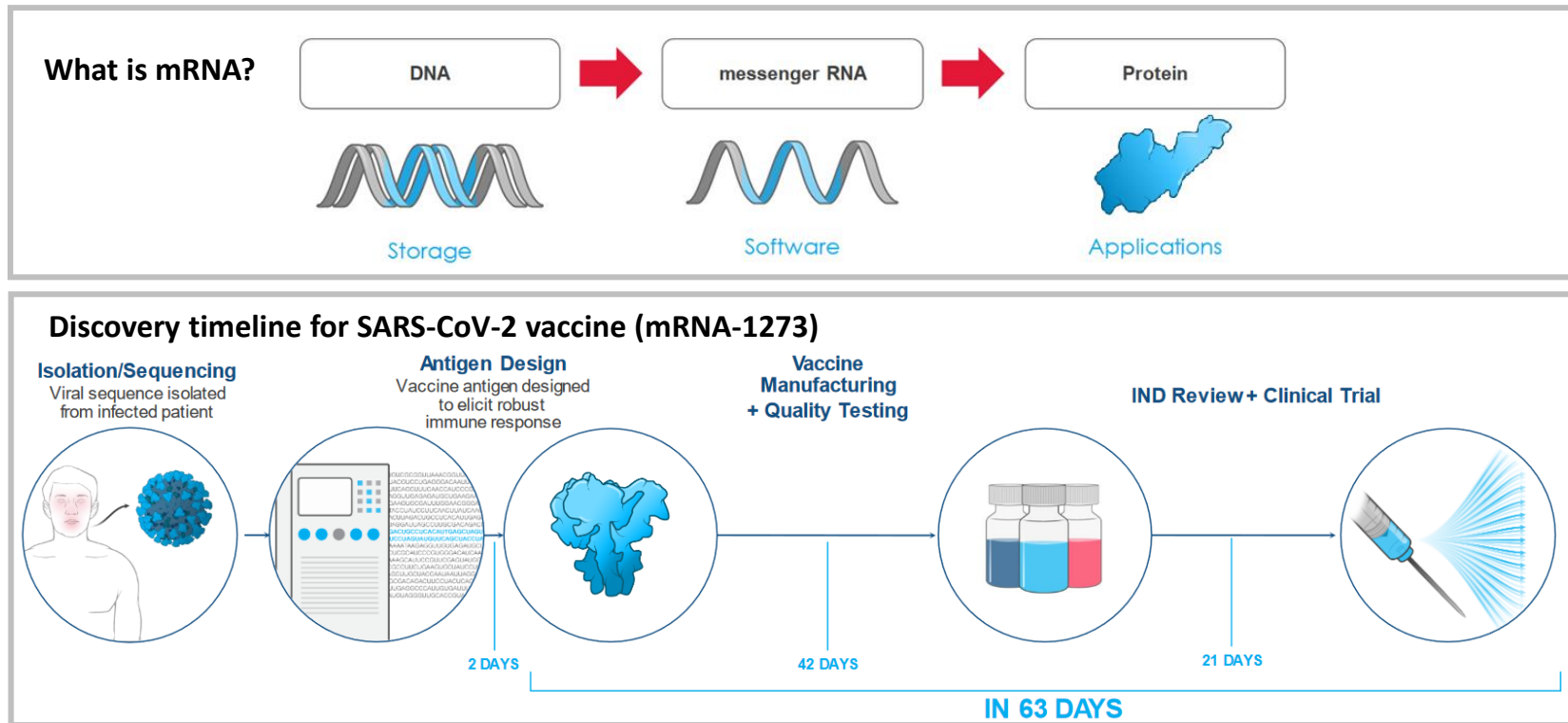


Source: Denali Therapeutics Corporate Presentation, Dec 2018

# Vaccines case study

Moderna mRNA – only 63 days to get from genetic sequence to vaccine entering clinical trials

moderna



# Genetic drugs case study

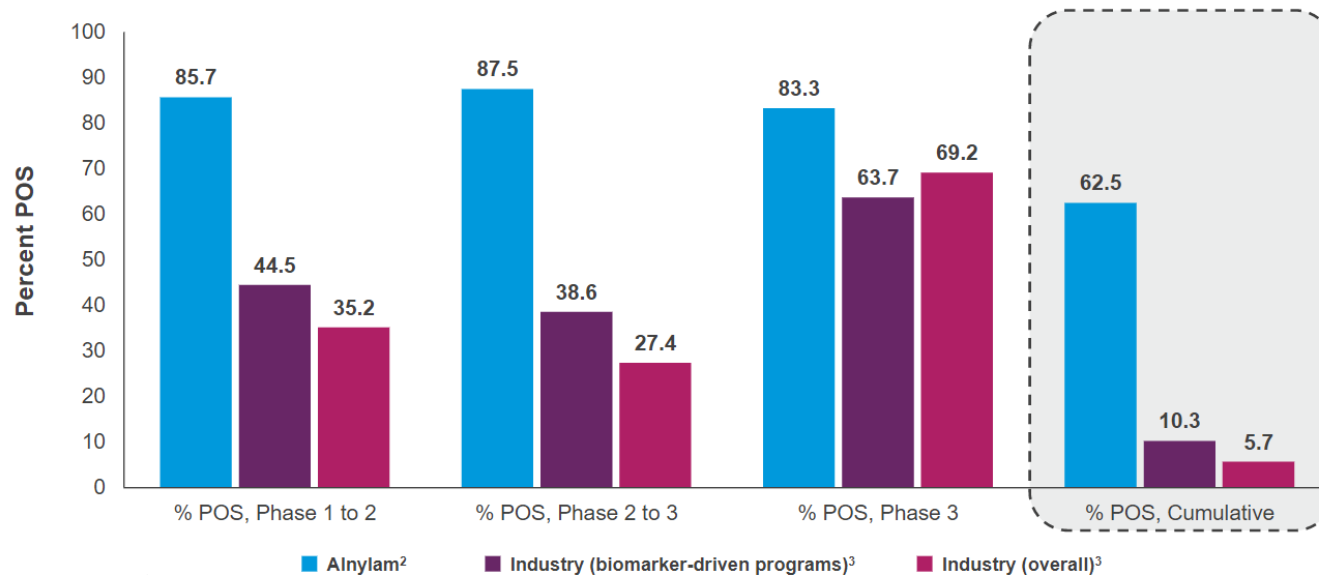
More targeted, higher success rate



## High-Yield Productivity of Alnylam RNAi Therapeutics Platform

Comparison of Historical Industry Metrics to Alnylam Portfolio<sup>1</sup>

### Probability of Success (POS) by Phase Transition



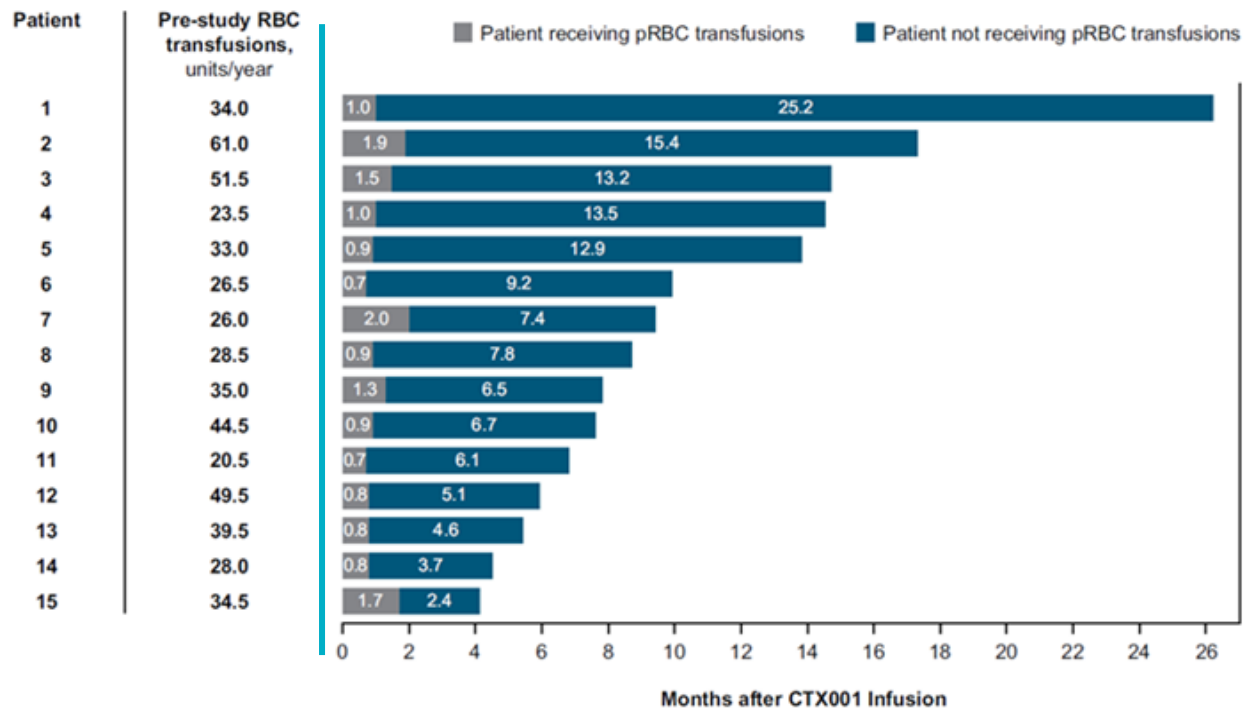
Source: Alnylam corporate presentation

# Gene editing case study

In patients now, transforming lives



All patients free of transfusions within two months of a single treatment with CTX001



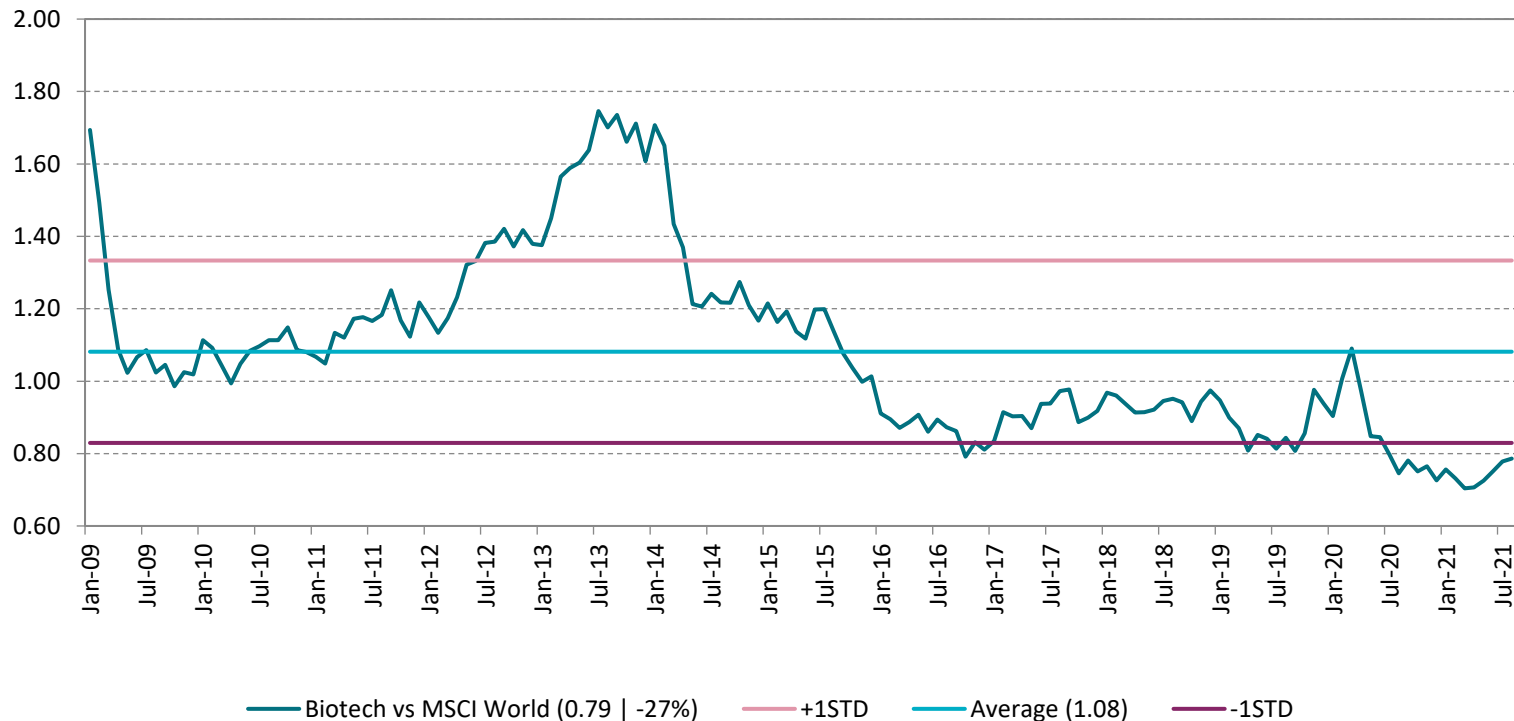
Source: Bernstein April 2021



# Valuation Biotech vs market

Looking interesting – forward P/E next 12 months vs market

## Biotech vs MSCI World (0.79 | -27%)

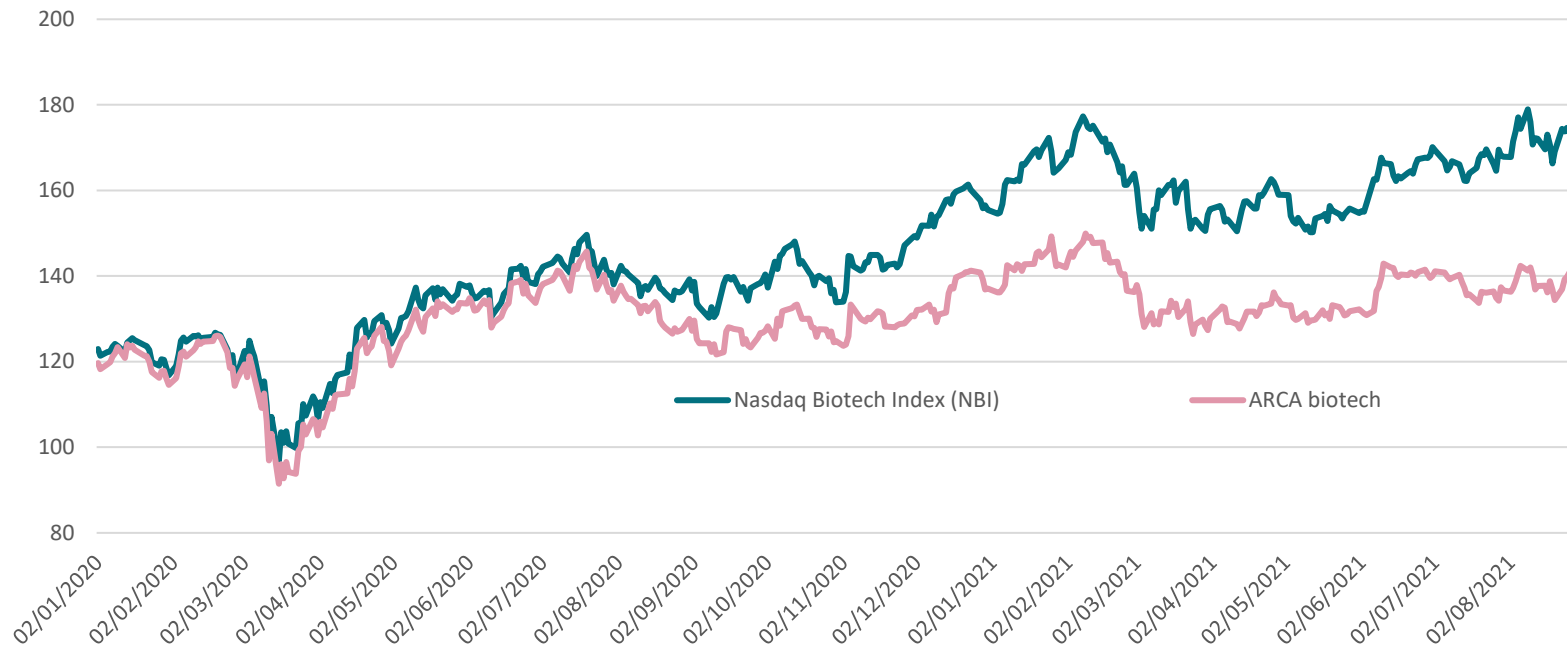


Source: FactSet as at 31/08/21

# Valuation NYSE ARCA biotech vs NBI

SMID cap biotech has underperformed year to date

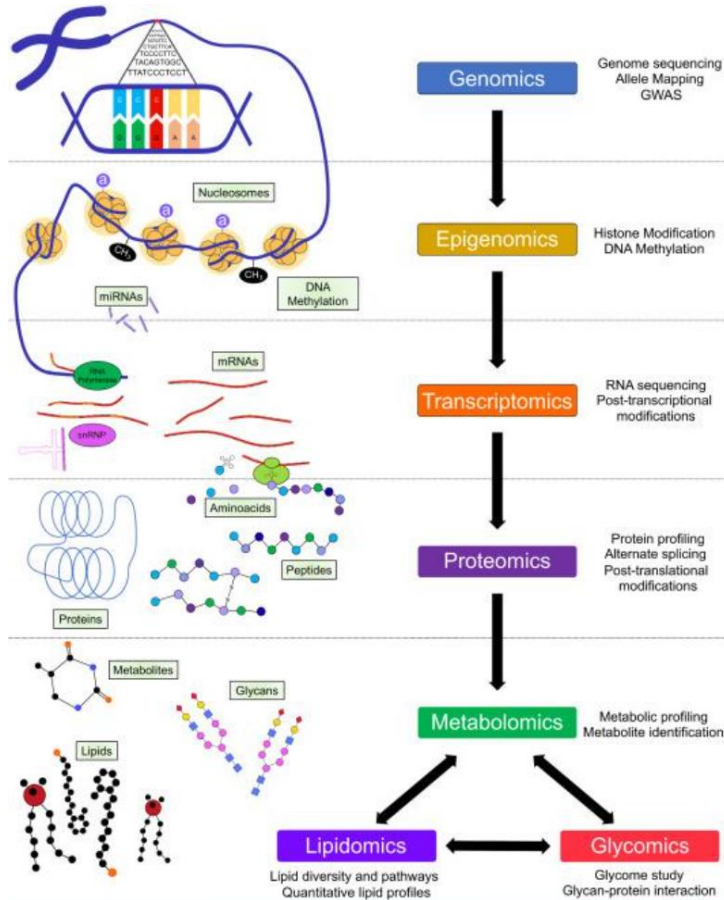
## Price performance of large cap vs smid cap biotech UTD



Source: Bloomberg, as at 31/08/2021

# Continuous cycle of innovation

Still a lot more to come



Source: Bernstein, April 2021

Improving disease understanding; identifying additional potential targets

## Hepatocellular carcinoma

- Proteomics identified novel therapeutic targets (e.g., SOAT1)

## Various cancers

- Proteomic signatures shared by different types of aggressive cancers identified as playing a role in cell survival and migration

## ALS / dementia

- Proteomics identifies and characterizes key proteins, including TDP-43, SOD1, and tau

## Inflammatory disease

- Transcriptomics enables detection of biomarkers and identifies new targets for rheumatoid arthritis

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