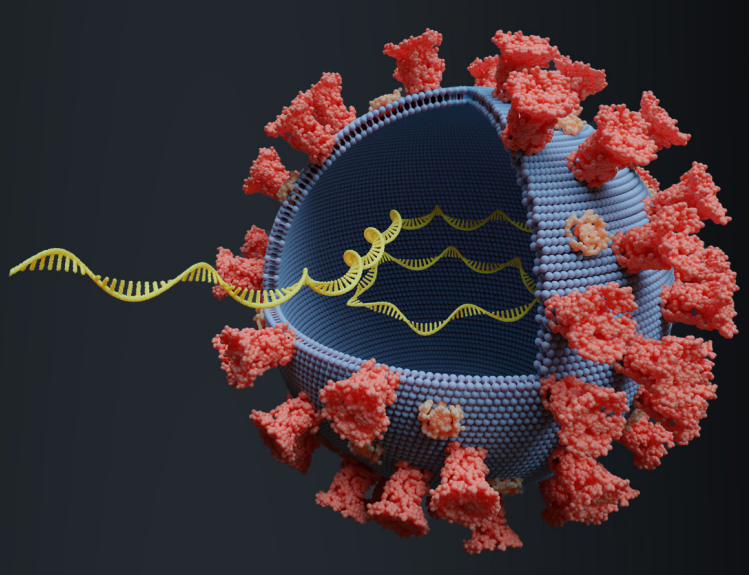
RNA Biotherapeutics — A New Approach to an Old Problem



Drug development has been focused on traditional small molecule and protein therapies for many years, but these approaches have provided means to address only a small fraction of desired targets and diseases. Discovery of the RNA interference (RNAi) process opened a new door to therapeutics discovery and development. RNA-based biotherapeutics are on the rise and positioned to provide a rapid, cost-effective, and readily adaptable way to address previously "undruggable" targets.

This infographic provides a brief history of RNA-based therapy and outlines how Bio-Rad™ Droplet Digital™ PCR (ddPCR™) technology supports this field of work.

The RNA Biotherapeutics Difference

14%

Percent of the human genome targetable by traditional drug therapies[1]

Small molecule, protein, and other traditional approaches to drug discovery have plateaued in their ability to affect clinically meaningful targets.

3,624

RNA therapeutics publications released in 2021[2]

The delivery of RNA to cells to affect the expression of target proteins is a relatively new approach that holds great promise to target previously undruggable proteins and change the standard of care for many diseases. RNA therapeutics are also relatively fast and cost-effective to develop and are more easily adaptable than traditional therapies.[1]

Timeline and Metrics

RNA biotherapeutics are based on the RNAi process that was discovered less than 25 years ago.

1998 Nature paper[3] by Craig Mello and Andrew Fire is published to first describe RNAi.

2006 Craig Mello and Andrew Fire receive The Nobel Prize and RNAi is recognized as a new opportunity for drug discovery and development.

2018 Patisiran is the first FDA approved therapeutic using RNAi.

While relatively new, RNAi has quickly been recognized as an opportunity for unique drug development and a pipeline of RNA-based biotherapeutics has been developed.

Type of RNA	FDA or EU Approved (including EUA)	In Phase I/II Trials
Messenger RNA (mRNA)	2	21
Antisense oligonucleotides (ASO)	4	—
MicroRNA (miRNA)	—	3
Aptamer (miRNA)	1	2
Small interfering RNA (siRNA)	2	—

TOTAL 35
RNA-based therapies approved for use or in current clinical trials[1]

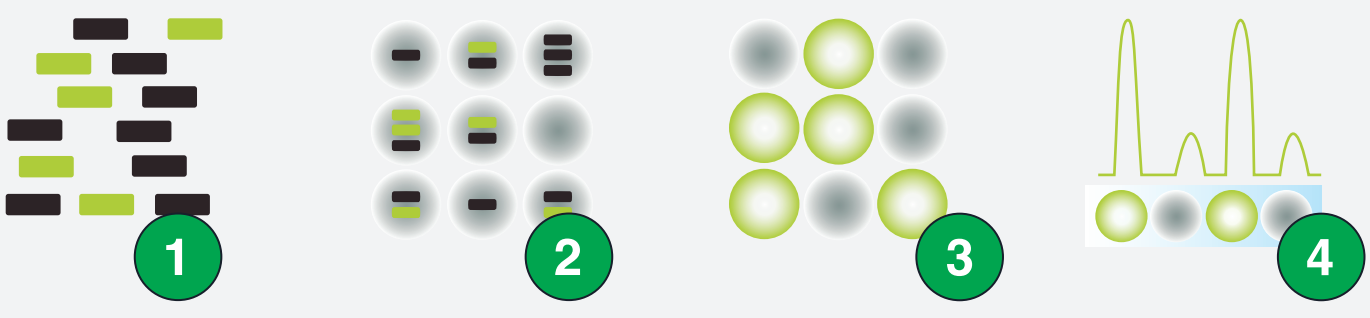
New Targets Available

Developers have overcome challenges of using RNA as a therapeutic (e.g., avoiding degradation, delivering across the cell membrane, and managing immunotoxic cell response)[1] to produce RNAi-based drugs to help with the following diseases and conditions:

- Cancer
- Cardiovascular disease
- Viral infections
- Eye-related disorders
- Renal injury and failure
- Hemophilia

ddPCR Technology and Application in RNA Therapeutics

Bio-Rad ddPCR technology provides absolute quantification of RNA and gene expression for low copy number templates.



1. RNA sample with target sequence is partitioned into droplets
2. Target and background RNA are randomly distributed among 20,000 droplets
3. Target sequence is amplified by end-point PCR in each droplet
4. Positive droplets are counted to give precise quantification of target sequences in sample

Development, testing, and production of RNA therapeutics is supported by ddPCR technology in the following ways:

Biomarker discovery

Copy number variant analysis

Rare variant detection

Ratio analysis for multivalent therapies

Gene expression analysis
Used to establish a positive correlation between CRED9 and *CEBPA* mRNA expression in multiple cancer cell lines[4]

RNA therapeutic titer
Demonstrated to provide sensitivity, accuracy, reproducibility, and scalability for higher-throughput capabilities in AAV viral genome titration across multiple transgenes and serotypes[5]

Poly(A) tail level determination
Cited as a Poly(A) determination method by developer of a commercially available SARS-CoV-2 mRNA vaccine[6]

Biodistribution studies
Used for RNA biodistribution studies based on sensitivity, precision, reproducibility, and ability to detect low copy numbers, and reduced interference form endogenous RNA[7]

Visit **bio-rad.com/RNA** to learn more.

References

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