RNAConnect

Yale Innovation Summit

Ryan Muldoon, CEO

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RNAConnect, Inc.

Biotechnology enzymes are scientific hardware.

When hardware is improved, one can do everything better, faster, and innovate in ways not previously imaginable.

RNAConnect was formed to create, develop, & sell high performance biotech enzyme hardware.

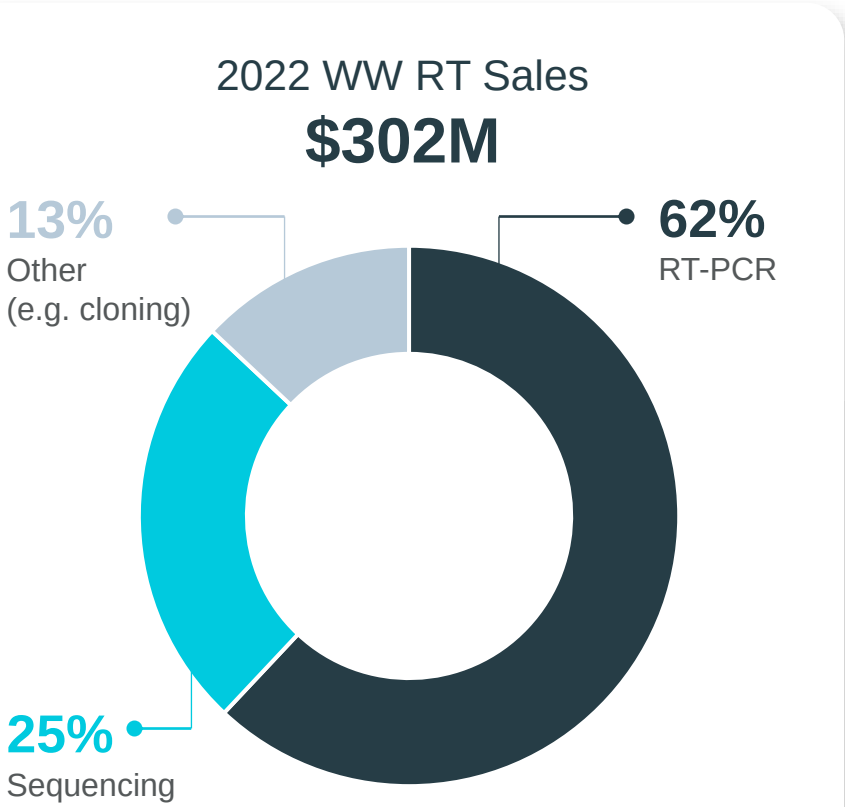
Key Innovation: We discovered and optimized a vastly superior reverse transcriptase that enables:

- New categories of companion diagnostics in cancer & neurodegenerative diseases
- Superior viral pandemic surveillance
- Unbiased whole-transcriptome RT-PCR, single-cell sequencing, & spatial transcriptomics

Reverse Transcriptase (RT)

An attractive growing market

The Reverse Transcriptase Market



Reverse Transcriptase enzymes convert single-stranded RNA into single-stranded cDNA for:

- **PCR amplification**
  e.g., HIV and COVID-19 testing
- **RNA Sequencing**

Inherent limitations of leading RTs

Processivity
RTs can only read ~100 bases, but natural RNAs are 2,000-30,000 bases long

Thermal Activity
Operate best at high temperatures – which degrade the RNA templates

Unwinding Power
RNAs “fold” into structural motifs, but existing RTs stop reading and fall off when they encounter structures

MarathonRT: Our First Product

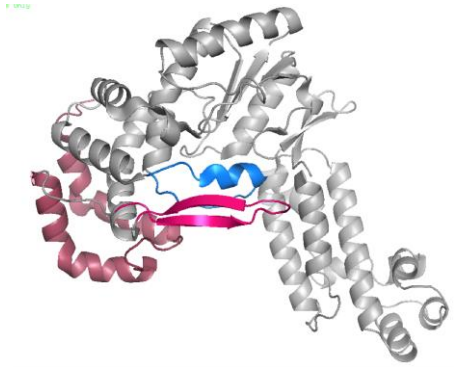
The science behind the enzyme

Innovation

Structure

The Pyle lab discovered this novel RT, solved its structure, and showed it is ultraprocessive.

Novel features



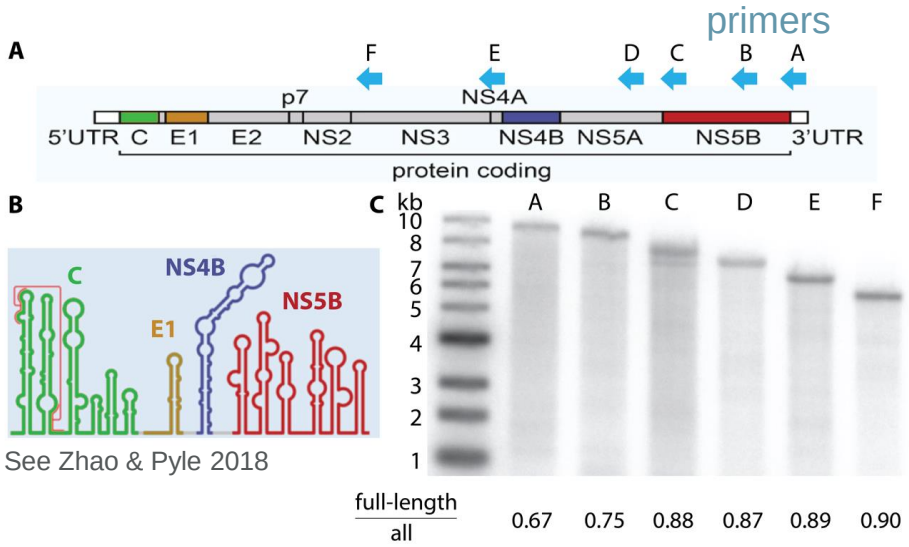
α- loop
processivity factor and “pin” for melting template structures

RT0 domain
holds RNA template strand in place with high affinity

β-hairpin
melts template structures it its path

Function

We put MarathonRT to the test by creating full-length cDNAs of the entire, highly structured hepatitis C genome (10 kb).



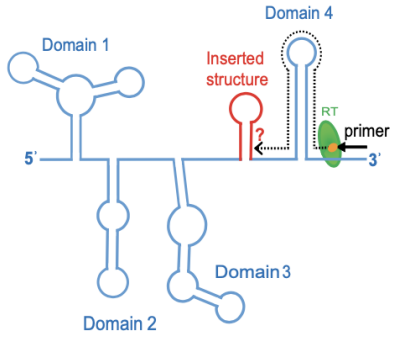
This novel RT architecture confers ultraprocessivity: MarathonRT can copy any RNA end-to-end

MarathonRT

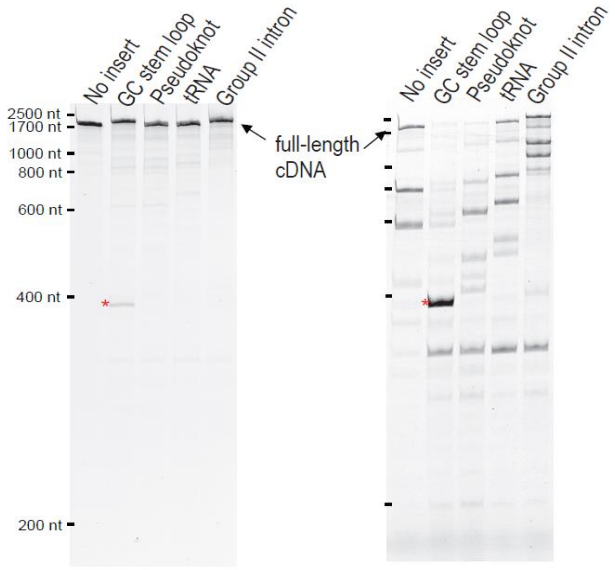
Specifications

MarathonRT outperforms competitors by powering through template structures at ambient temperature

Long, structured RNA template



RNA template with structural obstacles **Inserted** by design



MarathonRT **Superscript IV**

Only MarathonRT

- Copies entire kb transcripts in a single pass without falling off (single-cycle function)
- Unwinds RNA structures in its path, making it insensitive to RNA motifs and repeats in the template
- Maintains high reactivity at ambient temperature

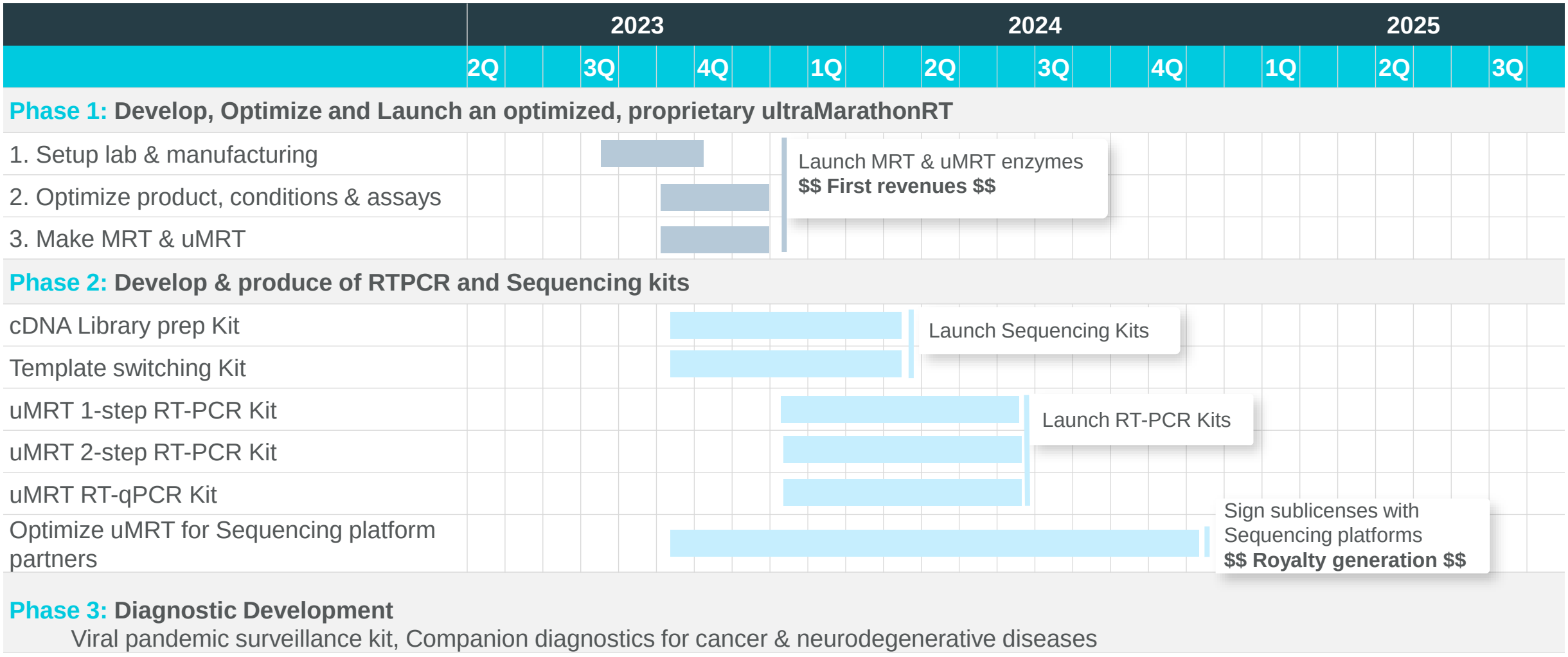
Applications

Sequencing:
Long read RNA-seq, single cell RNA-seq, spatial transcriptomics

Epitranscriptomics:
RNA modification detection

RNA Structure Determination:
Vaccine design

Multiple product platforms to launch in rapid succession



Better RNA Hardware from the People who Innovate with RNA

Anna Marie Pyle, PhD
Founder, SAB Chair
Professor of Molecular, Cellular and Developmental Biology and Chemistry at Yale; Howard Hughes investigator; Past-President of the RNA Society.

Li-Tao Guo, PhD
Co-Founder & Lead Developer
Associate Research Scientist at Yale, Leader of the MarathonRT development and innovation team.

Brent Graveley, PhD
Co-Founder, SAB Member
Chair of the Dept of Genomics and Associate Director of the Institute for Systems Genomics at Univ. of Connecticut.

Emmanuel Saliba, PhD
Co-Founder, SAB Member
Group Leader at the Helmholtz Institute for RNA-based Infection Research.

Ryan Muldoon
Co-founder, Director, CEO
President & CEO of RNAConnect.
Co-Founder of PrEP Biopharm Ltd.

Craig Crews PhD
Board Chair
Prof. of Molecular, Cellular and Developmental Biology at Yale; Founder of Arvinas, Proteolix, Siduma and Halda Therapeutics.

Spencer Glantz PhD
Director, SAB Member
Co-Founder and Head of R&D at Detect Inc, a viral diagnostic testing company.

Additional SAB Members:

Sigrid Nachtergaele PhD, Assistant Professor, Yale

Anthony Mustoe PhD, Assistant Professor, Baylor

Eric van Nostrand PhD, Assistant Professor, Baylor