Genomic expression

RNA Platform For Next Generation Cures

Mission: to save lives and make healthcare more effective

Vision: By analyzing **RNA** we can monitor **health**, detect **disease** and design next generation **cures**

STAGE: Commercial, growing 250% over last year

REGULATORY APPROVALS: Obtained (CLIA Lab)

By Gitte Pedersen, CEO and co-founder and member of ESIR2

Core Competencies

- **NUCLEIC ACID CHEMISTRY: Design new chemistries using nucleic acids (RNA/DNA) informatics and enzymes**
- **IT/INFORMATICS: Building regulatory compliant backend platforms to analyze massive amounts of data efficiently and make clinical sense og it**
- **UNDERSTANDING OF BIOLOGY: Deep domain knowledge in oncology**
- **REGULATORY: Operating a CLIA lab and experience with FDA EUA**

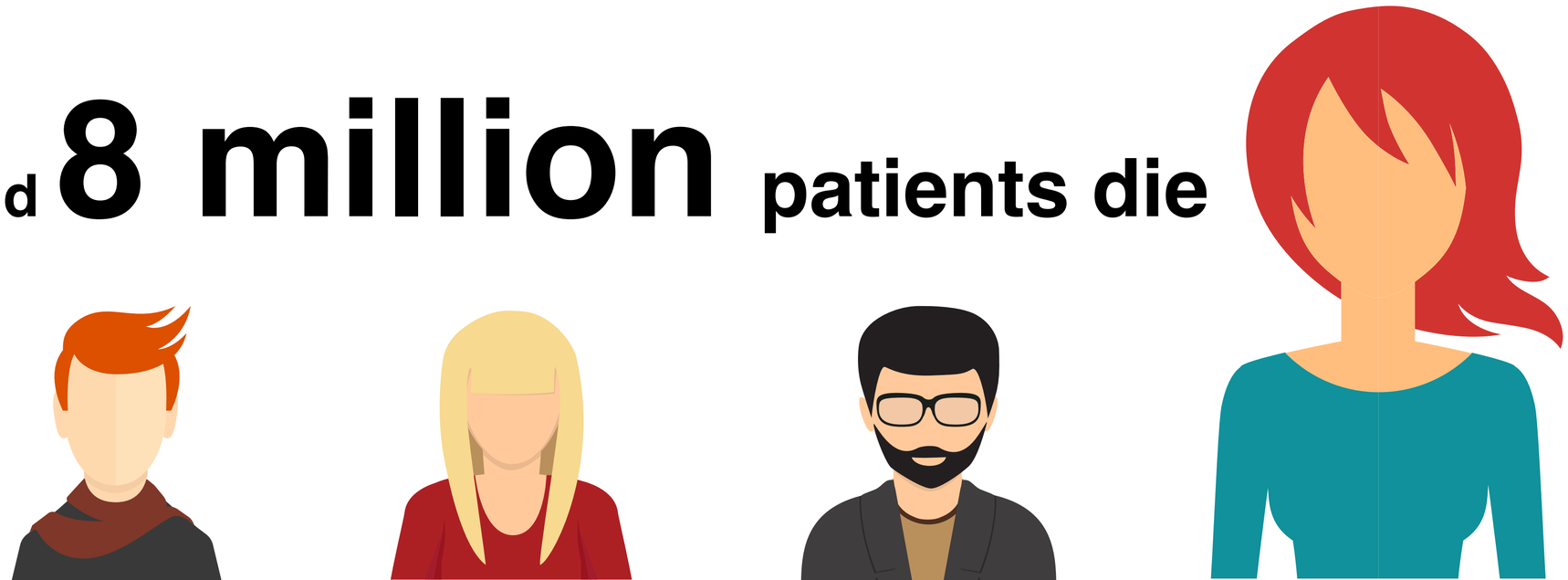
3 commercial product

1. COVID-19 PCR in saliva, NP and AN FDA EUA
2. OneRNA® Platform
3. BRACA in saliva, blood and tumor tissue

Standard of Care: Only **1 out of 4** cancer treatments prolong life while we spend

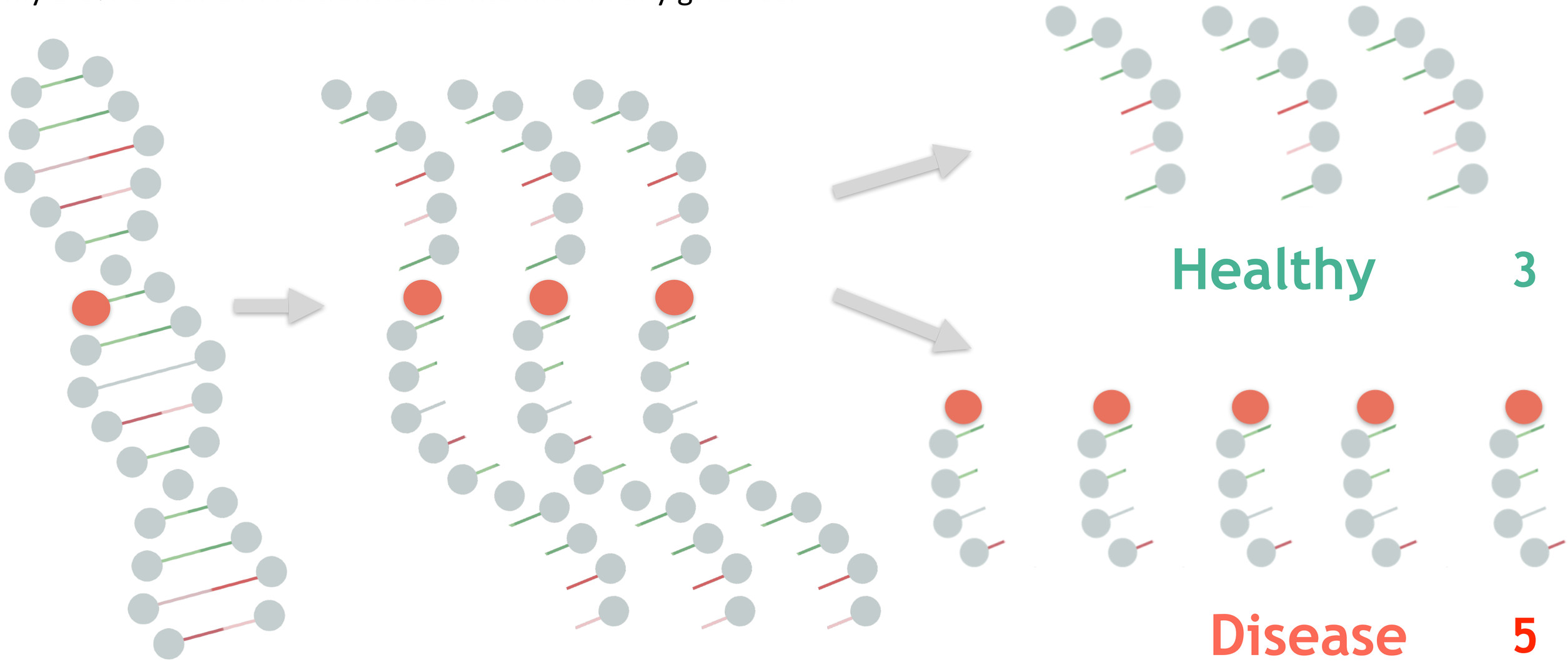
$100 billion on drugs

And 8 million patients die



DNA tell us what the cell *CAN* whereas RNA tells us what the cell *IS* doing

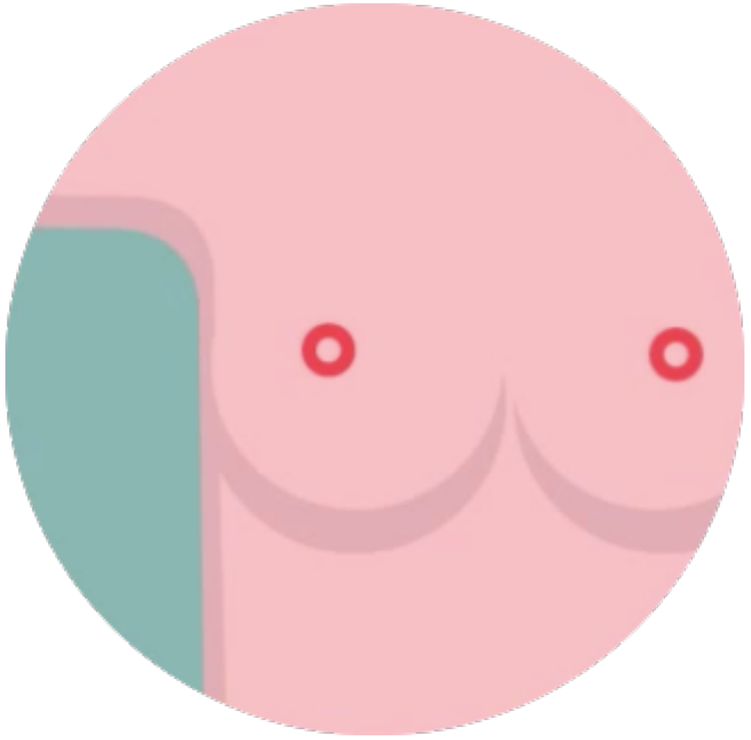
Only 2-3% of our DNA is translated into RNA in any given cell



DNA: Information storage

RNA: Information carrier - *quantitative*

Cancer is a disease caused by genetic changes



Program A = drug A

Program A = drug A

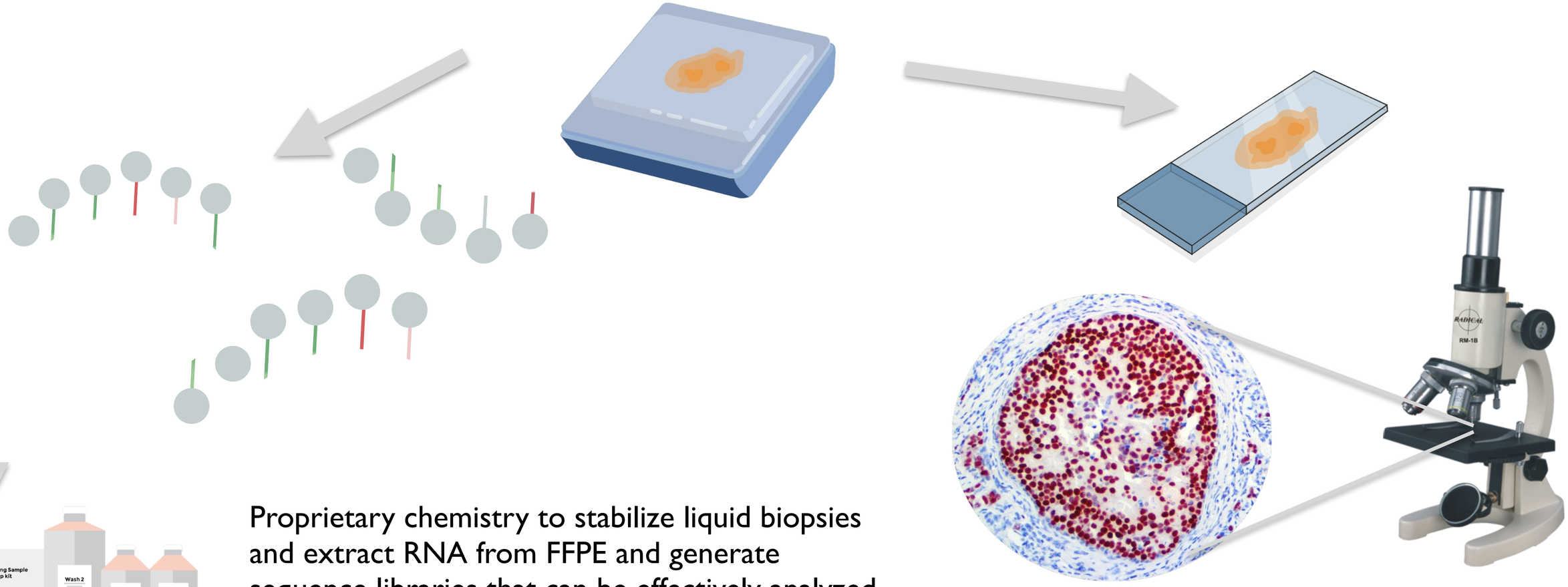
A drug developed in breast could work in lung

3 Barriers making RNA possible and actionable in real clinical samples

1. RNA is not stable in clinical samples
2. Quantitative -> Compare to reference samples
3. Identify treatment options based on RNA

1) RNA is destroyed in clinical samples

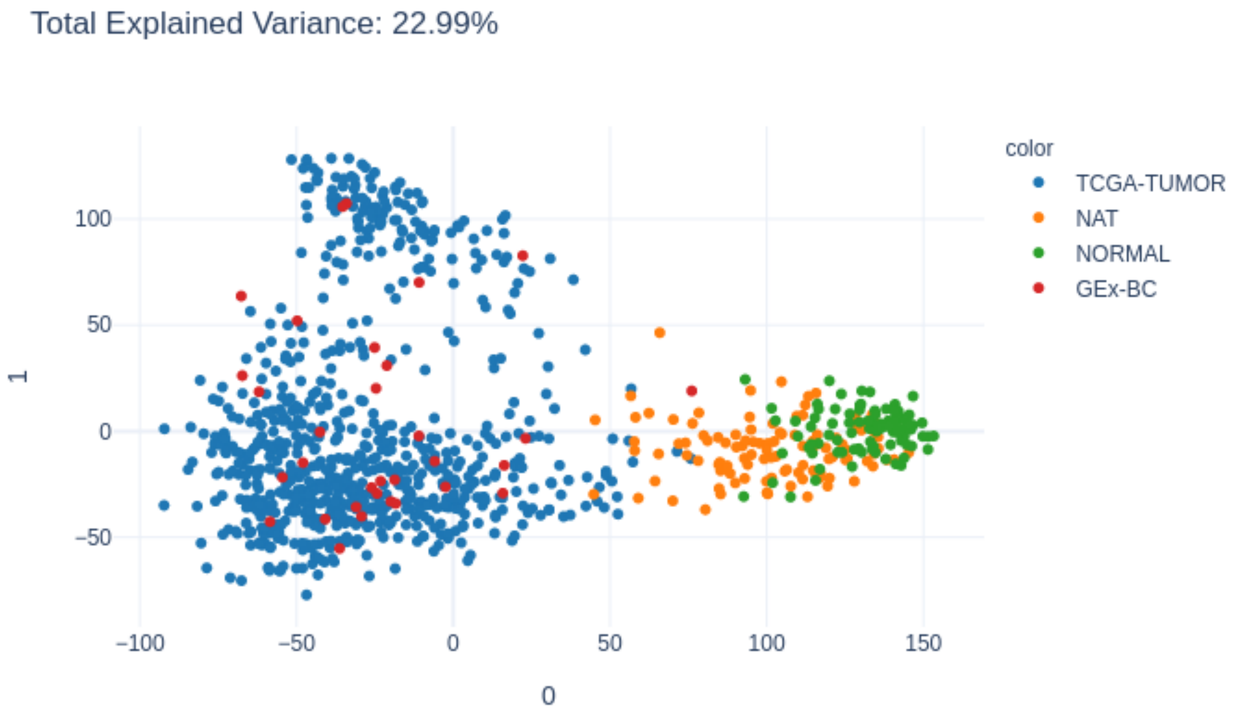
a) In tissue samples, because they are formalin-fixed and paraffin-embedded (FFPE) in order to provide the ability to slice the tissue and color cells to detect abnormal-looking cells
b) In liquid biopsies such as blood, saliva, urine and stool because of RNAses that naturally destroy it

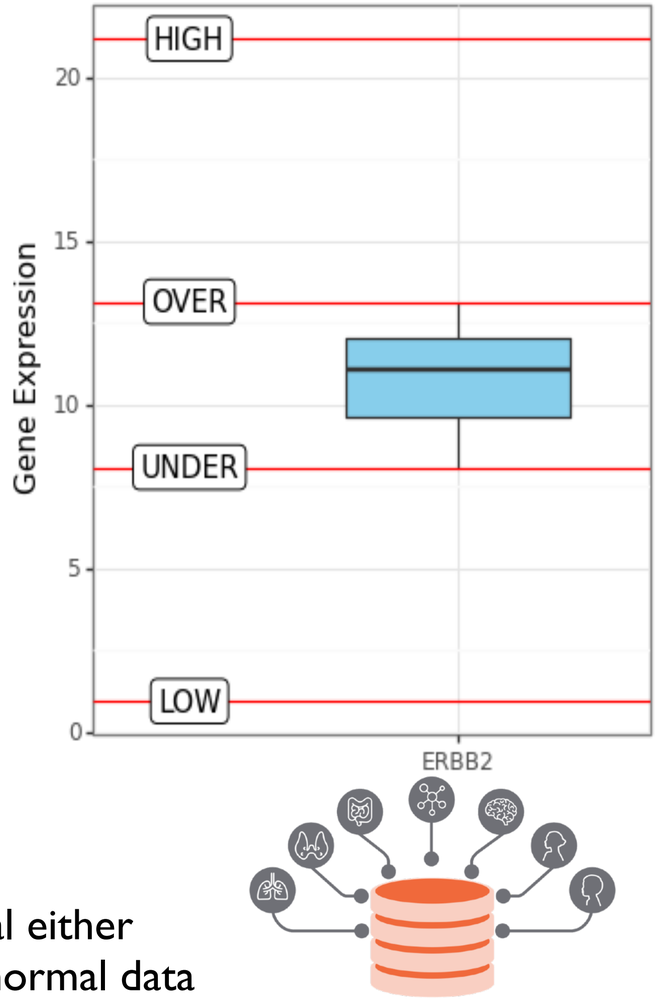


Proprietary chemistry to stabilize liquid biopsies and extract RNA from FFPE and generate sequence libraries that can be effectively analyzed and quantified

2) Comparing to RNA expression ranges in true normal samples

a) Adjacent normal is not normal - identification of pre-cancerous lesions and aberrantly expressed genes involved in tumorigenesis
b) Adjacent normal biopsy from same patient is not going to be adopted in the clinic as its a 2nd invasive procedure
- > Solution Comparing to a database of true normal either from GTEX + our own OneRNA normal data

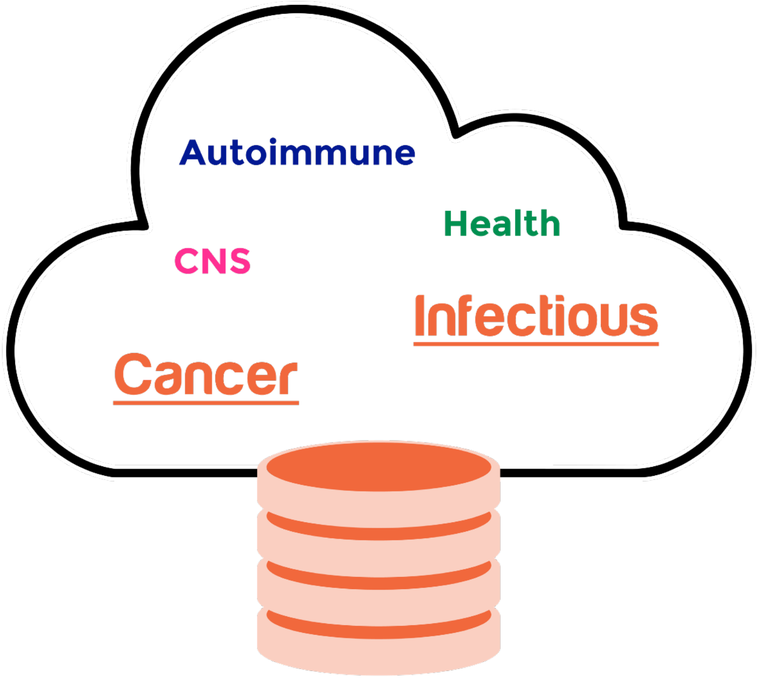




OneRNA® database of true normal either from GTEX + our own OneRNA normal data

Database of all FDA approved cancer drugs, targets, ligands and biomarkers

Proprietary database manually curated by PhD-level scientists using multiple sources.



Actionable genes are defined as genes that code proteins that:

1) Are direct targets of drugs,
2) Are ligands for the drug targets
3) Are treatment selection biomarkers listed on the FDA label

Our data are based on patient data. We do not rely in cell or animal data

OneRNA®

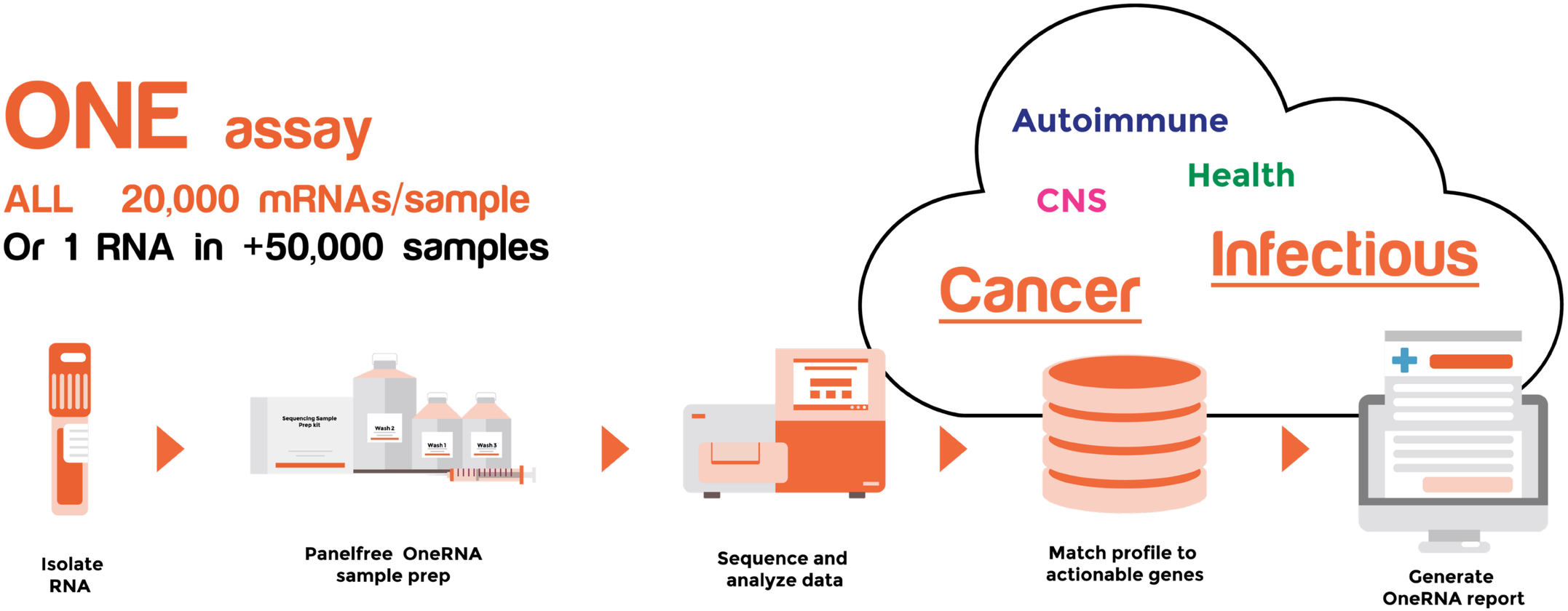
Exponentially scalable platform for Next Generation Cures

Genomic expression

ONE assay

ALL 20,000 mRNAs/sample

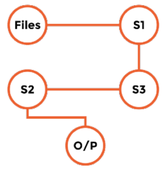
Or 1 RNA in +50,000 samples



By analyzing RNA we can monitor health, detect disease and design next generation cures

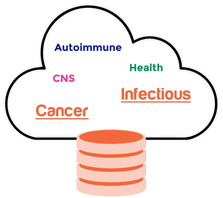
OneRNA® Technology Stack

Proprietary quantitative RNA-seq sample prep chemistry for in FFPE and liquid biopsies:
Clinically validated quantitative RNA-seq chemistry and bioinformatics pipeline that produces robust data in paraffin embedded tissue samples (FFPE) and FF (Fresh Frozen) samples. Reagents and kits to collect and stabilize RNA in self collected liquid biopsy samples. OneRNA® kit commercially available for FFPE.



Automated cloud- based data analysis pipelines:
Fully automated primary, secondary, and tertiary pipelines, including clinical report generation. Exponentially scalable and performed in compliance with HIPAA privacy and security standards.

Database of normal tissue expression ranges:
Databases of normal expression ranges in normal tissue. Aberrantly expressed genes are called by comparing data from one sample to healthy true normal tissue gene expression range. This approach eliminates the need for a second biopsy from patients, which would drive up cost and create friction in the implementation. Finally adjacent normal is no longer normal.



Database of gene expression biomarkers and targets for FDA approved drugs:
Proprietary database manually curated by PhD level scientists using multiple sources. Actionable genes are defined as genes that code proteins that (1) are direct targets of drugs, (2) are ligands for the drug targets, or (3) are treatment selection biomarkers listed on the FDA label.

Actionable Clinical report:
The OneRNA® report displays tumor gene expression levels alongside normal tissue gene expression reference ranges for aberrantly expressed genes that can be matched to approved drugs. Aberrantly expressed genes are grouped into virtual panels based on mechanism and/or target category.

Virtual Care Connection Platform
Access to doctors' and patients' data in the cloud, connecting the dots between the patient and care providers, aggregating data over time that allows the patient and physician to make better care decisions. Integrates with Electronic Medical Records (EMR).

Machine Learning Algorithms:
Combining aberrantly expressed genes with clinical and patient data to produce algorithms of probability for response to standard of care and in the future also novel approached to intervention.

OneRNA

20,000

Exponentially scalable - tissue and disease agnostic
No guessing and future proof, *AI enabled*

↓

5 actionable markers in 100% of the patients

↓

improved outcome for ALL

OneRNALiquid TBD

<>

DNA panels

500

Limited to cancer
Outdated before its validated
Fail to predict response to immune therapy

↓

1 actionable marker in 40-80% of the patients

↓

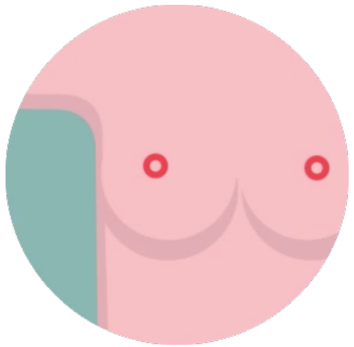
improved outcome for only 7-16%

DNA Liquid **25 %** of early-stage cancers detected

Repurposing of drugs - on an individual patient bases

OneRNA® typically identify 5 already approved drugs in 100% of the patients

A paradigm shift from the static standard of care model to a dynamic truly Individualized treatment



ONE Disease

Her2

ONE Marker

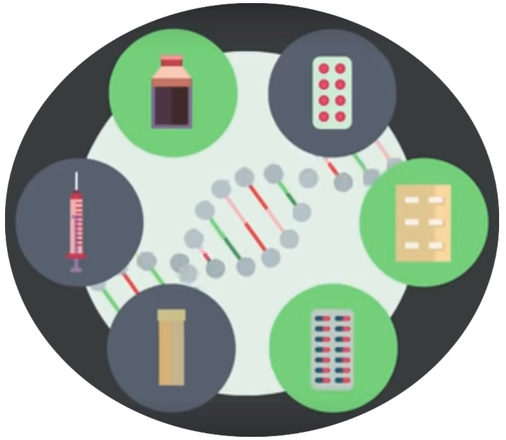
50%

20%

ONE Drug

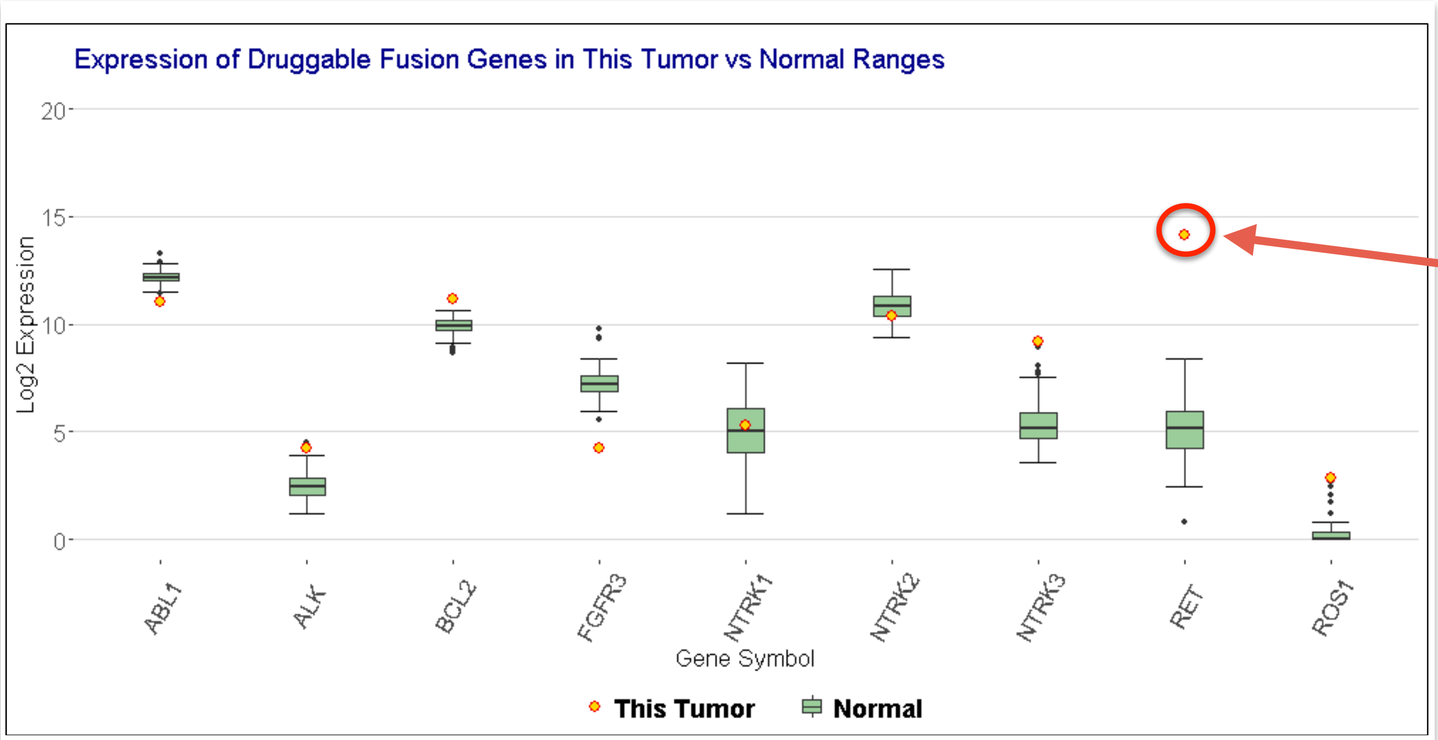
ONE Patient

Many Markers



Multiple Treatments

Saving Lives NOW OneRNA Patient treated at Memorial Sloane



Gene(s)	Relevant Therapies	Comments
NTRK3	Larotrectinib	Larotrectinib is approved in any solid tumor harboring a NTRK fusion
RET	LOXO-292, BLU-667	LOXO-292 and BLU-667 are being studied in patients with RET fusion-positive solid tumors including medullary thyroid cancer (NCT03157128, NCT03037385)
ALK, ROS1	Alectinib, crizotinib	Although ALK and ROS1 are overexpressed, their absolute count levels are still very low; thus no treatment suggestions are being made based on these genes

Patient has **Metastatic Thyroid cancer** with very few treatment options.

OneRNA® identified **RET over expression**

LOXO had a **drug in phase II targeting RET** now FDA approved (Retevmo (selpercatinib -LOXO-292)

Patient is treated at Memorial Sloane Kettering and entered this trial

Patient is responding and continue to be in remission **+3 years now**

Pharma Partnering Opportunity

1) Development of Companion Diagnostics AI (CDx)

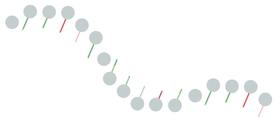
Saving +$1B by de-risking, reducing trial size and enabling at home collected liquid biopsies - 80% of clinical studies fail due to lack of enrollment

2) At home collected liquid biopsies enabling decentralized studies

Faster enrollment, more datapoints, reaching community hospital where 80% of patients are treated

3) Expanding label on drugs & repurposing of drugs

Most drugs are approved only for one disease and one tissue type



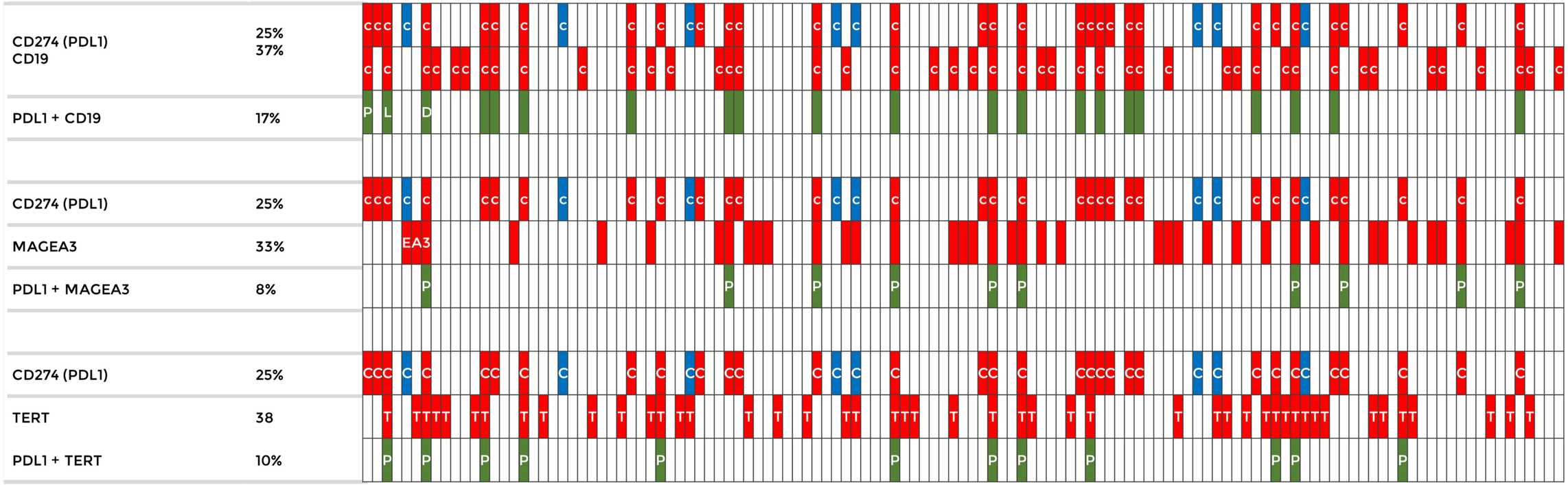
4) Designing Next Generation Personal Cancer Cures

OneRNA design of mRNA vaccines from code to drug in less than 7 days (In Development)

Article on LinkedIn on #1 here https://bit.ly/OneRNACDxBlog

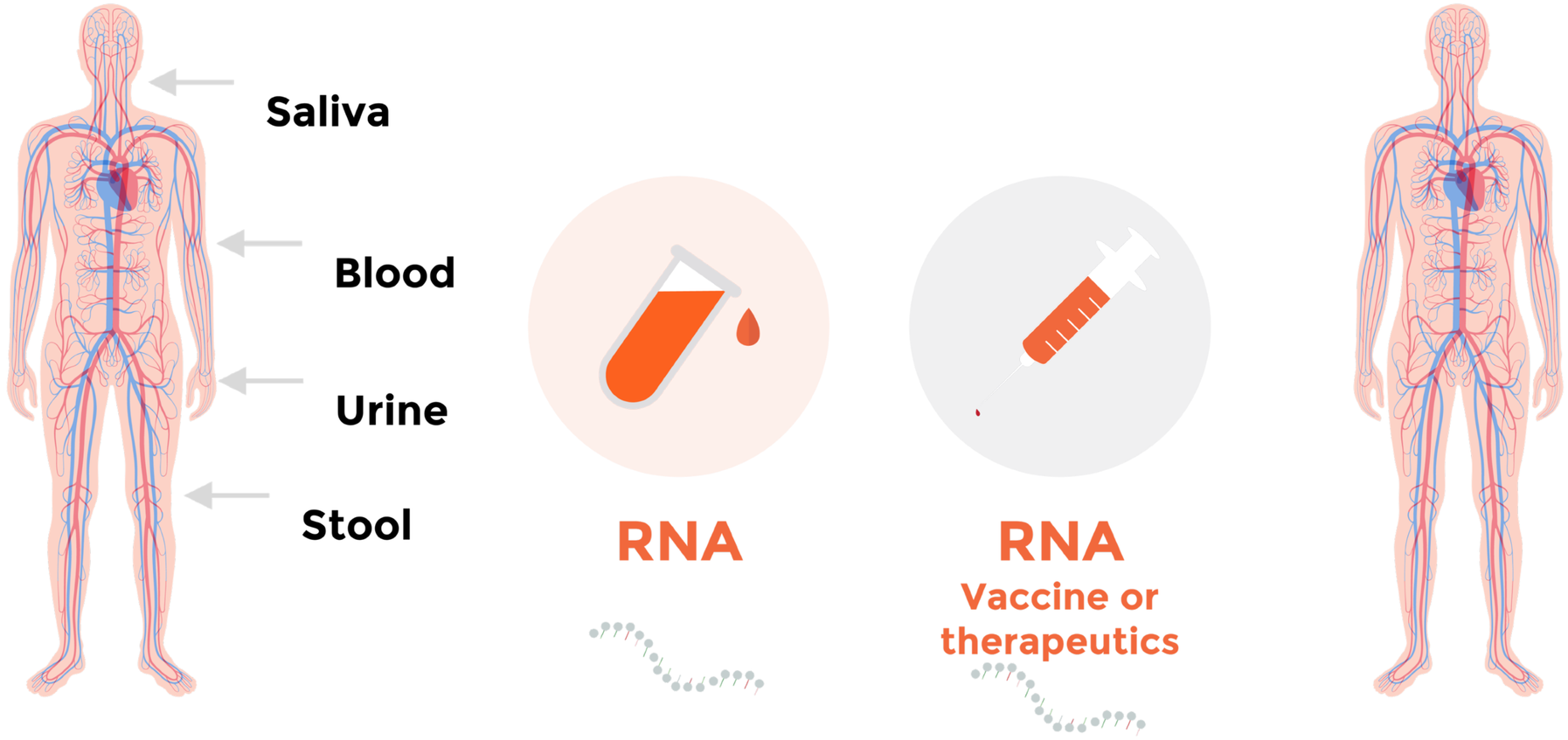
In-silico design of combinatorial clinical studies leveraging existing datasets

Using aberrantly expressed RNA as inclusion criteria can address significant (+20%) of a patient population in a trial design with one checkpoint + tumor antigen, thus with 4 drugs. This approach is impossible using mutations due to the single digits penetration of DNA alterations

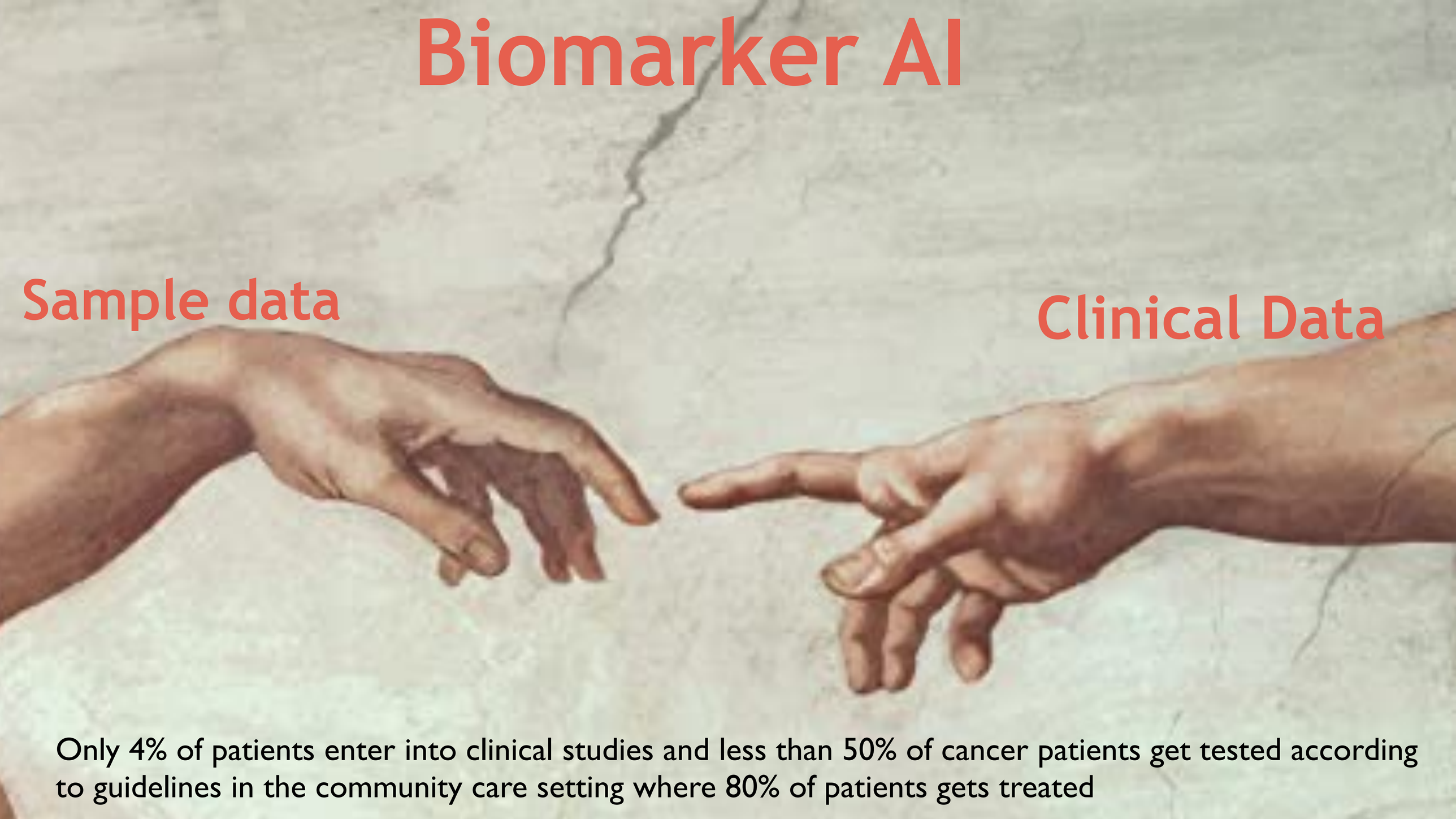


In conclusion: Using an RNA-based high-resolution biomarker AI platform enables clinical learning that allows the data to be utilized to discover new targets and design better clinical studies and drugs in the future

From RNA code to Approved mRNA Vaccine in 12 month



Biomarker AI



Only 4% of patients enter into clinical studies and less than 50% of cancer patients get tested according to guidelines in the community care setting where 80% of patients gets treated

Algorithms based on RNA *quantification* is already adopted in the clinic

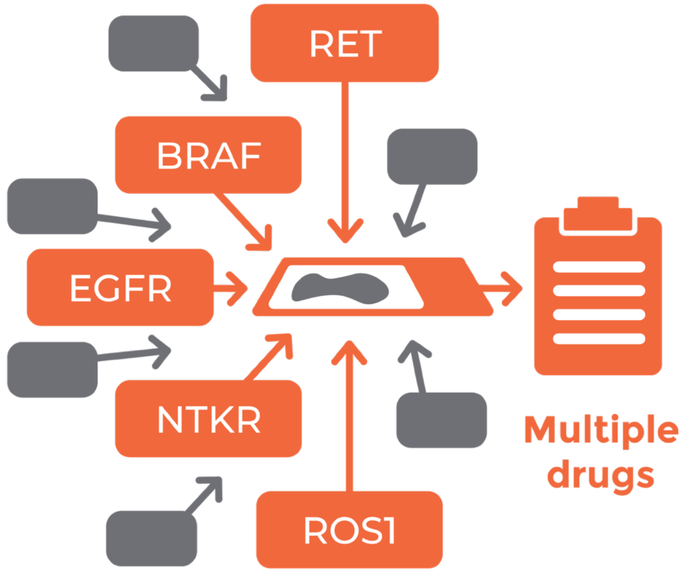
OneRNA® detects ALL mRNA in

ONE assay

Thus these diagnostic
Products becomes algorithms
On the OneRNA® platform

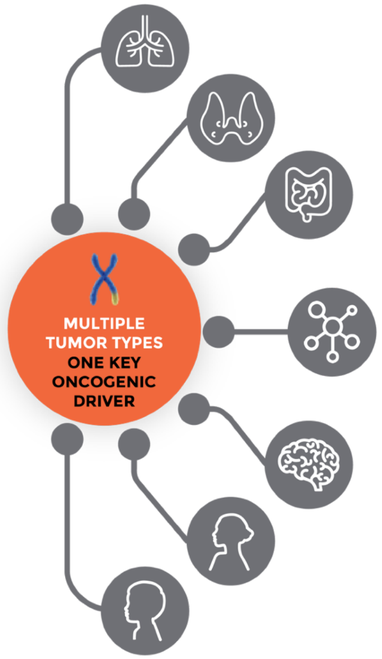
Binary Relationship Between Biomarker and Drug Rapidly Changing

One Assay multiple drugs



Example OncomineDx

One drug multiple cancers



Larotrectinib for solid tumors with NTRK gene fusions

Biomarker in the clinic enables:

Reduction of trial size (orphan status?)

Faster enrollment and completion

Increase approval rate/ risk reduction

Combined $1 Billion in Savings

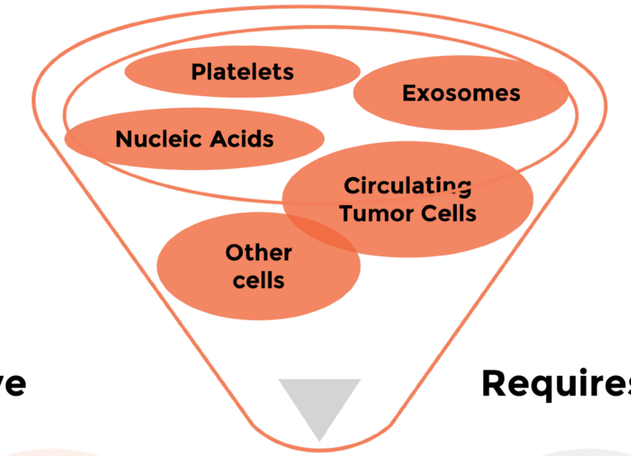
Effective Cost Per Successful Oncolog Drug w/CDx

$1B in cost reductions from reduced trial size and improved approval rates

Source: ARK Investment Management LLC[2]

Sample types and enrichment methods

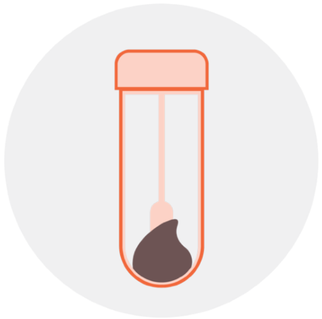
Enrichment methods



Self-collected samples, non-invasive

Requires a visit to the lab - invasive

Saliva



Stool

Urine

Cerebrospinal Fluid

Blood

OneRNA® CLIA validated liquid biopsy collection kits and proprietary RNA stabilizers

Tracking everything in the cloud from order to report

- Health 2.0, distributed diagnostics enabling effective virtual care and monitoring of health
- Decentralized, responsive, digital-first and consumer-centric
- HIPAA and CLIA compliant

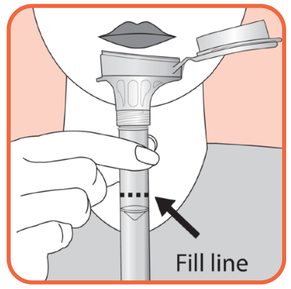
Purchase

Register an account with us

Buy a single test
or many to get discounts

Saliva collection kits will be
Sent to your home

Spit in a tube



Collect the sample

Collection kit includes
everything you need

RNA is stabilized at sample Collection

Mail Back

Register sample online prior to shipping

Ship overnight and track it on our platform

Receive Results

Receive an email notification when results are ready

Log in to download your report in a HIPAA Compliant manner

Regulatory CDx co-development path

Biomarker

Biomarker Test

Source or Materials for Measurement

- Subject
- Specimen

Assay

- Supplies
- Equipment
- Software
- Instructions

Method/Criteria for interpretation

Biomarker Measurements

Qualified Use in Drug Development

Analytical Validation

Establishing that the performance characteristics of the biomarker test are acceptable for the proposed context of use (COU)

Clinical Validation

Establishing that the correlation between the biomarker and the outcome of interest are acceptable for the proposed COU

Publications at Society for Immunotherapy of cancer

2021 SITC Poster: "Novel RNA-seq Platform Improves Patient Outcome in Clinical Oncology and enable implementation of AI in the clinic". https://bit.ly/SITC2021OneRNA. The platform is an end-to-end analysis of RNA-seq data to actionable report and can also work with 3rd party RNA-seq data.

2022 SITC Poster: "Novel RNA-seq Platform Enables Repurposing of Approved Drugs in Rare Cancers, Improving Outcomes". Anecdotal outcome data from our OneRNA® platform in rare cancers download here https://tinyurl.com/2022SITCRareCancer

2022 White paper: "Increase clinical success using novel high-resolution biomarker strategies and AI". How to leverage the OneRNA(R) platform to de-risk clinical programs. Download a draft here

In draft from:

1) **"What is normal - validation of RNA sequencing pipeline data from various sources"**. We demonstrate that adjacent normal from cancer patients are no longer normal tissue rendering it unsuitable for establishing normal reference ranges. We also illustrate the steps to validate the bioinformatics pipeline for clinical practice and the development of novel tools required to analyze a single sample to generate actionable insight.

2) **"Clinical validation of novel RNA platform leveraging next-generation sequencing to quantify RNA expression in clinical formalin-fixed and paraffin-embedded tissue samples (FFPE)"**. Comparison of Truseq and OneRNA® chemistry in FFPE and FF using comparative informatics pipelines and concordance to FF and standard IHC assays.

Awards + $6.5M in grants and our collaborators

1 RNA detected
+50,000
samples/run
(XPRIZE semi
finalist)

XPrize Semifinalist Targets 300 Million Tests Per Day With Scalable COVID Self-Test

Collaborating with 180 CLIA labs
Scaled COVID19 testing in saliva
to 1 mill/day umbrella EUA

Seasoned Management team with **Start-Up RNA**

Gitte Pedersen, M.Sc.
CEO & Co-founder
- **Big Biotech +$1B deals**
- **MSc Chemical Engineering**
- **Advisor in ESIR2**

Morten L. Pedersen, Ph.D.
CTO & Co-founder
- **Inventor NGS Chemistry**
- **PhD in Genetics**

Tanya Kanigan, Ph.D.
CAO (Chief Analytics Officer)
- **Postdoc MIT**
- **Cofounded BioTrove**
- **Co-Inventor of OpenArray**
- **Diagnostic Big data AI**

Sugganth Daniel, MD, PhD
Medical Director
- **Foundation Medicine**
- **Quest**
- **Invite**

Jesper Zeuthen, D.Sc.
CMO
- **The Danish Cancer Society**
- **Co-founder of GenMab & Dandrit**
- **Leader in immune therapy**
- **Raised > $650MM for Bankinvest**

Bill Southworth
VP Data,
- **MIT, creator of products**
- **Coder**
- **CEO and VP public companies**

Board/Investors

- **Dan Adams**, Ex CEO Biogen, Founder/ Chairman Protein Sciences exit to Sanofi $740M
- **Geert Cauwenbergh**, Spun Barrier Therapeutic out of JnJ and IPO, RNA therapeutics. RNA Therapeutics
- **Melina Fan**, Harvard PhD, CSO and cofounder Adgene, Biobank (observer)
- **Kim Tennican,** co-founder Seattle Women's Impact Fund, Principal and Owner Berntson Porter & Company, PLLC (observer)
- **Kirsten Dinesen**, Founder and CEO Front Page IR and PR Company

Scientific advisory board with the Principal Investigators from our clinical studies

Genomic Expression Location: Beverly MA

62	448	$481 M	25
Companies	Jobs Created	Grants & Equity Raised	Graduates