

September 2024

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Challenges in cancer

- **90% of cancers could be effectively treated** if diagnosed in the earliest stage of disease. This is where our AI-enabled early diagnostics, oncology vaccine and upcoming test and potential treatment replacement for chemotherapy come into play. Approximately half of cancers are diagnosed late at Stage 3 and Stage 4, and only then with painful, time consuming and expensive diagnostics methods such as tissue biopsy and multiple imaging techniques.
- **60% of cancers are not effectively treated** resulting in the use of expensive and toxic chemotherapy which only allows the cancer to spread while damaging the immune system and health of the patient, often resulting in serious illness and, ultimately, death or a shorten lifespan.

Opportunities

Al-powered early diagnosis of cancers has the potential to increase patient quality of life while reducing premature death and the economic burden to healthcare systems.

Potential

Early diagnosis of cancer can result in a \$200B market opportunity.*

Source * https://www.ark-invest.com/articles/analyst-research/cancer-diagnostics

MULTIPLIER EFFECT DRIVES BUSINESS OPPORTUNTIES



Explainable AI Engine

Al system agnostic, trusted and versatile. Capable of handling data from multiple sources.

Diagnostics

Early diagnosis, recurrence and response to treatment. Can be applied to liquid biopsies.

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Therapeutics

A universal off the shelf approach for various indications. Allowing non-toxic universal treatment.

THE CLINICAL IMPACT IS CRYSTAL CLEAR

Lifespan extension of cancer patients



Source

https://seer.cancer.gov/statistics

 While cancer treatment has improved significantly in past years, the overall improvement in patient QoL has only seen linear improvements.

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- Since 1975-today, therapy advances have added ~1.5 years of life per decade and average lifespan of cancer patients has increased by ~5.5 years.
- Over half of this advance is courtesy of technologies that enable diagnosing cancer early. This has led to life expectancy outcomes that otherwise wouldn't have occurred until 2035.
- Liquid biopsy-based diagnostics can accelerate the life expectancy tremendously at a fraction of the costs of new therapeutic advances.

network/explorer/application.html?site=1&data_type=1&graph_type=2&compareBy=sex&chk_sex_3=3&chk_sex_2=2&rate_type=2&race=1&age_range=1&hdn_stage=101&advopt_precision=1&advopt_show_ci=on&hdn_view=0&advopt_show_ap

https://prevention.cancer.gov/sites/default/files/2023-02/Liquid-Bx-Day2-07-Canzi.pptx

 <u>https://www.ark-invest.com/articles/analyst-research/cancer-diagnostics</u>

THE TIMING IS RIGHT



Source: National Human Genome Research Institute (NHGRI) Genome Sequencing Program; BCG analysis.

The timing is right for reduction as both WGS costs and also the acceleration of GPU power and AI powered super computing allows the data sequenced from WGS to be analysed more deeply which would not have been possible a few years ago. Both of these elements together are what are driving a new era of Healthcare Diagnostics.

New technology has **dramatically** reduced costs of genetic testing and opened new frontiers for molecular testing. The cost of whole genome sequencing (WGS) dropped from \$2.7 1 million in 1990 to \$300 in 2020.2

- Liquid biopsy in oncology is the biggest frontier for application of WGS based diagnostics.
- The current ceiling for potential reimbursement is sub-\$1,000/ liquid biopsy test. Reaching that threshold will open up a €150B market. 3
- Tremendously active market → 2 serious deals in recent years such as Quest acquiring Haystack for €450M.

Sources:

- . https://biology.mit.edu/the-human-genome-project-turns-20-heres-how-it-altered-the-world/#:~:text=The%20original%20project%20cost%20%242.7.over%20a%20two%2Dyear%20span.
- https://emea.illumina.com/science/technology/next-generation-sequencing/beginners/ngs-cost.html
- 3. https://prevention.cancer.gov/sites/default/files/2023-02/Liquid-Bx-Day2-07-Canzi.pptx
- 4. https://www.bcg.com/publications/2024/how-genomic-sequencing-may-change-advanced-diagnostics

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Breaking Through High Predictive Value Testing Requires Innovation that RenovaroCube is Tackling Now

Cancer-related ctDNA to background cfDNA



The main challenge

Detecting mutant-ctDNA in healthy-cfDNA is the main challenge to early detection

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Needle-in-a-haystack

VAF¹ quantifies the 'needle-in-a-haystack' problem and its proportional to tumor size

1. VAF = Variant allele frequency.

Source: The Exploitable Genomics of Cancer: Earlier Cancer Detection Part II - ARK Invest https://prevention.cancer.gov/sites/default/files/2023-02/Liquid-Bx-Day2-07-Canzi.ppt

MAKING BLOOD COUNT FOR MORE

A Vial of Blood Delivers a Wealth of Interpretable Clinical Information

Advanced Genomics

- One routinely applicable assay
- Multi-signal & Multi-Omics
- From a single vial of blood
- Utilizing Oxford Nanopore technology

AI Powered Data Analysis

- 10.000 biomarkers
- 13 tumors validated in-silico
- Developing collaboration with NVIDIA for supercomputing and open AI architecture
- Platform is agnostic
- Differential diagnostic report



 Using samples obtained from ongoing collaborations, solid proof-of-principle has already been obtained.

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- Our multi-omics models clearly show an accuracy benefit over single omics analysis. Accuracy of 0.84 for multi-omics vs 0.7 using single omics.
- Future **goal to reach accuracy of 0.95-0.99** in order to deliver clinically meaningful NPV (Negative Predictive Value) and PPV (Positive Predictive Value).
- More sophisticated Deep Learning models being developed.

What's needed:

- Training our multi-omics models on data from up to 1000 new samples with matching clinical data
- Access to aforementioned 1000 samples.
- Validation in a prospective clinical trial

PATIENT JOURNEY

TREATMENT CYCLE

- Early Detection: Identifying cancer at an initial stage when it is more treatable and manageable.
- **Treatment Selection**: Choosing the most effective therapy based on the specific characteristics of a patient's cancer.
- Treatment Monitoring: Continuously assessing a patient's response to therapy to adjust treatment plans as needed.
- **Recurrence Screening:** Regularly testing patients to detect cancer recurrence or emergence of new cancers at an early stage.



LIQUID BIOPSY

Measuring the level of cell tumour DNA with recurrent liquid biopsy sampling throughout entire patient journey.



PATIENT JOURNEY VS PLATFORM

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PLATFORM OVERVIEW

PLATFORM OVERVIEW

Transform raw molecular data from patient samples into clean, analyzable formats using advanced sequencing and alignment technologies.

> Utilize unique algorithms and multiomic pipelines to identify biologically relevant cancer biomarkers.

Employ sophisticated machine learning models to predict cancer presence, origin, and stage, based on extracted biomarker features.

Provide an interactive interface for visualizing data, generating clinical reports, and gaining actionable insights across various omic layers and biomarkers.



AI FACTORY

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Feature Store

Centralized repository that organizes and stores extracted features from the processed data, making them readily available for machine learning tasks.

ML Training

Utilize machine learning algorithms to train models on the stored features, optimizing them to accurately predict cancer in patient samples.

Inference

Apply trained models to new data to generate predictions and insights for clinical decisionmaking.

PRODUCT DEVELOPMENT

VALUE CREATION | LUNG CANCER PLAN



ROADMAP & DELIVERABLES



MARKET OVERVIEW

HIGH POTENTIAL MARKET OPPORTUNITY THROUGHOUT PATIENT CARE CONTINUUM



New Approach to Market Development

Broad Base Assessment	Precision Diagnostic	Precision Therapy	Precision Monitoring / Adapting	Definitive Cost Savings / Effective Recovery
Personalized			1	



REFERENCES

Precision Medicine Market: https://www.precedenceresearch.com/precision-medicine-market

Al in Oncology Market: https://www.marketresearch.com/Grand-View-Research-v4060/AI-Oncology-Size-Share-Trends-34337452/

Liquid Biopsy Market: https://www.precedenceresearch.com/liquid-biopsy-

market#:~:text=The%20global%20liquid%20biopsy%20market.forecast%20period%202023%20to%202032

A SEGMENTED, \$100B+ MARKET IS OUR OPPORTUNITY

U.S. Liquid Biopsy Market Opportunity By Application



Early Detection: \$65B

30M *lower-risk* patients, ~\$1,000/test
35M *high-risk* patients, ~\$1,000/test
Therapy Guidance: \$2.1B
0.7M patients, ~\$3,000/test

Monitoring & Surveillance: \$45B

15M patients (survivors), ~\$3,000/test

Note: price per screening test may vary significantly across indications at stages. Market estimates are conservative Sources: GRAIL S-1, Guardant Health Annual Report, SEER Database, ARK Invest. https://prevention.cancer.gov/sites/default/files/2023-02/Liquid-Bx-Day2-07-Canzi.pptx

COMPETITION

WHERE IS THE MARKET GAP?

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Source: company websites, investor relations reports and scientific publications, 'Integrating liquid biopsies into the management of cancer' (Nature) https://prevention.cancer.gov/sites/default/files/2023-02/Liquid-Bx-Day2-07-Canzi.pptx

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WHERE IS THE MARKET GAP?





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VALUE CREATION PLAN



Q	3 2024	Q4 2024	Q1 2025	Q2 2025	Q3 2025	Q4 2025	Q1 2026	Q2 2026	Q3 2026	Q3 2027	Q1 2028	
	•	•	•	•	•	•	•	•	• •	• •		
		OWN CLIA LAB ESTABLISHMENT				SEQUENCING & BIOINFORMATIC SERVICES PIPELINE						
	L	Cash out Mileston and servi	tflow = €2M e achieved = Ow ces to external pa	vn lab for sequencing rties	2	Cash infl €2,5M/yea	ow = €0,6M in 2028 onwards	2025 increasing to				
Proof-of-principle PRODUCT 1 PROOF-OF-CONCEPT (>1000 sample and validation) PROD		T (>1000 samples lidation) PRODUC	nples used for training ADUCT 1		ASSAY DEVELOP	ASSAY DEVELOPMENT + PARTNERING DEAL PRODUCT 1			CLINICAL VALIDATION PRODUCT 1			
	Toot for ro	Cash out Mileston Inflection	flow = €10,6M e achieved = NPV n point = Multi-om	and PPV of >95% hics model validated		Cash outf Milestone ready for d Inflection lab in US a	ow = €3,5M + Ope achieved = Cor eployment in atlea point = Partnerin nd EU e.g. Labcor	ex mmercial LDT assay ast 2 geographies ng deal with a CLIA p		Cash inflow = -€12M via LDT sale -€75M via LDT sale Milestone achier validation in a larg Inflection point = -Regulatory appro -Commercial scale	es in 2026 es in 2030 ved = Prospective e clinical cohort val in EU and US e-up ensued	
prediction in receiving surgic	lung can cal resectio	cer patients		Proof-of-princ PRODUCT	iple 2	PR	OOF-OF-CONCEF or training and va	PT (>1000 samples u alidation) PRODUCT	sed 2	ASSAY DEVELO VALIDATION	PMENT + CLINICAL FOR PRODUCT 2	
-PRODUCT 2 = Test for cancer								PRODUCT 3 deve	lopment			
cancer patients										PRODUCT 4 deve	lopment	

THANK YOU