circio

Disruptive circRNA technology for genetic medicine

Dr. Erik Digman Wiklund - CEO

Redeye Fight Cancer Event 24 January 2024

Circio is developing a unique portfolio of cancer vaccines and next generation RNA therapeutics





- Targets KRAS mutations, found in 30% of all cancer patients
- Clinically validated target, both by industry and academia
- Potential upcoming USD 3m milestone from Chinese partner





- Circular RNA (circRNA) is a **next generation mRNA format**
- Potential to disrupt the genetic medicine and vaccine fields
- Versatile platform with broad commercial opportunities

KRAS cancer vaccine program

The RAS gene is mutated in 30% of all cancers

Frequency of RAS mutations

Global cancer incidents per 10,000 (xx) = no. of cancer patients



- RAS is the most frequently occurring cancer driver mutation
- RAS is a clinically validated shared neoantigen
- RAS mutations likely to become a future **"genetic marker" indication**

Fernandez-Medarde; RAS in Cancer and Developmental Diseases; Genes & Cancer 2011

Phase 1 study completed with TGO1 cancer vaccine in pancreatic cancer

Pancreatic Cancer chemotherapy combination

> Phase 1 post-surgery *n = 32 patients*

British Journal of Cancer

www.nature.com/bjc



ARTICLE

Clinical Study

TG01/GM-CSF and adjuvant gemcitabine in patients with resected RAS-mutant adenocarcinoma of the pancreas (CT TG01-01): a single-arm, phase 1/2 trial

Daniel H. Palmer^{1,2}, Juan W. Valle ^{3,4}, Yuk Ting Ma^{5,6}, Olusola Faluyi², John P. Neoptolemos¹, Trine Jensen Gjertsen⁷, Berit Iversen⁷, Jon Amund Eriksen⁷, Anne-Sophie Møller⁷, Anne-Kirsti Aksnes⁷, Robert Miller⁷ and Svein Dueland⁸

- TG01 targets seven different RAS mutations in parallel
- Mutant RAS immune response detected in 94% of patients
- Six month survival benefit vs. chemotherapy

TG01 drives robust anti-RAS T-cell immune responses

CD4+ T-cells

mutRAS specific CD4+ T-cells isolated from vaccinated patient





mutRAS specific CD8+ T-cells isolated from vaccinated patient



CD8+ TILs

mutRAS specific CD8+ T-cells isolated from the tumor of vaccinated patient

The same CD8+ T-cell clone found both in circulation and in the tumor



TG01 RAS immune responses were associated with six month survival benefit in pancreatic cancer



Time to overall survival (months)

Cancer vaccine data presented at ASCO 2023 provides external proof-of-concept for KRAS vaccination

AMPLIFY-201 Waterfall Plot: Biomarker Reduction/Clearance



- O Product: ELI-002 KRAS vaccine
- KRAS 12D + 12R mutations only
- Monotherapy only, no PD1 combo



circio

Product: TG01 KRAS vaccine O

- Covers 7 KRAS mutations •
- Monotherapy & IO combinations •

Next steps: TGO1 program expanded into multiple cancer settings

Pancreatic Cancer chemotherapy combination

> Phase 1 post-surgery *n = 32 patients*

Multiple Myeloma monotherapy Phase 1 post 1L treatment *n = 20 patients*

Pancreatic Cancer PD-1 double combination

> Phase 1/2 post-surgery *n = 24 patients*

Lung & Pancreatic Cancer triple combination CD38/PD1

Phase 2 Immunotherapy resistant tumors *n = 54 patients* Sponsored by:



THE UNIVERSITY OF KANSAS Cancer Center **agenus**



Georgetown University (^{III} Bristol Myers Squibb[™]

Completed trials 🚽 Ongoing Trials

TGO1: Additional opportunity in China

Pancreatic Cancer chemotherapy combination

> Phase 1 post-surgery *n = 32 patients*



- License option for TG01 in China
- IND-review in process for two clinical studies in China
- USD 3m milstone payable upon IND approval





RNA financing has flowed from mRNA towards circular RNA during 2021-23



Source: BioEquity Note: Other includes ASOs, saRNAs and tRNA private financing deals

Circular RNA (circRNA) is a novel disruptive RNA format



Circio leadership established the circRNA field



 THE EMBO JOURNAL
 EMBO Press
 30 September 2011
 922 citations

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miRNA-dependent gene silencing involving Ago2mediated cleavage of a circular antisense RNA

Thomas B Hansen, Erik D Wiklund, <mark>J</mark>esper B Bramsen, Sune B Villadsen, Aaron L Statham, Susan J Clark, Jørgen Kjems

nature reviews genetics

2,291 citations

Review Article | Published: 08 August 2019

The biogenesis, biology and characterization of circular RNAs

Lasse S. Kristensen 으, Maria S. Andersen, Lotte V. W. Stagsted, Karoline K. Ebbesen, Thomas B. Hansen & Jørgen Kjems

The circVec expression system: making circRNA from a DNA starting point

DNA

circRNA



Protein

circVec DNA or viral vector

Inject

circRNA biogenesis

Intra-cellular protein expression

circVec substantially outperforms the expression level and durability of mRNA-based systems

Increased expression level

Prolonged durability

Enhanced therapeutic potency

"Due to its significant advantages, circRNA systems can be expected to replace mRNA-based expression for DNA format therapeutics in the future – just as synthetic circRNA can be expected to replace current mRNA formats"

> Dr. Alex Wesselhoeft Scientific founder oRNA Therapeutics

circVec vs. mRNA luciferase reporter expression; time course



In vivo reporter pilot study: circVec 2.1 substantially outperforms mRNA durability



Major opportunities identified for the circVec platform in gene therapy and vaccines



'Remove & replace' conceptwith durability and safetyadvantages

Enhanced potency, single dose vaccine concept with simplified administration

Broad pipeline potential

Early partnering option

Efficient and durable expression of therapeutic proteins in solid tumors

Expansion opportunity

Designed for intra-cellular circRNA supply driving strong and durable protein expression

Circio investment case – executive summary



Clinical stage cancer vaccine

- Ongoing phase 2 program creates **multiple shots on goal**
- Low cost, financed through partnerships and grants
- Potential upcoming USD 3m milestone from Chinese partner



- Unique circRNA pipeline
- Deep expertise: the discoverers of circRNA work for Circio
- Differentiated approach , substantially improved durability
- Platform potential, lead applications in gene therapy and vaccines



Value drivers

- TG01 out-licensing following strong phase 2 data package
- Aiming for several circRNA partnering dealsduring 2024-2025