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EXECUTIVE SUMMARY

DISRUPTIVE ANTI-AGEING DRUG

- Developing transformative gene therapies targeting the upstream biology of ageing
- GF-1002 (the Company's lead candidate)
 extensive preclinical data suggests extension
 of life and health span



DIVERSIFIED PLAN

- The company is undertaking pre-clinical trials following admission
- The company intends to develop its lead compound for the treatment of Werner Syndrome (WS) patients (an accelerated ageing disease)
- Risk is mitigated with an additional focus on the veterinary program



EXPERIENCED TEAM

- Exceptional team with decades of experience in the pharmaceutical and health industries
- First rate academics from top universities and industry leaders





SCIENTIFIC ADVISORY BOARD



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ABOUT GENFLOW BIOSCIENCES

Genflow Biosciences Plc is a UK based biotech company with R&D facilities in Belgium and an office in Cambridge, MA, driven by one mission: to deliver medicines that potentially halt, slow, or reverse the ageing process in humans and dogs.

Genflow is listed on the London Stock Market (GENF.L)

Genflow's lead compound, GF-1002, works through a **centenarian variant** (a variant gene found in people living to 100 years or more) of the **SIRT6 gene** and has yielded promising preclinical results.

Managed by an experienced team with decades of experience in the pharmaceutical and biotech industries, the company is optimistic that development programs will continue at pace in the next 24 months.



AGEING

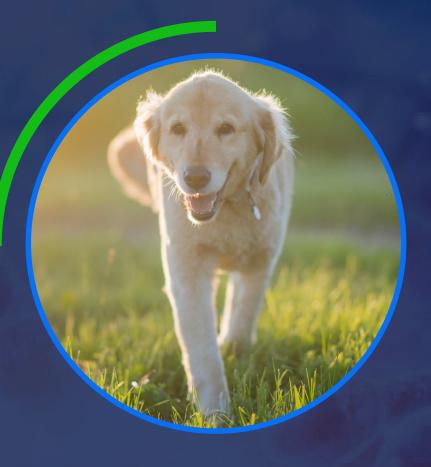
Age related diseases are the biggest health burden we face

Genflow treats ageing as the underlying risk factor for these diseases

Given the key role of genes in determining how we age Genflow focuses on gene therapeutics



2 years
life expectancy



10-13 years life expectancy



88 years*
life expectancy

Source: Morgan AE, Davies TJ, Mc Auley MT. The role of DNA methylation in ageing and cancer. Proc Nutr Soc. 2018 Nov;77(4):412-422. doi: 10.1017/S0029665118000150. Epub 2018 Apr 30. PMID: 29708096



^{*}expected LE in relation to baby boys born in the UK in 2018

GENE REGULATION IN AGEING

Ageing is a function of overworked epigenetic regulator genes unable to respond to cellular DNA damage.

Many genes regulate ageing: we are focusing on the SIRT6 gene.

Sirtuin 6 Gene (SIRT6)

Output

Gene (SIRT6)

Gene (SIRT6)

Output

Sources:

R. White. J. Vijg. Do DNA DSB drive Ageing? Molecular Cell 63, September 1, 2016
Mao, Z et al SIRT6 promotes DNA repair under stress by activating PARP1. Science 332, 2011,1443-1446
F. Wang, CH Chan, K. Chen, et al. Deacetylation of FOXO3 by SIRT1 or SIRT2 leads to Skp2-mediated FOXO3 ubiquitination and degradation. Oncogenes 31, no. 12. March 2012: 1546-57



Ageing is driven by 9 interlinked Hallmarks, all rooted in DNA damage. Targeting one individual factor is unlikely to be effective.



SIRT6 – REPAIRING DNA

SIRT6 gene/protein repairs DNA damage (especially double strand breaks (DSB)) and prevents senescence of our cells

- SIRT6 gene codes for SIRT6 protein
- Stronger SIRT6: Longer lifespan
- DSB repair coevolves with maximum lifespan (MLS) in rodents
- The activity of SIRT6 in stimulating DSB repair coevolves with MLS in rodents
- 5 amino acids determine the differential activities of mouse and beaver SIRT6

SIRT6 Efficiency Double Strand Break Repair

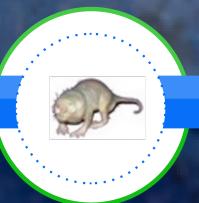
LIFESPAN

SIRT6 activity









Lifespan

DSB repair

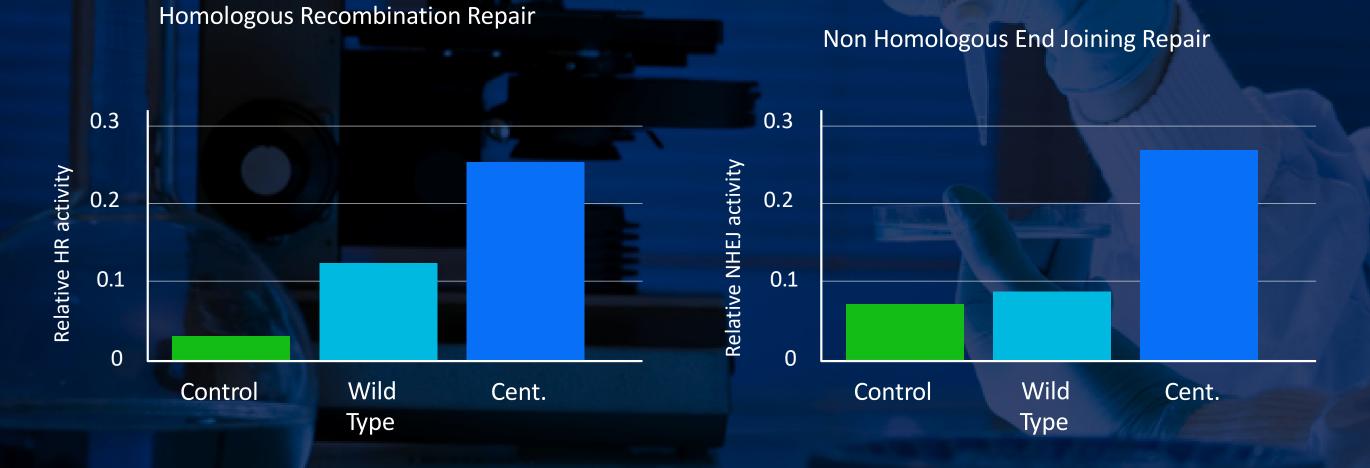
High activity SIRT6 5 amino acids OW activity SIRT6

Source: Tian et al., 2019, Cell 177, 622-638 April 18, 2019



FOCUS ON CENTENARIAN SIRT6

SIRT6 centenarian variant gene has more efficient DNA repair properties





Relative PARP1 Ribosilation

ACTING UPSTREAM

As organisms become more sophisticated, the biology of ageing becomes more complex.

This makes it more difficult to solve the problem, and increases the importance of acting early in managing ageing.

SIRT6 has been shown to extend the lifespan of virtually every organism on which it has been tested.



Mouse

Lifespan x 1.35

Sources: P. Oberdoerffer, S. Michan, M. McVay, et al. DNA damage-induced alterations in chromatin contribute to genomic integrity and age- related changes in gene expression. Cell 135. no. 5. Nov. 2008. 907-18 M. De Cecco, S. W. Criscione et al. Genomes of replicatively senescent cells undergo global epigenetic changes leading to gene silencing and activation of transposable elements. Ageing Cell 12. no. 2 April 2013:247-56





DELIVERY SYSTEM: SAFE AND COST-EFFECTIVE

The patent-pending technology has already been tested in several preclinical studies



ADVANTAGES OF EXOSOME BASED DELIVERY

Exo-AAV can mediate efficient, specific, and more durable SIRT6 expression in liver compared to conventional AAV

No Immunogenicity

Lack of local and systemic immunogenicity

Targeted Delivery

Engineered exosome to direct to specific cell types

Potency Advantage

Improved transduction versus free AAVs Rapid uptake and sustained

Therapeutic Window

Potency improvement.

Local retention.

Lack of systemic leakage

Efficient loading of AAVs into the exosome lumen



INTELLECTUAL PROPERTY

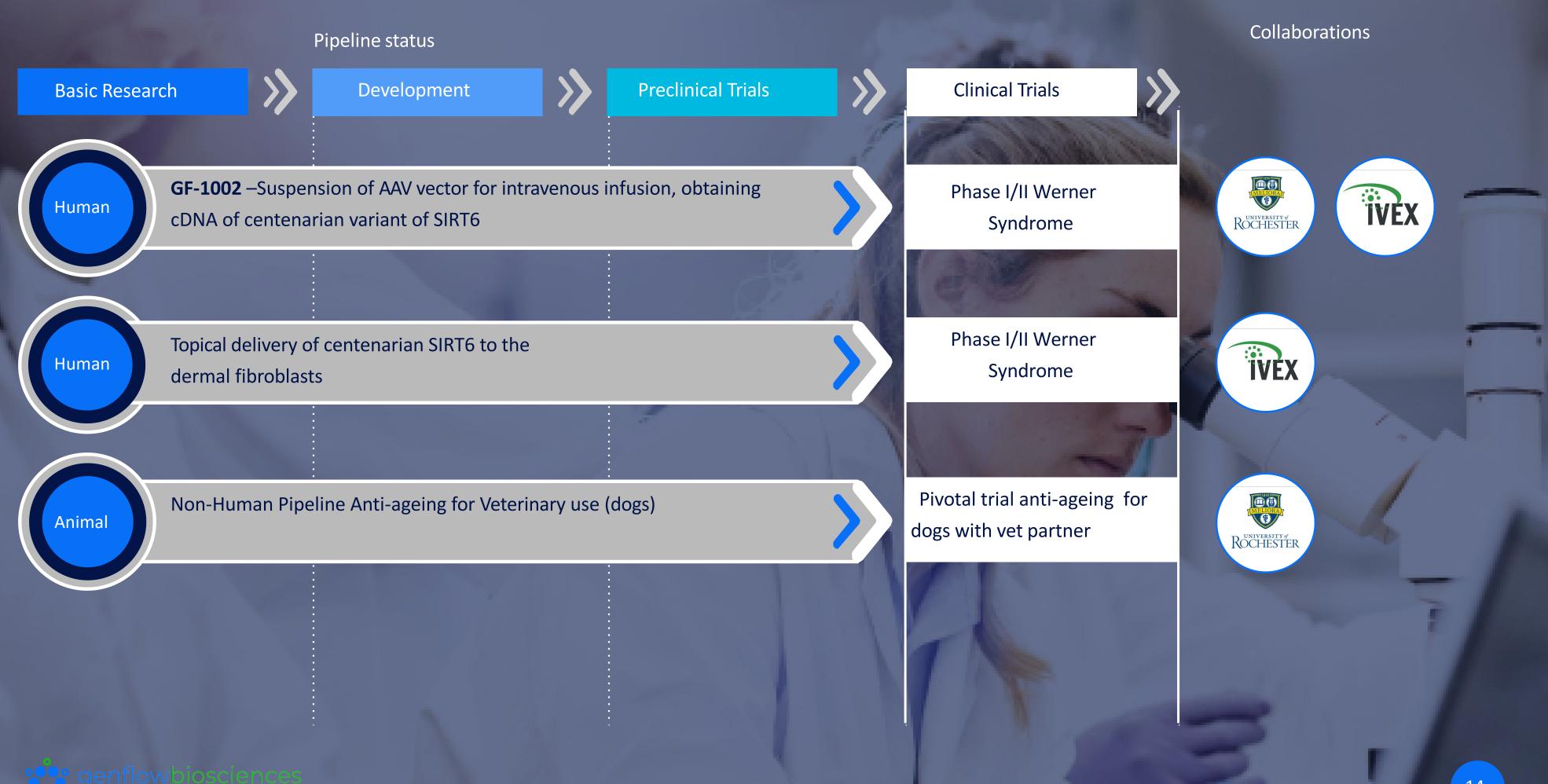


	EFS ID	1-21069	43268050
į	Application Number	US 63/188,573	US 63/222,557
	Title of Invention	Variants of SIRT6 for use in preventing and/or treating age-related diseases	Method of in vivo administration of the coding sequence of the SIRT6 gene via Adeno-Associated-Virus
	First Named Inventor	Vera Gorbunova, Seluanov and Suh	Eric Leire
Ĭ	Receipt Date	May 14, 2021	July 16, 2021
	Ownership	Worldwide Exclusive license from University Rochester New York / Columbia University / Albert Einstein College of medicine	Genflow Biosciences SRL

Applications are being made to the USPTO to patent Genflow's proprietary technology.



PRODUCT PIPELINE



LONGEVITY LANDSCAPE

COMPANY	OVERVIEW	TECHNOLOGY	HALLMARK OF AGEING FOCUSED ON	LOCATION
BIOTECHNOLOGY	Clinical stage (osteoarthritis Phase 2) public (Nasdaq) biotech	Anti-senescence (small molecules senolytic)	Senescence	USA, San Francisco, CA
Samumed	Private biotech developing therapeutics to address a range of degenerative diseases, regenerative medicine and	Regenerative medicine Stem cell and small molecules	Stem cell exhaustion	USA, San Diego, CA
BIOAGE	Private biotech developing medicines to treat ageing and ageing-related diseases	Hypoxia-inducible factor-prolyl hydroxylase (HIF-PH) inhibitor	Proteostatis	USA, Richmond, CA
FREQUENCY THERAPEUTICS	Public (Nasdaq) biotech	Small molecules to activate progenitor cells Hearing loss	Stem cell exhaustion	USA, Woburn, MA
11fe BIOSCIENCES	Private biotech targeting ageing	Epigenetic reprogramming; Autophagy; mitochondrial dysfunction	Mitochondrial dysfunction	USA, Boston, MA
⊗ ALKAHEST°	Private biotech developing drugs to fight age- related neurological diseases	Protein-based drugs	Proteostatis	USA, Boston, MA
REJUVENATE BIO	Private biotech developing gene therapy for dogs with mitral valve pathology.	Gene therapy	Proteostatis	USA, San Carlos, CA



VETERINARY PROGRAM

Genflow is developing the same delivery system for dogs. This has several advantages.



Dogs must be used as part of development for the human program



Owners are interested in prolonged health and life extension for their pets



The regulatory hurdle is much lower than for the human program



Short-term possibility for out-licensing following completion of the preclinical studies in dogs

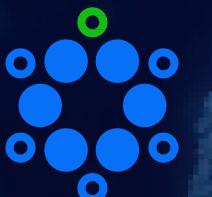


Results will be obtained at no extra cost to the main program



Demand is adequate to justify a separate program





genflowbiosciences longer better life

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