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Wave Life Sciences

First Quarter 2020

May 11, 2020

Forward-looking statements

This document contains forward-looking statements. All statements other than statements of historical facts contained in this document, including statements regarding possible or assumed future results of operations, preclinical and clinical studies, business strategies, research and development plans, collaborations and partnerships, regulatory activities and timing thereof, competitive position, potential growth opportunities, use of proceeds and the effects of competition are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause the actual results, performance or achievements of Wave Life Sciences Ltd. (the "Company") to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "aim," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this presentation are only predictions. The Company has based these forward-looking statements largely on its current expectations and projections about future events and financial trends that it believes may affect the Company's business, financial condition and results of operations. These forward-looking statements speak only as of the date of this presentation and are subject to a number of risks, uncertainties and assumptions, including those listed under Risk Factors in the Company's Form 10-K and other filings with the SEC, some of which cannot be predicted or quantified and some of which are beyond the Company's control. The events and circumstances reflected in the Company's forward-looking statements may not be achieved or occur, and actual results could differ materially from those projected in the forward-looking statements. Moreover, the Company operates in a dynamic industry and economy. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties that the Company may face. Except as required by applicable law, the Company does not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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Paul Bolno, MD, MBA
President and CEO

Wave Life Sciences: Recent business highlights

1. **PRECISION-HD clinical trials ongoing in Huntington's**
2. **Clinical and early-stage neurology pipeline advancing**
3. **First non-human primate RNA-editing data announced**

Wave priorities amidst COVID-19

- **Safeguarding health & well-being of our employees and patients**
- **Advancing our programs**
- **Creating opportunity in a new operating climate**

Delivering transformative medicines for patients

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Innovative pipeline led by neurology programs

THERAPEUTIC AREA	TARGET	DISCOVERY	PRECLINICAL	CLINICAL	ESTIMATED U.S. PREVALENCE*	PARTNER
NEUROLOGY						
Huntington's disease	**WVE-120101** mHTT SNP1			Phase 1b/2a and OLE	~10,000 / ~35,000	Takeda 50:50 option
	WVE-120102 mHTT SNP2			Phase 1b/2a and OLE	~10,000 / ~35,000	Takeda 50:50 option
	mHTT SNP3				~8,000 / ~30,000	Takeda 50:50 option
ALS and FTD	C9orf72				~1,800 (ALS) ~7,000 (FTD)	Takeda 50:50 option
Spinocerebellar ataxia 3	ATXN3				~4,500	Takeda 50:50 option
CNS diseases	Multiple†					Takeda milestones & royalties
OPHTHALMOLOGY						
Retinal diseases	USH2A and RhoP23H					100% global
HEPATIC						
ADAR RNA-editing	Multiple					100% global

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*Estimates of U.S. prevalence and addressable population by target based on publicly available data and are approximate; for Huntington's disease, numbers approximate manifest and pre-manifest populations, respectively.
†During a four-year term, Wave and Takeda may collaborate on up to six preclinical targets at any one time.
ALS: Amyotrophic lateral sclerosis; FTD: Frontotemporal dementia; CNS: Central nervous system; OLE: Open-label extension

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David Gaiero
Interim Chief Financial Officer

First quarter 2020 financial results

	Three Months Ended Mar 31, 2020	Three Months Ended Mar 31, 2019
Figures are in thousands		
Revenue	$4,161	$3,026
Operating Expenses:		
Research and Development	41,158	40,113
General and Administrative	12,996	10,901
Total Operating Expenses	54,154	51,014
Loss from Operations	(49,993)	(47,988)
Total Other Income, Net	2,500	3,788
Net Loss	($47,493)	($44,200)
Net Loss per Share	**($1.38)**	**($1.36)**

As of Mar 31, 2020 **Shares Outstanding:** 34.6 million **Cash Balance:** $121 million

Wave expects that its existing cash and cash equivalents, together with expected and committed cash from its existing collaboration, will enable Wave to fund its operating and capital expenditure requirements into 3Q 2021.

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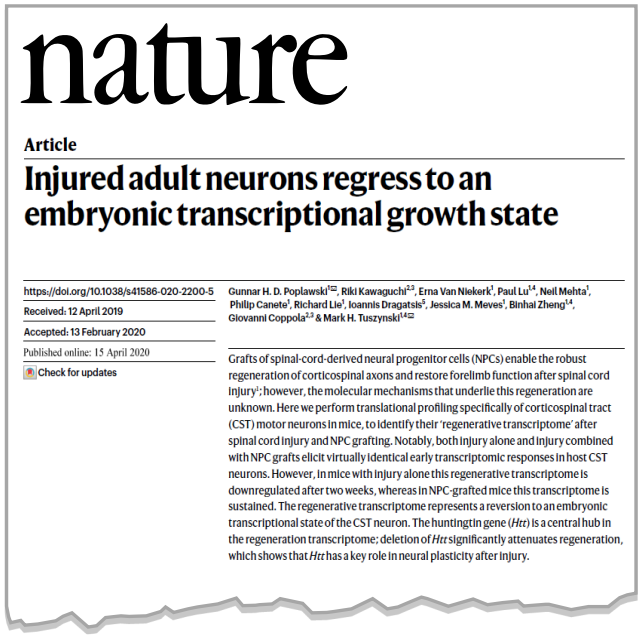
Michael Panzara, MD, MPH
Chief Medical Officer

Recent publication contributes to weight of evidence on importance of wild-type huntingtin



nature

Article

Injured adult neurons regress to an embryonic transcriptional growth state

https://doi.org/10.1038/s41586-020-2200-5
Received: 12 April 2019
Accepted: 13 February 2020
Published online: 15 April 2020
Check for updates

Gunnar H. D. Poplawski[1✉], Riki Kawaguchi[2,3], Erna Van Niekerk[1], Paul Lu[1,4], Neil Mehta[1], Phillip Canete[1], Richard Lie[1], Ioannis Dragatsis[5], Jessica M. Meves[1], Binhai Zheng[1,4], Giovanni Coppola[2,3] & Mark H. Tuszynski[1,4✉]

Grafts of spinal-cord-derived neural progenitor cells (NPCs) enable the robust regeneration of corticospinal axons and restore forelimb function after spinal cord injury[1]; however, the molecular mechanisms that underlie this regeneration are unknown. Here we perform translational profiling specifically of corticospinal tract (CST) motor neurons in mice, to identify their 'regenerative transcriptome' after spinal cord injury and NPC grafting. Notably, both injury alone and injury combined with NPC grafts elicit virtually identical early transcriptomic responses in host CST neurons. However, in mice with injury alone this regenerative transcriptome is downregulated after two weeks, whereas in NPC-grafted mice this transcriptome is sustained. The regenerative transcriptome represents a reversion to an embryonic transcriptional state of the CST neuron. The huntingtin gene (*Htt*) is a central hub in the regeneration transcriptome; deletion of *Htt* significantly attenuates regeneration, which shows that *Htt* has a key role in neural plasticity after injury.

- Conditional knock-out of Htt in 4-month old mice (post-neuronal development)
- Results suggest that:
  1) Htt plays a central role in the regenerating transcriptome (potentially influencing genes such as NFKB, STAT3, BDNF)
  2) Htt is essential for regeneration

> **"Indeed, conditional gene deletion showed that Htt is required for neuronal repair. Throughout life, neuronal maintenance and repair are essential to support adequate cellular functioning"**

Poplawski et al., *Nature*, April 2019; Htt: Huntingtin protein

Neurology: Clinical pipeline update

WVE-120101 (SNP1)
WVE-120102 (SNP2)
Huntington's disease

- PRECISON-HD1 and PRECISION-HD2 ongoing; working to help sites adapt to challenging environment created by COVID-19 pandemic
- 32 mg data from PRECISION-HD2 trial on track for 2H 2020
- Initiated 32 mg cohort for PRECISION-HD1; data from PRECISION-HD1 trial on track for 2H 2020

SNP3 program
Huntington's disease

- Third allele-selective HD program; ~40% of HD population has SNP3
- Expected to initiate clinical development in 2H 2020

C9orf72 program
ALS and FTD

- Selectively targets the transcripts containing the hexanucleotide repeat expansion (G4C2) in C9orf72 gene
- Expected to initiate clinical development in 2H 2020

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ALS: Amyotrophic lateral sclerosis; FTD: Frontotemporal dementia

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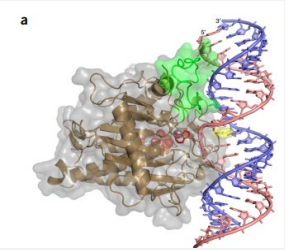
Chandra Vargeese, PhD
SVP Drug Discovery

RNA editing: A promising new therapeutic modality for treatment of genetic diseases

Potential benefits versus gene editing

- Ability to use endogenous proteins (e.g. ADAR)
- Ease of delivery
- Titratable, repeatable dosing
- Reversible effects, avoids potential long-term risks associated with permanent off-target DNA editing

ADAR
(adenosine deaminases acting on RNA)

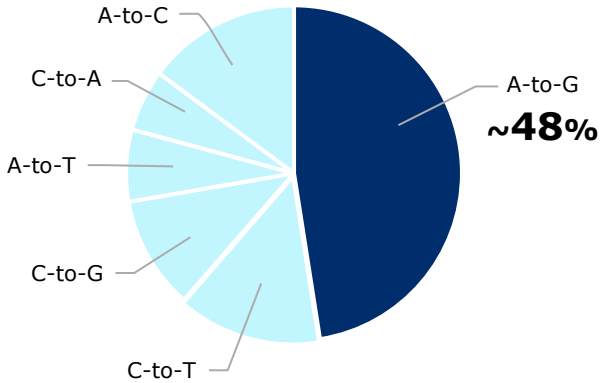


- Endogenous proteins that catalyze A-to-I RNA editing
- Upon translation, I recognized as G, leading to A-to-G editing

A-to-I(G) RNA editing opportunity is significant

- Nearly half of known human genetic pathogenic SNPs are G-to-A mutations[1]
- Tens of thousands of potential disease variants A-to-I(G) editing could target[2]

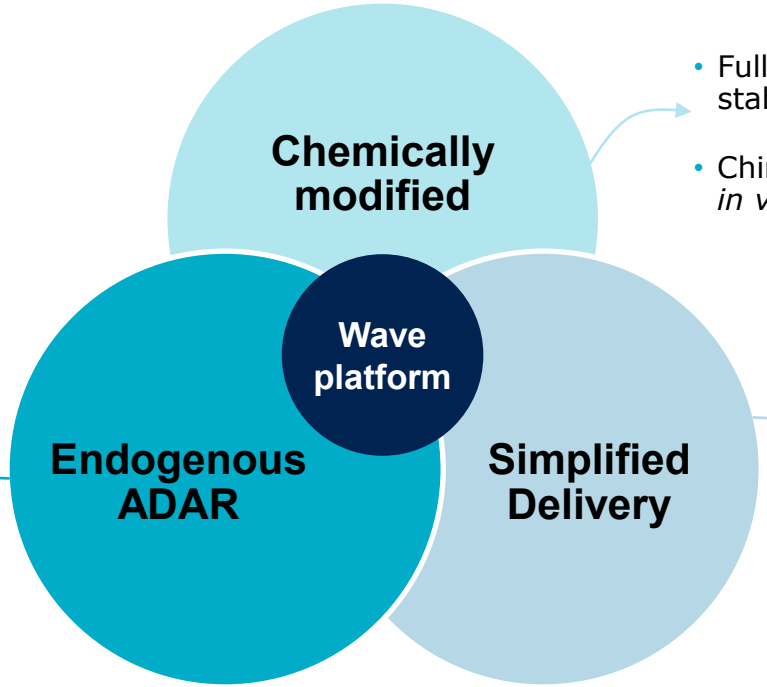
Pathogenic human SNPs by base pair corrections



>32,000 pathogenic human SNPs[1]

SNP: single nucleotide polymorphism A: Adenosine I: Inosine G: Guanosine
[1] Gaudeli NM et al. *Nature* (2017). [2] ClinVar database

Advantages of Wave ADAR-mediated RNA-editing platform



- Fully chemically modified to increase stability *in vivo*
- Chirally-controlled backbone to maximize *in vitro* activity

- No immunogenicity from exogenous proteins
- Reduced off-target effects[1]

- GalNAc-conjugated for targeted delivery into liver
- No requirement for AAV / nanoparticles

Building RNA-editing capability for PRISM platform

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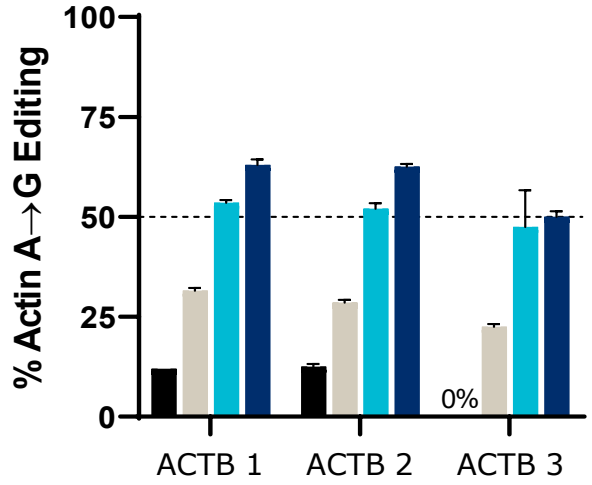
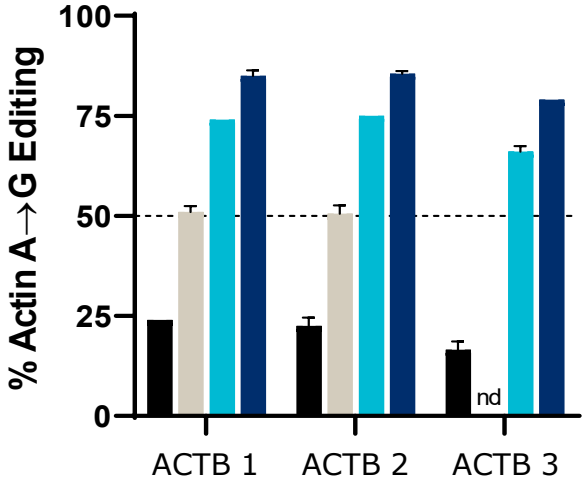
[1]Chen et al. Biochemistry 2019

In vitro RNA editing demonstrated in non-human primate and human hepatocytes

NHP Hepatocytes



Human Hepatocytes

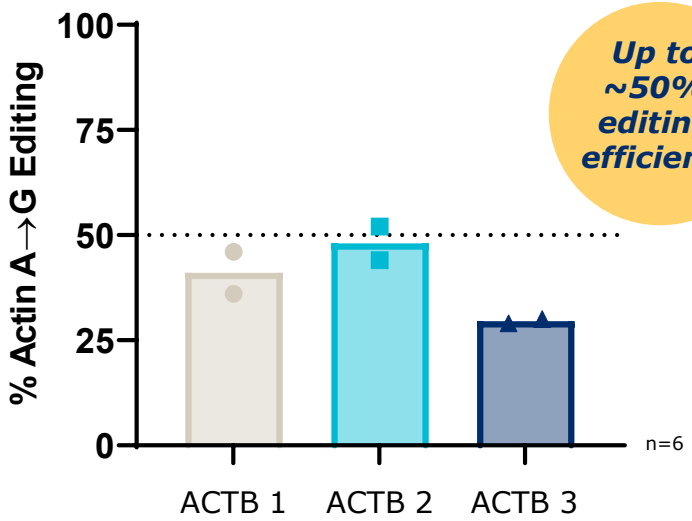


Potent, dose-dependent RNA editing demonstrated via free uptake with GalNAc-conjugated stereopure oligonucleotides

NHP: non-human primate; ACTB: Beta-actin; nd= not determined
Total RNA was harvested, reverse transcribed to generate cDNA, and the editing target site was amplified by PCR.

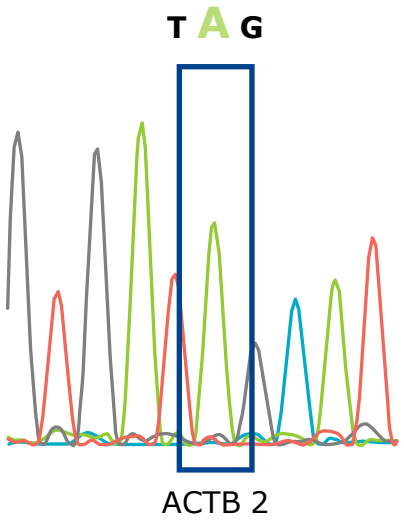
First non-human primate RNA editing

***In vivo* – NHP**

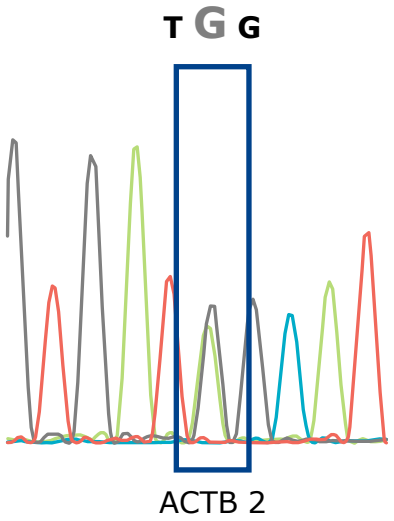


Up to ~50% editing efficiency

Baseline



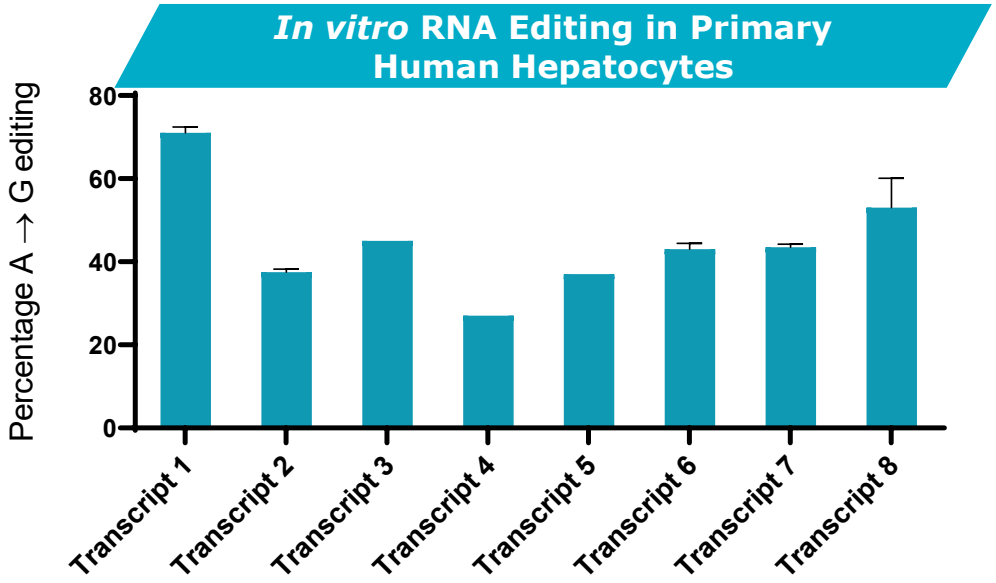
Post-treatment



Liver biopsies conducted at baseline and 2 days post last dose
RNA-editing efficiencies of up to 50% with GalNAc conjugate in liver of NHP

NHP – non-human primate; ACTB: Beta-actin; Left: 5mg/kg SC: Day 1,2,3,4,5; Liver Biopsy for mRNA (ACTB Editing) & eASO Exposure: Day 7 Right: % Editing quantified from Sanger sequencing using EditR program.

RNA-editing design applicable across targets



- Editing achieved across several distinct RNA transcripts
- Supports potential for technology to be applied across variety of disease targets

Additional *in vivo* ADAR-mediated RNA-editing data and first RNA-editing program expected to be announced in 2020

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Data presented at 1st International Conference on Base Editing – Enzymes and Applications (Deaminet 2020); See poster for full dataset

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Paul Bolno, MD, MBA
President and CEO

Anticipated upcoming Wave milestones

Neurology

- **2H 2020:** PRECISION-HD2 data from 32 mg cohort in Huntington's disease
- **2H 2020:** PRECISION-HD1 topline data, including 32 mg cohort, in Huntington's disease
- **2H 2020:** Initiate clinical development of SNP3 program in Huntington's disease
- **2H 2020:** Initiate clinical development of C9orf72 program in ALS and FTD

Ophthalmology

- **2020:** Advance USH2A and RhoP23H programs

Hepatic

- ✓ **2020:** *In vivo* ADAR editing data
- **2020:** Additional *in vivo* ADAR-mediated RNA-editing data and announce first RNA-editing program

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Q&A

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Realizing the potential of genetic medicines

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