



rippletherapeutics

Keeping Patients in Sight

OIS XV
November 22nd, 2025

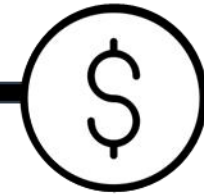
Advantages of Ripple's Prodrug Technology Platform



- Higher loading/smaller implants
- Zero-order release kinetics
- Tunable dose and duration

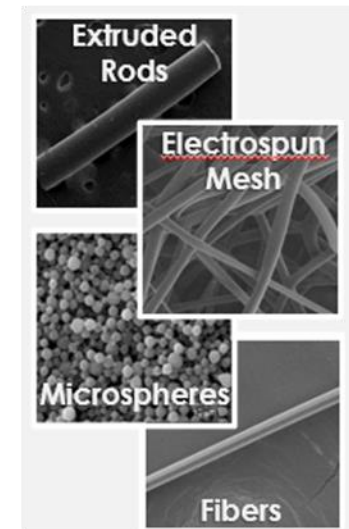
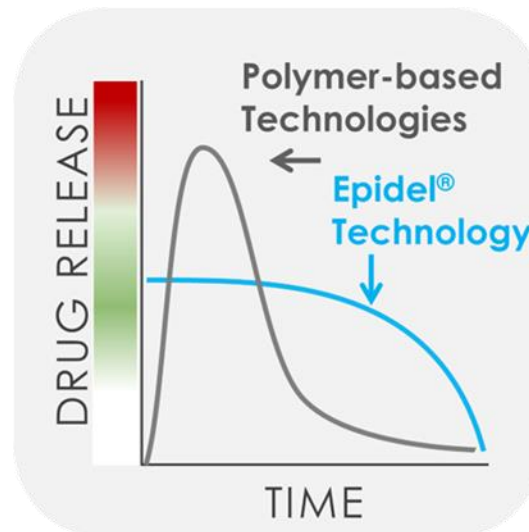
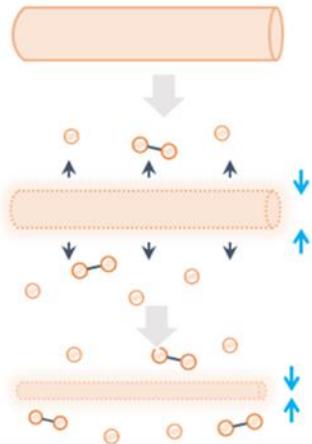


- Minimum effective dose
- Reduced treatment burden
- Improve long term outcomes



- Composition of Matter patents
- Standard processing techniques
- Scalable manufacturing

Surface Erosion-based Release



Ripple's Prodrug Engineering Versatility

Ripple has more than **fifty (50)** patents and patent applications

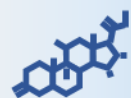
Includes granted composition of matter patents.

Dexamethasone Prodrug Compositions and Uses Thereof

(12) United States Patent Parrag et al.		(10) Patent No.: US 10,959,954 B2
(45) Date of Patent: *Mar. 30, 2021		
(54) Dexamethasone Prodrug Compositions and Uses Thereof		(58) Field of Classification Search None See application file for complete search history.
(71) Applicant: Ripple Therapeutics Corporation, Toronto (CA)		(56) References Cited
(72) Inventors: Ian Charles Parrag, Mississauga (CA); Matthew Alexander John Statham, Milton (CA); Kyle Rattinas, Toronto (CA); Dimitra Louka, Toronto (CA); Hans Christian Fischer, Toronto (CA); J. Paul Santner, Toronto (CA); Wendy Allison Naimark, Toronto (CA); Rosetta Leland, Mississauga (CA)		U.S. PATENT DOCUMENTS
(73) Assignee: RIPPLE THERAPEUTICS CORPORATION, Toronto (CA)		3,910,412 A 7/1971 Akita et al. 3,663,790 A 5/1972 Smith et al. A01K 47/50 552,509
		4,024,871 A 5/1977 Stephenson
		4,532,316 A 7/1985 Blum
		4,933,215 A 5/1990 Reddy et al.
		4,916,193 A 4/1990 Tang et al.
		5,013,341 A 5/1991 Matsuura et al.
		5,217,493 A 6/1993 Raul et al.
		5,796,524 A 10/1993 Kozawa et al.
		5,321,099 A 6/1994 Goldwasser et al.
		5,347,598 A 2/1995 Rosenberg
		5,412,126 A 7/1995 Goldwasser

Granted

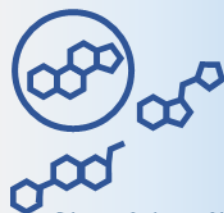
Platform Expansion



Dexamethasone



Steroids



Steroids with 2nd Drugs



Opioid Inhibitors



Prostaglandins



TKIs



Undisclosed compounds



Prostacyclin Agonists



Aptamers



Peptides

New drug classes

2017 - Discovery

2018

2019

2020-22

2022-24

Ongoing and Future Work



Demonstrated



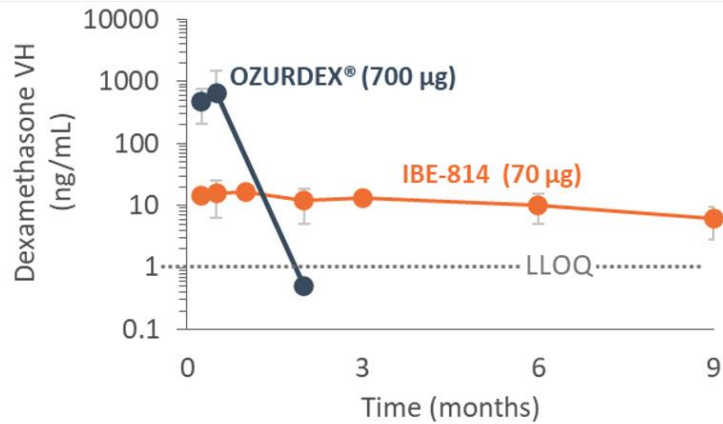
Platform expansion

The Ripple Difference

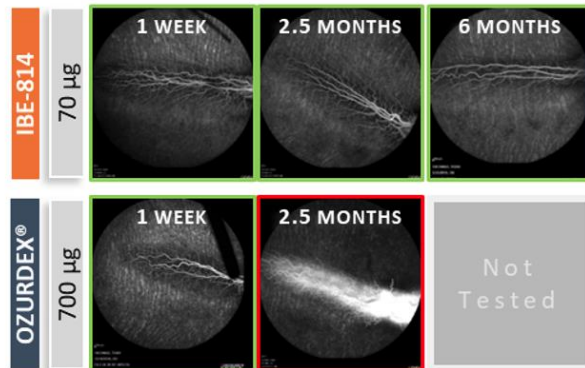
Proven clinical translation (IBE-814 example)

Preclinical PK/PD POC

Pharmacokinetics



Pharmacodynamics



Clinical Translation

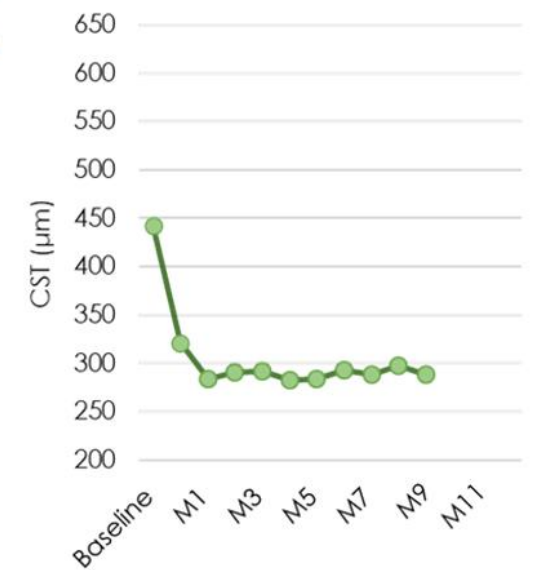
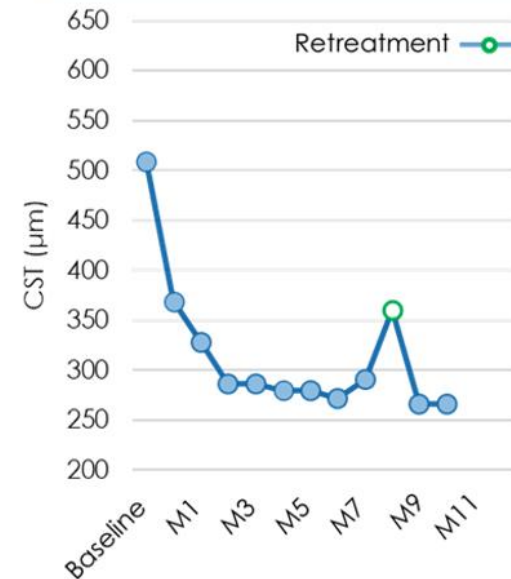
RIPPLE-1 Phase II 60 pt DME/RVO Study

DME – Long Treatment History

Disease Duration: **22 years**
 Tx History: Avastin, Lucentis, Eylea
9 years

RVO – Long Treatment History

Disease Duration: **10.5 years**
 Tx History: Avastin, Lucentis
9.5 years



Ripple Commercial Strategy

Balance of Proprietary Products and Partner Programs



RIPPLE
Proprietary
Products



**Funded
Partner
Programs**

**RIPL Internal
Development**

**Product Licensing
Deals**

**Development Funding
with Licensing Option**

Intermediate Dry AMD

RTC – 4202 IVT
CFB Inhibitor

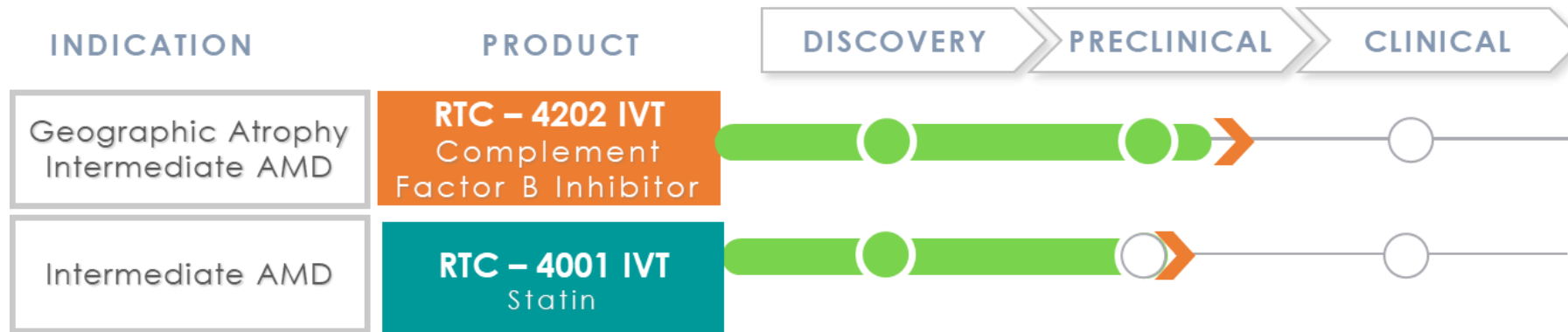
RTC – 4001 IVT
Statin



Ripple's proprietary product focus is on Dry AMD and GA with two active programs

6

Ripple TPP: 6-month dosing, 100% prodrug implant

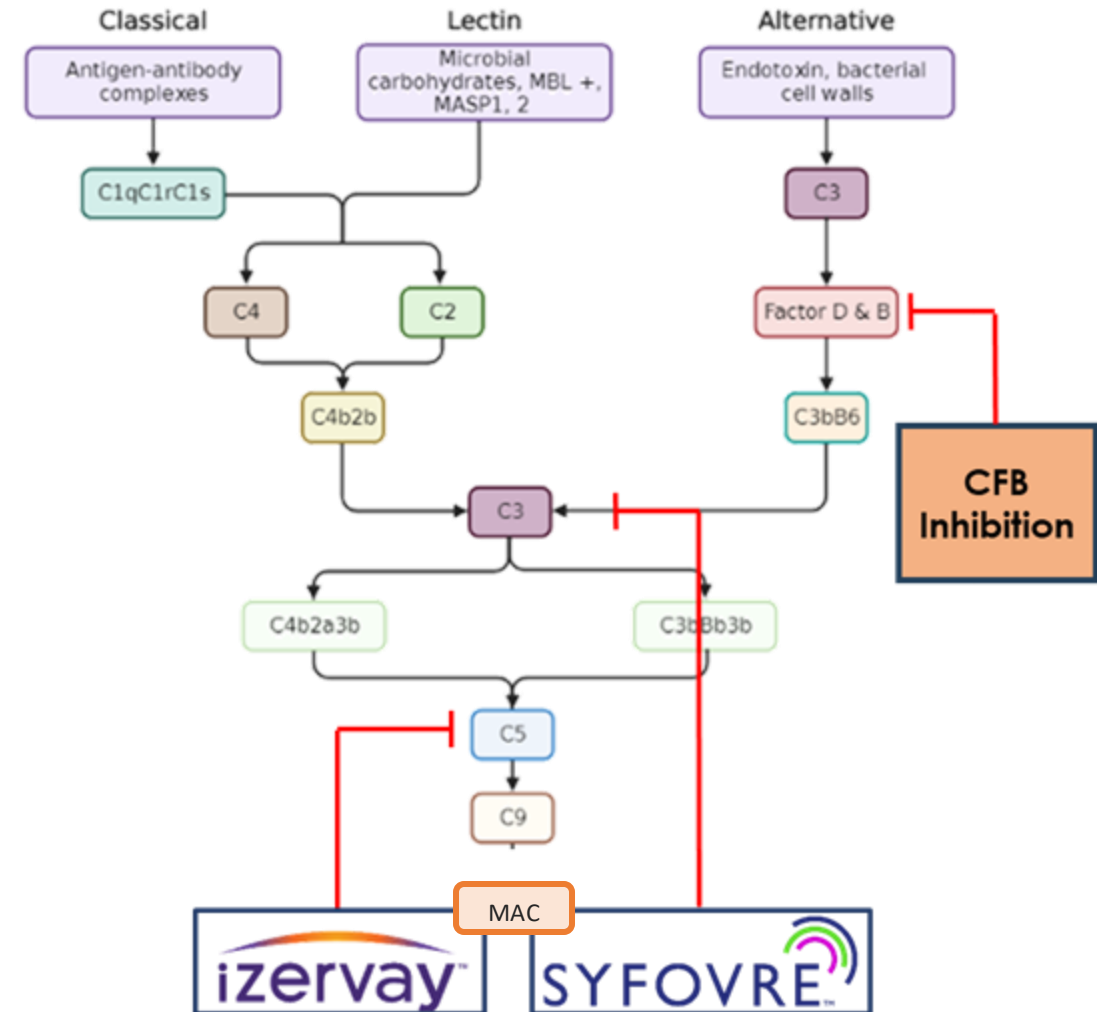


- ❑ Dry AMD 2030 market size ~\$17B¹
 - Izervay and Syfovre have ~\$2B in combined revenue since approval in 2023
- ❑ Challenges with current therapies
 - High treatment burden (monthly injections) with limited improvement in vision
 - Potential safety concerns with continuous injections

¹DataM Intelligence: Geographic Atrophy Market Size, Share, Industry, Forecast and Demand

Complement Factor B is an attractive target for sustained local drug delivery

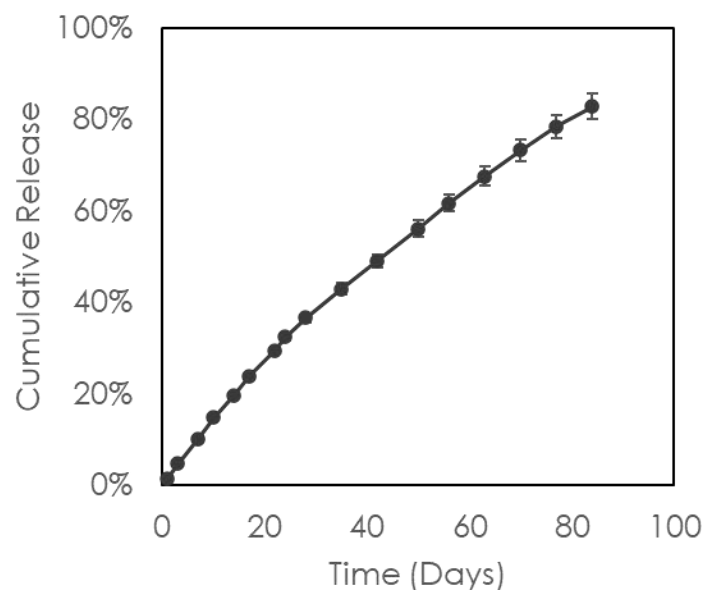
- ❑ Genetic evidence links CFB with progression of dry AMD^{1,2}
- ❑ CFB inhibitors switch off the alternative pathway amplification loop that drives downstream complement activity on drusen and Bruch's membrane³
- ❑ Local drug delivery is more effective than systemic approaches
- ❑ Ripple CFB implant with 6-month duration and zero-order release kinetics is designed to reduce treatment burden, improve safety and provide better patient outcomes



1. Am J Epidemiology 2012;176(5):361-72.
2. JAMA Ophthalmology 2014;132(5):528-34.
3. Front Immunology 2017;8:1778

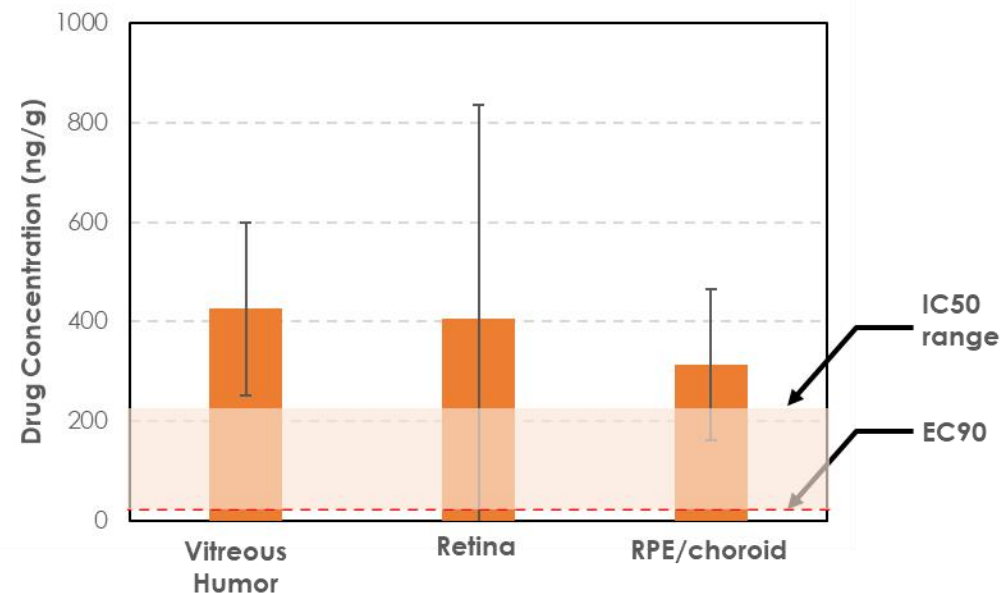
RTC-4202 IVT: Continued progress on preclinical safety and efficacy

Sustained release and *in vivo* safety



Controlled drug release & favorable ocular tolerability observed *in vivo*

RTC-4202 1-month PK data



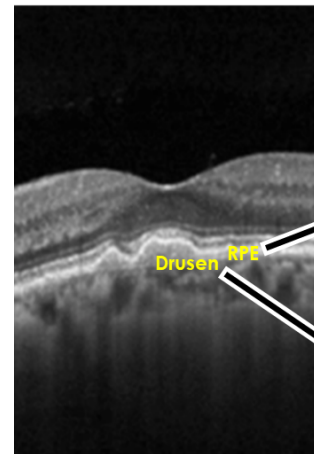
Drug levels in retina & RPE/choroid are in anticipated therapeutic range

Intravitreal statins have the potential to impact multiple aspects of dry AMD pathogenesis

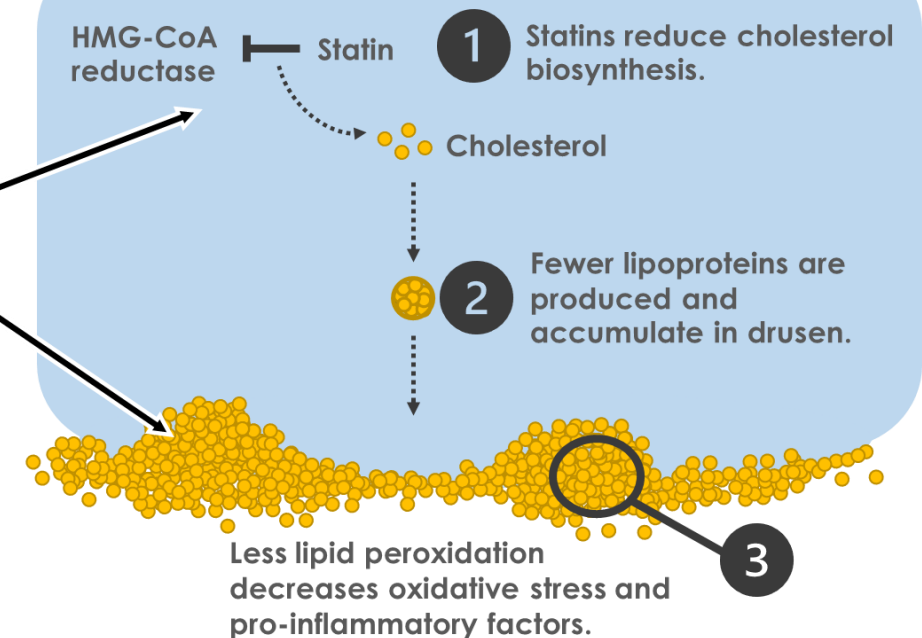
- ❑ Pleiotropic properties of statins offer potential to have significant impact on Dry AMD^{1,2}
- ❑ Reducing local cholesterol synthesis reduces drusen formation
- ❑ Reducing drusen can reduce chronic inflammation and complement activation
- ❑ Intravitreal delivery overcomes the barriers of oral statin therapy to treat Dry AMD

Intravitreal statins:

- ↓ Cholesterol synthesis
- ↓ Drusen formation
- ↓ Oxidative stress
- ↓ Inflammation

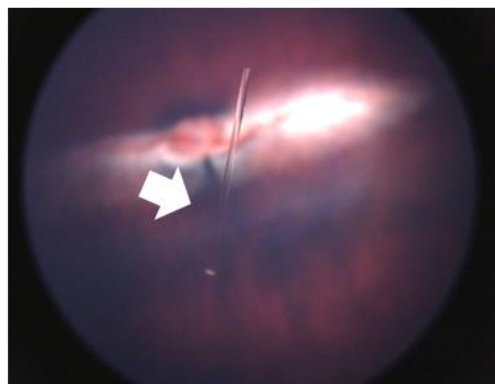
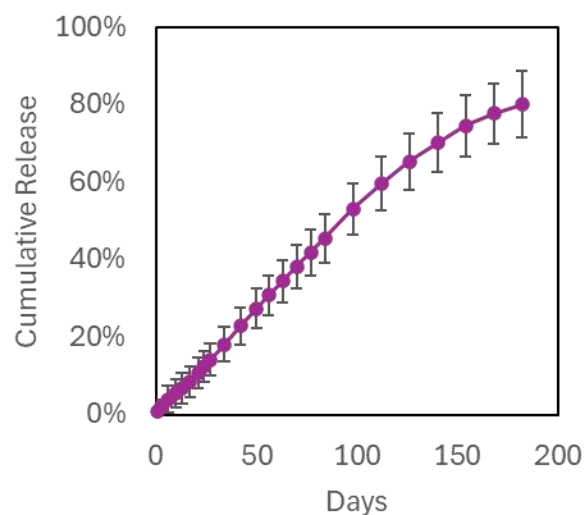


Retinal Pigment Epithelium (RPE) Cell



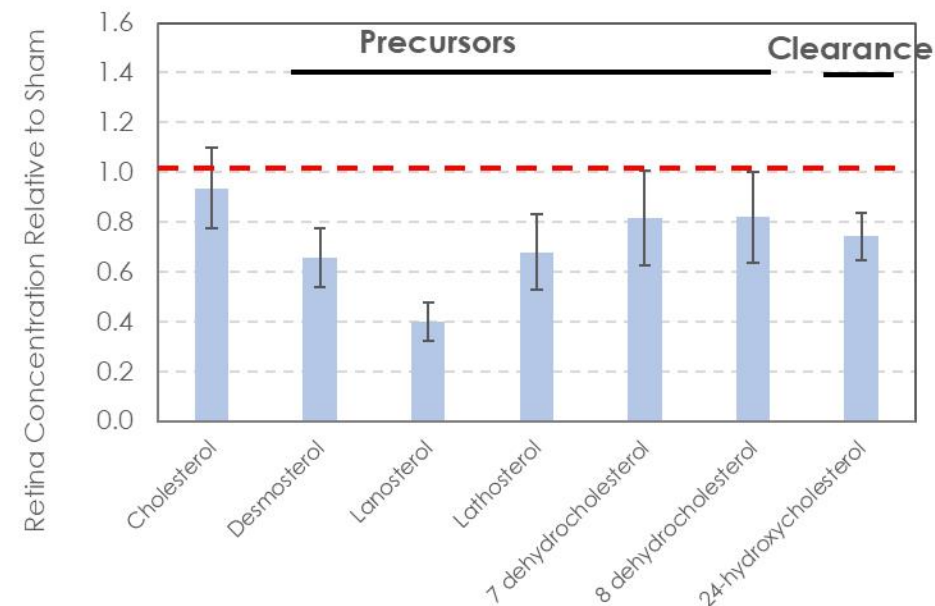
RTC 4001 IVT: Continued progress on preclinical safety and efficacy

RTC-4001 Drug Release



Surface erosion drug release
in vitro and *in vivo*

RTC-4001: 1-mo PD Lipid Study



Rosuvastatin impacts cholesterol
biosynthesis in retina

Ripple Series B Financing

Clinical Data for Dry AMD Program(s)

Complement Factor B Inhibitor

\$15M to support IND-enabling studies through Ph 1 completion

- PD, PK, and GLP tox studies
- Clinical batch manufacturing
- Completion of Phase 1/2a Clinical Trial

Statins

\$15M to support IND-enabling studies through Ph 1 completion

- PD, PK and GLP tox studies
- Clinical batch manufacturing
- Completion of Phase 1/2a Clinical Trial

Ripple Commercial Strategy

Balance of Proprietary Products and Partner Programs



RIPPLE
Proprietary
Products



**Funded
Partner
Programs**

**RIPL Internal
Development**

**Product Licensing
Deals**

**Development Funding
with Licensing Option**

Intermediate Dry AMD

Glaucoma

RTC – 4202 IVT
CFB Inhibitor

RTC – 4001 IVT
Statin

RTC-620 IC
Bimatoprost



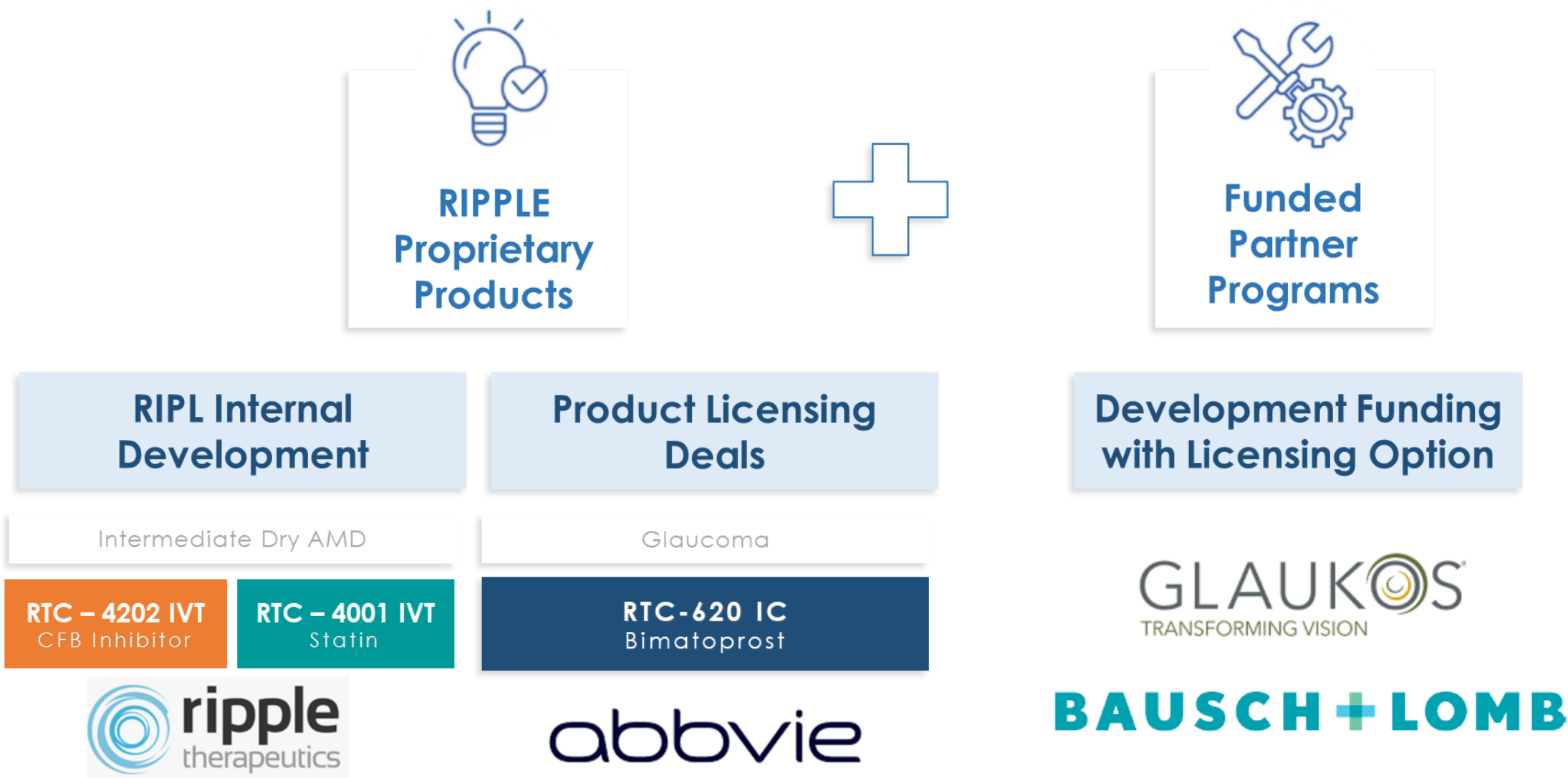
abbvie

AbbVie RTC-620 Collaboration and License Option Agreement is Transformative for Ripple

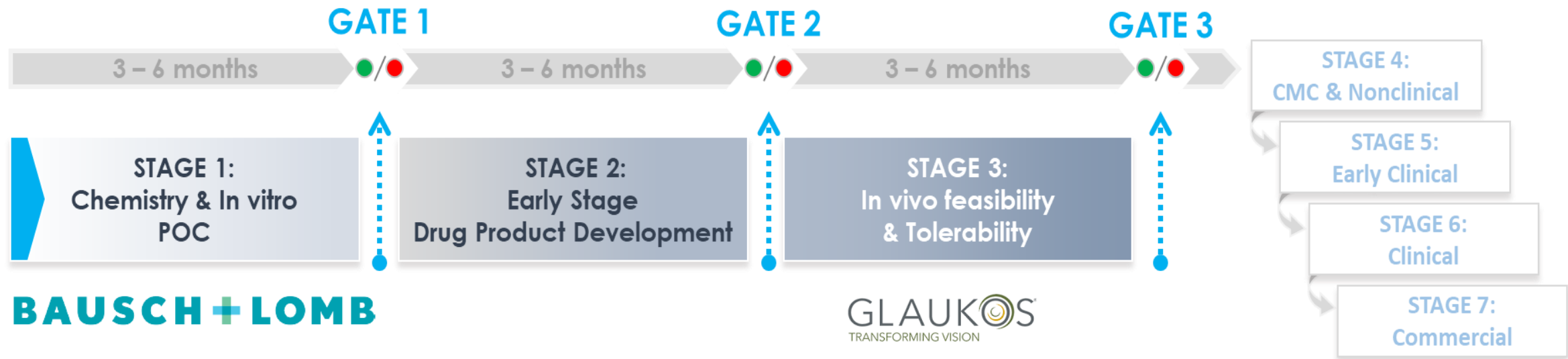
- ❑ Validation of Ripple technology approach for sustained drug delivery
- ❑ Confirmation of compelling preclinical data-set for RTC-620
- ❑ Significant economics
 - \$21.8M USD up-front payment (received Oct 2024)
 - \$290M USD milestones
 - Tiered royalties

Ripple Commercial Strategy

Balance of Proprietary Products and Partner Programs



Funded partner programs follow a staged-gate development process with a licensing option



- ☐ Partner's molecule
- ☐ Funded development program with licensing option
- ☐ Economics (milestones, royalties) negotiated in advance

The Ripple Difference

Experienced leadership team and world class advisory boards

Management Team



THOMAS P. REEVES

Co-Founder & President & CEO



WENDY NAIMARK, PH.D

Co-Founder & Chief Technology Officer



DEFNE GARNER, CA

Co-Founder & Vice President, Finance



IAN PARRAG P.ENG, PH.D

Co-Founder & Vice President, R&D



FRAÏDIANIE SÉVIGNÉ

Vice President, Operations



KYLE BATTISTON, PHD

Vice President, R&D Pipeline



JULIE FOTHERINGHAM, MA, PCC

Vice President, Marketing, People & Culture

Board of Directors



JON TALAMO, M.D., CHAIR

Ophthalmologist & Principal, JHT Strategic Consulting



SANDRA BEACH LIN,

Retired President & CEO, Calisolar Inc.



DAVID GUYER, M.D.

Co-founder, President & CEO, EyeBio



JONATHAN PRENNER, M.D.

Retinal Specialist & Chief Medical Officer, EyeBio



PHIL ANZARUT

Vice President & Partner, Asset Management, BDC Capital



COLIN FRANCOU

Managing Director, Théa Open Innovation



STÉPHANE THUMELIN

Head of Business Development, Théa Open Innovation



TOM REEVES

President & CEO, Ripple Therapeutics

The Ripple Difference

Experienced leadership team and world class advisory boards

Retina



David Boyer, MD



Baruch D Kuppermann, MD, PhD



Elias Reichel, MD



Anat Loewenstein, MD, MHA



Philip Rosenfeld, MD, PhD



Sumit Sharma, MD

Glaucoma



Iqbal Ike K. Ahmed, MD FRCS



Thomas Samuelson, MD

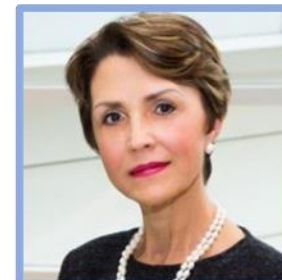


Sanjay Asrani, MD

Scientific Advisors



Christine Curcio, PhD



Irina Pikuleva, PhD



Simon Clark, PhD

The Ripple Difference

Capital efficiency and compelling economic potential

- ❑ Proprietary products targeting major underserved markets
 - Dry AMD 2030 market estimate ~\$17B¹
- ❑ Partner economic potential
 - Fully funded development programs; significant economic upside
- ❑ Capital efficiency
 - \$65M USD total funding; \$15M USD equity (Series A 2020)
- ❑ Series B Financing (\$30-40M)
 - Accelerate Dry AMD program
 - Proprietary product development/acquisition
 - Platform expansion

¹DataM Intelligence: Geographic Atrophy Market Size, Share, Industry, Forecast and Demand



www.rippletherapeutics.com
MaRS Centre, South Tower
101 College Street, Suite 300
Toronto, Canada

