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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

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**FORM 8-K**

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**CURRENT REPORT**  
**Pursuant to Section 13 or 15(d)**  
**of The Securities Exchange Act of 1934**

**Date of Report (Date of Earliest Event Reported): January 7, 2019**

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**Aerpio Pharmaceuticals, Inc.**  
(Exact name of registrant as specified in its charter)

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**DELAWARE**  
(State or other jurisdiction  
of incorporation)

**001-38560**  
(Commission  
File Number)

**61-1547850**  
(I.R.S. Employer  
Identification No.)

**9987 Carver Road**  
**Cincinnati, OH**  
(Address of principal executive offices)

**45242**  
(Zip Code)

**Registrant's telephone number, including area code: (513) 985-1920**

**Not Applicable**  
(Former name or former address, if changed since last report)

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Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

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**Item 7.01. Regulation FD Disclosure.**

Aerpio Pharmaceuticals, Inc. (the "Company") is furnishing a corporate presentation, attached as Exhibit 99.1 to this Current Report on Form 8-K, which the Company intends to use from time to time in meetings with investors and others beginning on January 7, 2019. The corporate presentation will also be available in the investor relations section of the Company's website at <http://aerpio.com>.

The information in this Item 7.01 and Exhibit 99.1 attached hereto shall not be deemed "filed" for purposes of Section 18 of the Securities and Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section, nor shall they be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, except as expressly set forth by specific reference in such filing.

**Item 9.01. Financial Statements and Exhibits.**

(d) Exhibits

<u>Exhibit No.</u>	<u>Description</u>
99.1	<a href="#">Aerpio Pharmaceuticals, Inc., corporate presentation.</a>

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: January 7, 2019

**AERPIO PHARMACEUTICALS, INC.**

By: /s/ Stephen Hoffman

Stephen Hoffman

Chief Executive Officer



# Corporate Presentation

January 7, 2019

# Forward looking statements

- *This presentation has been prepared by Aerpio Pharmaceuticals (“we”, “us” or, the “Company”) and includes forward-looking statements. All statements contained in this presentation other than statements of historical facts, including statements regarding our product candidates, their therapeutic potential and development plans, our future results of operations and our financial position, our business strategy and plans and our objectives for future operations, are forward-looking statements. Forward-looking statements speak only as of the date hereof unless it is stated otherwise. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to our strategy, our intellectual property position, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements including those contained in our public filings with the Securities and Exchange Commission.*
- *This presentation also contains estimates and other statistical data made by independent parties and by us. Management bases all estimates and projections as to events that may occur in the future (including projections of revenue, development plans and timing of clinical trial results) upon their best judgment as of the date of this presentation. Whether or not such estimates or projections may be achieved will depend upon the Company achieving its overall business objectives and the availability of funds. The Company does not guarantee that any of these projections will be attained. Actual results will vary from the projections, and such variations may be material. New risks emerge from time to time, and except as required by law, neither we nor any other person makes any representation as to the accuracy or completeness of such data or undertakes any obligation to update such data after the date of this presentation. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this presentation.*
- *This presentation may contain trade names, trademarks or service marks of other companies. The Company does not intend the use or display of other parties’ trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of, these other parties. Solely for convenience, the trade names, trademarks or service marks in this presentation are referred to without the symbols ® and ™, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.*

# Overview of Aerpio

- Diabetes leads to vascular leaks over time due to glucose insult. These leaks have three significant effects:
  - Diabetic macular edema (DME) driven by fluid leaking behind retina
  - Damage to kidneys leading over time to kidney dialysis (median survival <5 years)
  - Diabetic neuropathy and amputations
  - Erectile dysfunction
- Aerpio has developed AKB-9778, which is a Tie2 activator, which seals vascular leaks improving health
  - Delay or reduce DME (saving \$35,000/year)
  - Might delay or reduce kidney dialysis (saving \$50,000/year)
  - Might reduce multiple hospitalizations per year for other issues
- Aerpio is currently running a trial in diabetic retinopathy (DR) to demonstrate the ability to seal the leaky vasculature
- DR would represent a biomarker and the best moment to treat these patients to delay or prevent damage to the eye, kidney and other effects

# Overview of Aerpio

- The diabetic market is very large in the US
  - 30 million diabetics
  - 8.4 million estimated to have DR
  - 1.6 million diagnosed with DR
- Following only patients diagnosed with DR and assuming a price of \$10,000 per patient, the US market may be \$16 billion. Adding in Europe, Japan, Canada takes the market to over \$30 billion
- Aerpio has a very strong patent portfolio in TIE-2 activation
- Phase 2b data expected in March 2019

# Aerpio's IBD Drug

- Aerpio has entered into a partnership for its IBD drug with Gossamer (Faheem Hasnain & Sheila Gujrathi) for \$20 million upfront, \$400 million of milestones and mid-teens royalties as well as a percentage of the proceeds if the asset is ever sold
  - \$8 billion potential market
  - HIF drug with good safety profile distinguishing it from other IBD drugs like Humira and steroids
  - Strong efficacy data in mice
  - Phase 1b human trial completed by end of this year
  - Daily pill rather than an injection





## Tie2 Biology & the Critical Role of VE-PTP in Diabetes

# Diabetic complications are a result of progressive blood vessel damage due to chronic diabetes

- The Problem

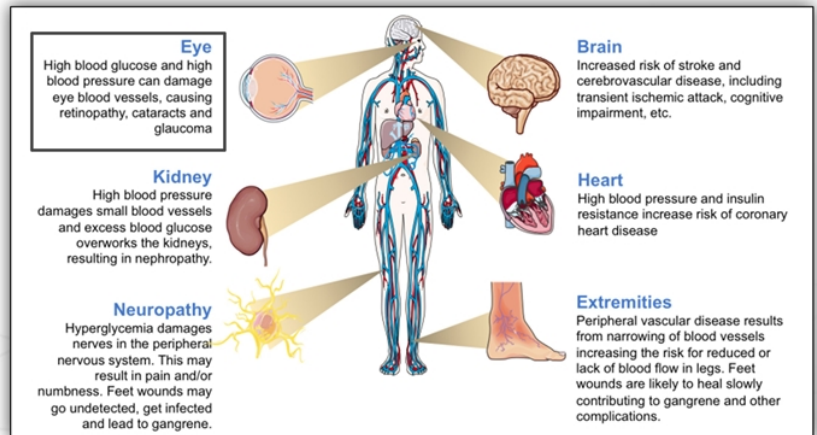
- Vascular leak and pathology leads to devastating consequences in diabetes

- The Solution

- Potential to reverse vascular leak by activating Tie2 with AKB-9778

- The Opportunity

- ~380 million diabetics world-wide increasing to 590 million by 2035
- ~132 million with retinopathy today
- Estimated 7 million Americans with NPDR
- Estimated 4-5 million Americans with NPDR and nephropathy



# Active Tie2 is essential for vascular stability

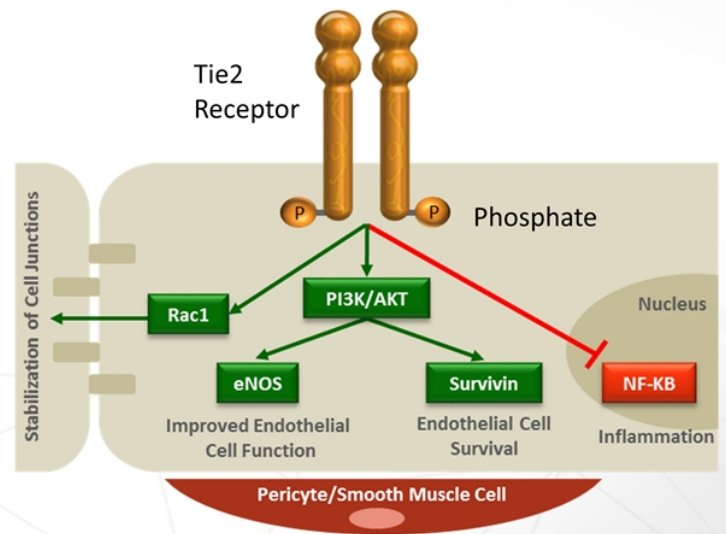
**Tie2** is a transmembrane receptor found on endothelial cells, the foundation for vascular stability

**Tie2** activity...

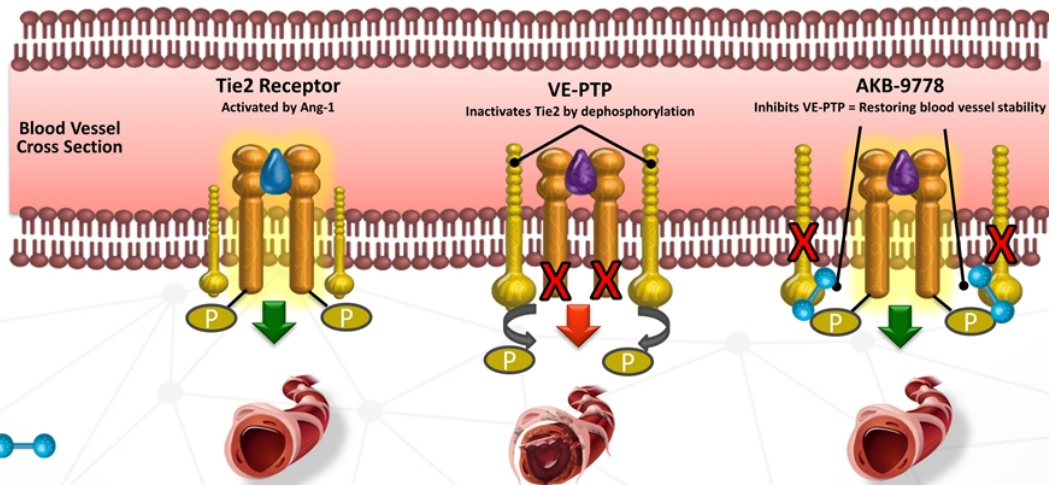
- Maintains integrity of endothelial cell junctions
- Enhances endothelial cell function and viability
- Inhibits vascular inflammation

**Inactive Tie2 = Vascular Destabilization**

- Promotes pathologic vascular leak and neovascularization



# Inhibiting VE-PTP with AKB-9778 reactivates Tie2 and restores endothelial cell stability even with Ang-2 present



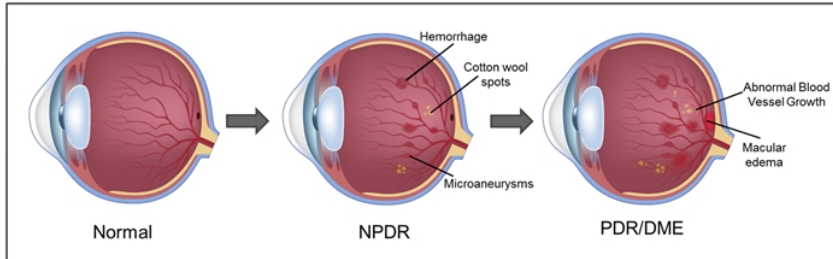
Ang-1 – Angiotensin 1  
Ang-2 – Angiotensin 2  
VE-PTP – Vascular endothelial protein tyrosine phosphatase



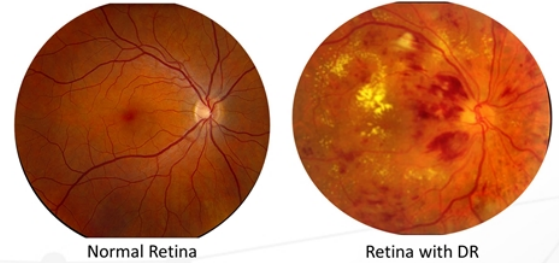
Diabetic Retinopathy and  
AKB-9778 TIME-2 Clinical Data

# Diabetic retinopathy progresses over time and can lead to blindness if untreated

## Progression of Diabetic Retinopathy



## Retinal Photographs



- Diabetic eye disease is a progressive disease characterized by worsening vascular damage
- Vascular damage in the eye leads to leakage of fluid and proteins in the surrounding retinal tissue
- Eventually the damage may be severe enough to cause significant vision loss and potentially blindness

NPDR – Non-proliferative diabetic retinopathy  
PDR – Proliferative diabetic retinopathy  
DME – Diabetic macular edema

# TIME-2 Design & Analyses

## Primary Analysis

- Patients with DME
- Three Arms (n = 144\*)
 

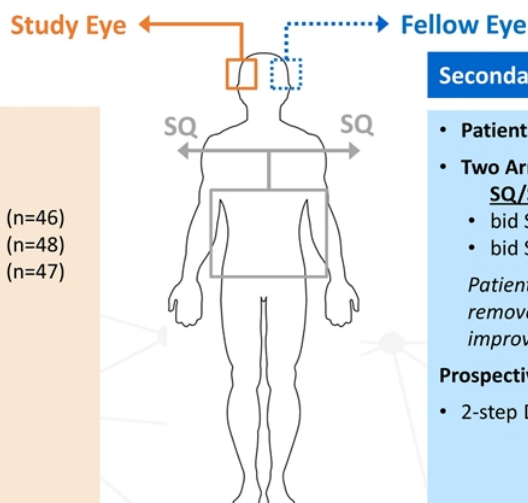
<u>SQ/Systemic</u>	+	<u>Study Eye</u>	
• bid SQ AKB-9778	+	monthly x 3 IVT Sham	(n=46)
• bid SQ AKB-9778	+	monthly x 3 IVT Lucentis	(n=48)
• bid SQ Placebo	+	monthly x 3 IVT Lucentis	(n=47)

### Primary Endpoint

- Change in retinal thickness at month 3

### Secondary Measurements

- 2-step DRSS change at month 3



## Secondary Analysis (Prospective)

- Patients with DRSS 2-6 in study and fellow eye
- Two Arms (n = 128)
 

<u>SQ/Systemic</u>	+	<u>Fellow Eye</u>	
• bid SQ AKB-9778	+	None	(n=90)
• bid SQ Placebo	+	None	(n=38)

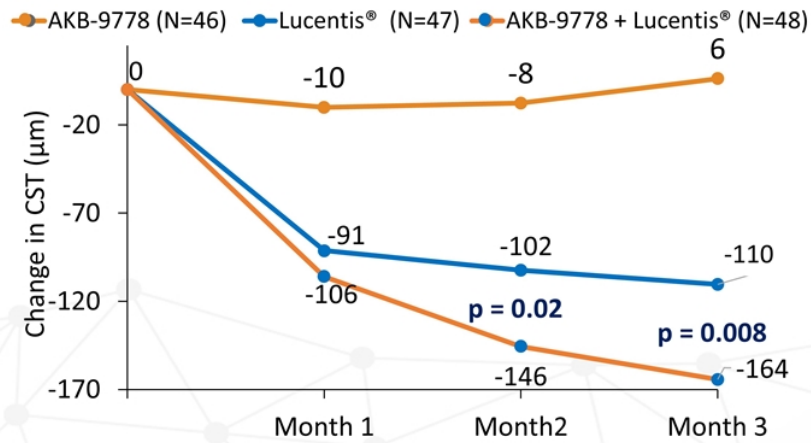
*Patients with DRSS of 1 in fellow eye removed (unable to measure 2-step improvement in DRSS)*

### Prospective Measurements

- 2-step DRSS change at month 3

- DRSS – Diabetic Retinopathy Severity Score
- bid – twice daily
- \* 3 patients withdrew from trial before efficacy measurements determined

## TIME-2: Change in retinal thickness over time



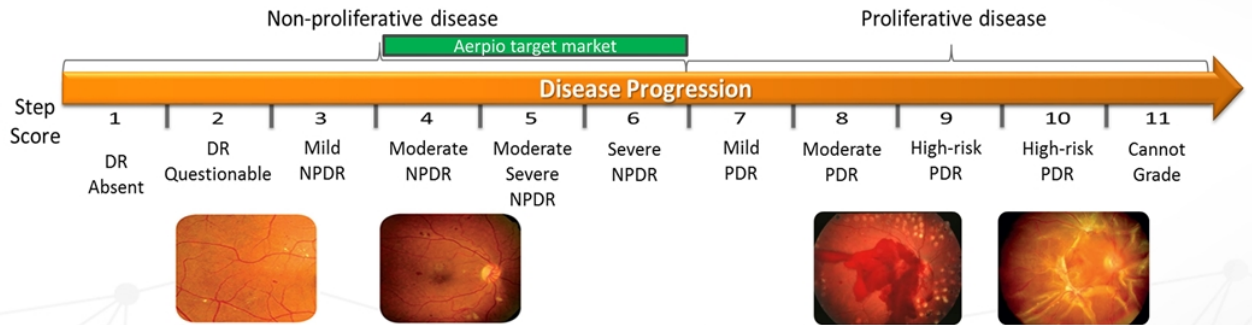
- Phase 1 data showed efficacy as monotherapy in DME prompting testing of monotherapy in phase 2a
- No efficacy seen as monotherapy in primarily VEGF-driven disease (DME)
- Vascular stabilizing effect of combination therapy significantly greater than either agent alone



# Progression of diabetic eye disease is measured using a discrete 11-step scale (Diabetic Retinopathy Severity Score - DRSS)

The FDA bar:  $\geq 2$ -step improvement at 12 months

AKB-9778 has already achieved 2-step improvement at 3 months in TIME-2 trial

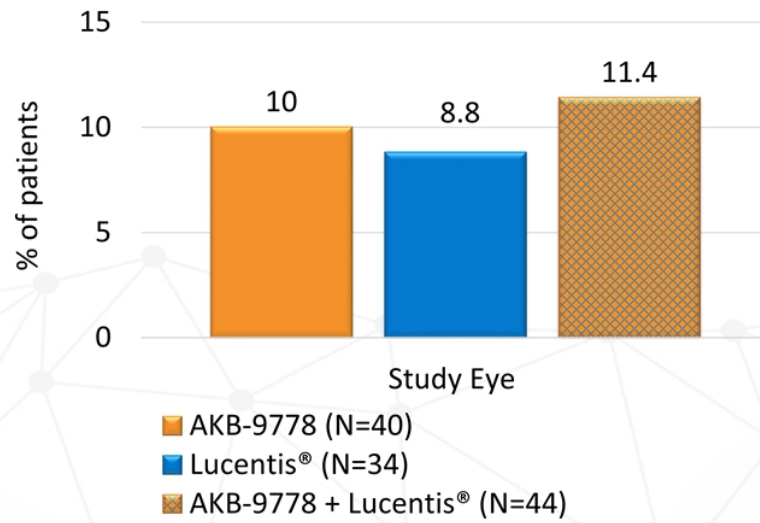


- Risk of vision-threatening events (DME, hemorrhage, retinal detachment, etc.) increases with each step
- Treatment of DR is generally not initiated until later in disease due to the drawbacks of currently available interventions (e.g. laser, intraocular injection)
- Early intervention could slow or prevent disease progression

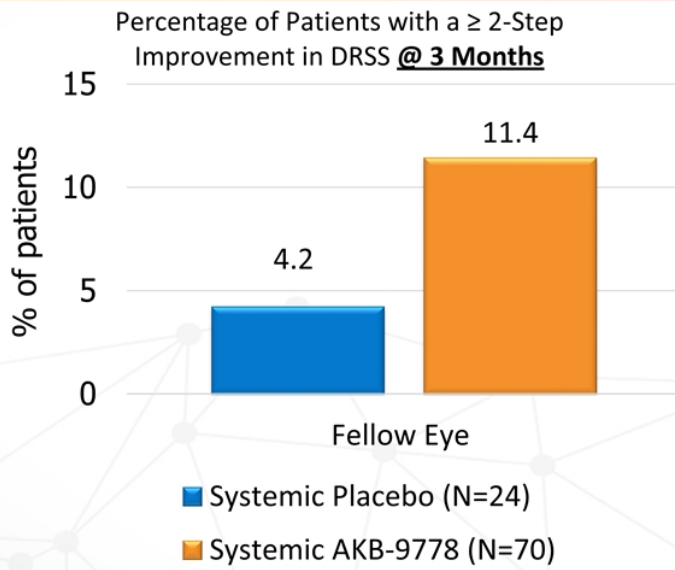
DME – Diabetic macular edema  
 DR – Diabetic retinopathy  
 NPDR – Non-proliferative diabetic retinopathy  
 PDR – Proliferative diabetic retinopathy  
 Klein R et al., *Arch Ophthalmol.*, 2001, Vol. 119.

# Study eye assessment of diabetic retinopathy improvement from TIME-2 study

Percentage of Patients with a  $\geq 2$ -Step Improvement in DRSS @ 3 Months



# Fellow eye assessment of diabetic retinopathy improvement from TIME-2 study

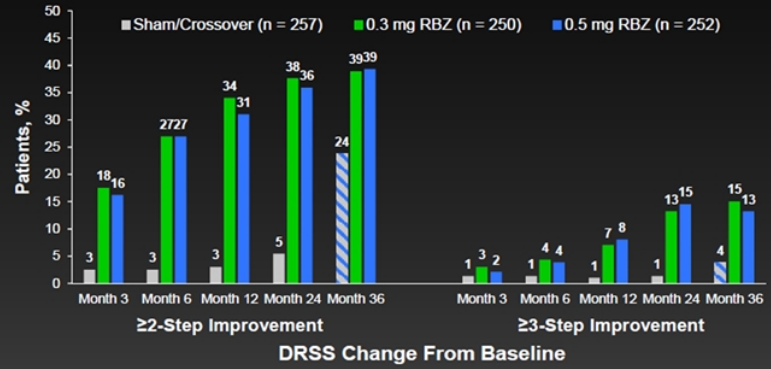


- 2-step improvement expected to increase at one-year timepoint (on-going TIME-2b study)
- Placebo rate of improvement consistent with sham control in Lucentis RISE/RIDE studies (3% at M3, M6 and 12)
- Consistent and bilateral 2-step improvement in DRSS from TIME-2 support biologic activity of AKB-9778

# RISE/RIDE: Improvement of DRSS over time

- Diabetic retinopathy does not improve on its own
- Active therapy improves DRSS over time

## RIDE/RISE: Rapid and Sustained Improvement in Diabetic Retinopathy Through Month 36

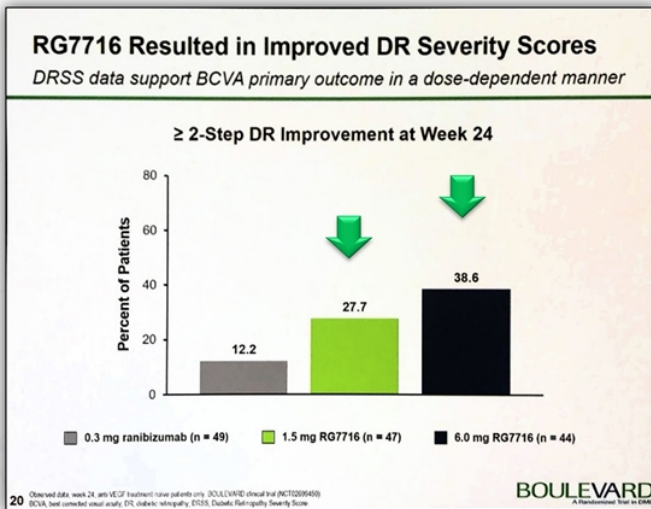


DRSS – Diabetic retinopathy severity score

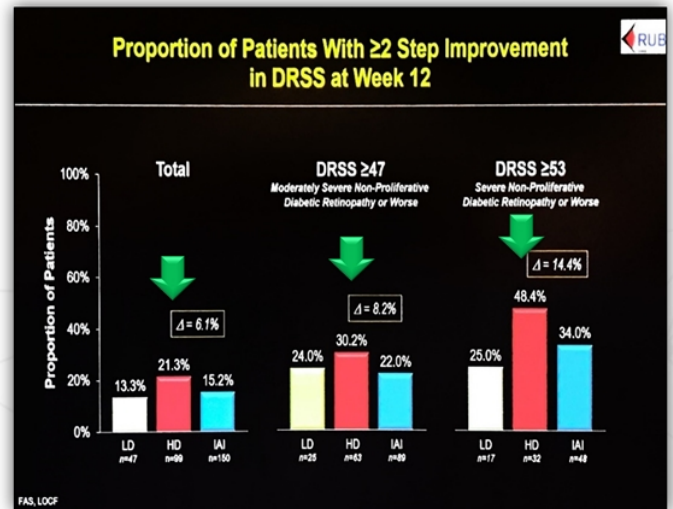
Ophthalmology. 2012 Apr;119(4):789-801; Ranibizumab for diabetic macular edema: results from 2 phase III randomized trials: RISE and RIDE

# Validation by Roche and Regeneron: Aerpio's approach to treating DR via Tie2 activation supported by anti-Ang-2 results

## Roche/Genentech BOULEVARD study (RG7716)



## Regeneron RUBY study (REGN-910)



Dugel, P. RG7716 in Diabetic Macular Edema: Results from the Phase 2 BOULEVARD Study. Angiogenesis, Exudation, and Degeneration; February 10, 2018; Miami, FL.  
Brown, D. Nesvacumab in Diabetic Macular Edema: Results from the Phase 2 RUBY Study. Angiogenesis, Exudation, and Degeneration; February 10, 2018; Miami, FL.

## AKB-9778 development: DR vs. DME

- Promising rationale for development in DR
  - AKB-9778 Monotherapy ability to control DR in equivalent manner to Lucentis (approved therapy for the treatment in DR)
  - Consistent effects seen bilaterally, study and fellow eye
  - Placebo performed in accordance with contemporaneous DR studies: no improvement in absence of therapeutic intervention
  - Regulatory path precedent set by Lucentis ( $\geq$  2-step improvement @ 1-year)
- AKB-9778 product attributes support a potential market-leading profile for patients with DR, good vision, and no center involved DME
  - No need for intraocular injections and no increase in frequency of visits to ophthalmologist
  - Treats both eyes via systemic delivery (>70% patients with DR have bilateral disease)
  - Potential to prevent progression to vision threatening events of PDR and DME
  - May improve diabetes-induced nephropathy and compromise of other vascular beds



Diabetic Retinopathy:  
Patient Numbers and Market Estimates

# NPDR is highly underdiagnosed and a very large market

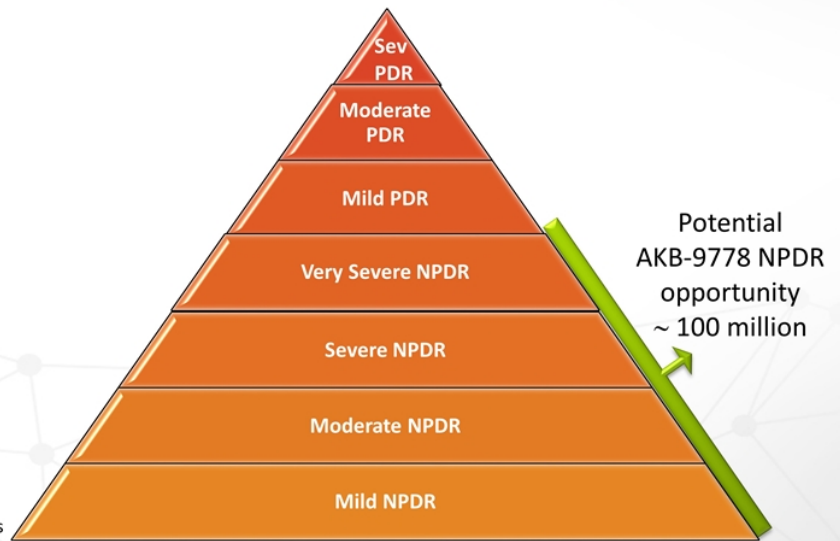
Geography	Estimated Prevalence Diabetes (1)*	Estimated Prevalence of DR (2)*	Estimated Prevalence of NPDR (2,3)*
U.S.	24	8.4	6.7
Europe	50	17	14
China	98	34	27
Japan	12	4	3
ROW	196	69	55
<b>TOTAL</b>	<b>380</b>	<b>132</b>	<b>106</b>

\* Patients Millions

1. Guariguata, L., et al. *Diabetes Res and Clin Practice*, 2014; 103: 137-14

2. Yau J, et al. *Diabetes Care*. 2012;35:556-564. ([10.2337/dc11-1909](https://doi.org/10.2337/dc11-1909))

3. NPDR = all DR minus PDR







AKB-9778:  
TIME-2 Study – Kidney Function Analysis

# Progression of diabetic eye and kidney disease suggest a common pathologic process

Progression of diabetic microvascular disease

**Diabetes with Chronic Endothelial Injury**

↓ Tie2 Activity  
(↑ VE-PTP, ↑ Ang2)

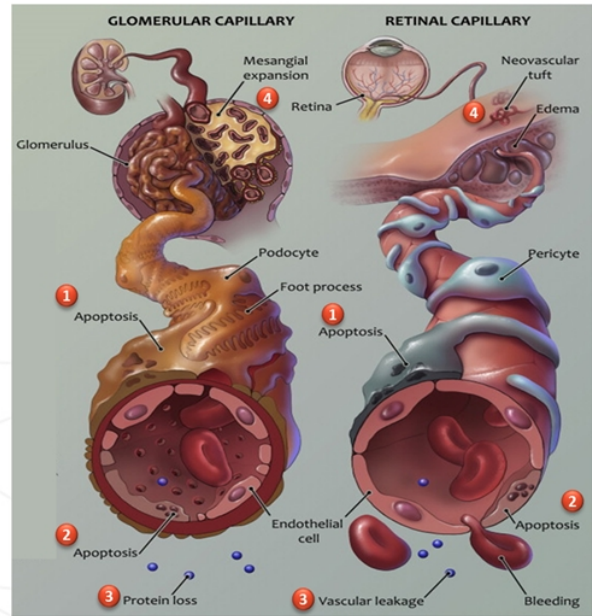
**Vascular Destabilization**  
(support cell loss/endothelial dysfunction) 1

**Vasoregression**  
(endothelial cell death/capillary loss) 2

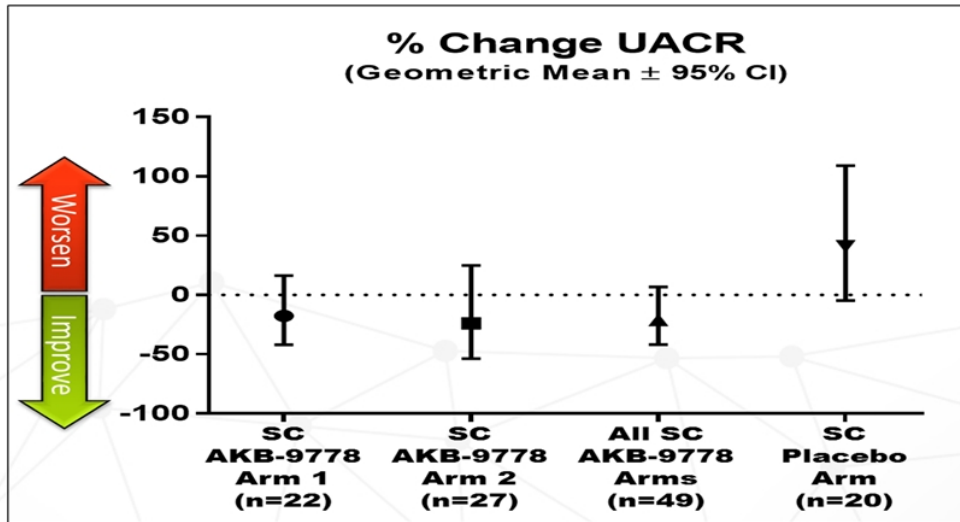
↑ Ischemia

↓ Tie2 and ↑ VEGFR Activity  
(↑ VE-PTP, ↑ Ang2, ↑ VEGF)

**Vascular Leak and Neovascularization** 3 4



# TIME-2 UACR data: Baseline proteinuria subgroup ( $\geq 30$ mg/g)



SC – Subcutaneous

UACR – Urine albumin/creatinine ratio

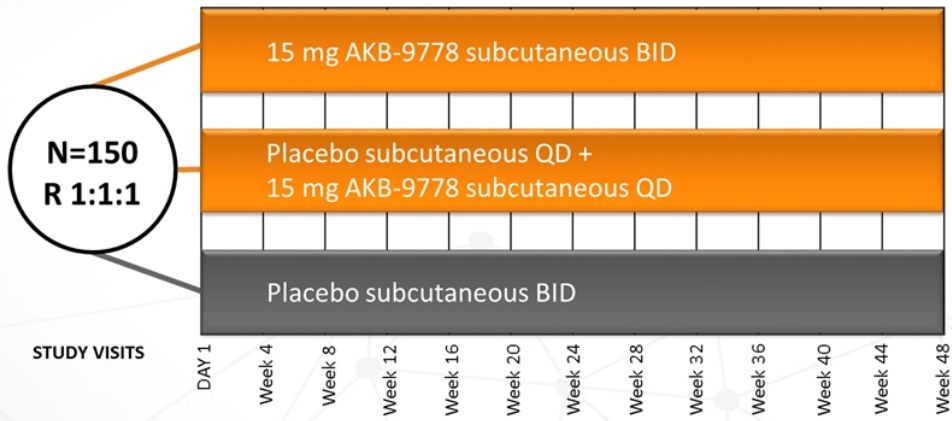
p = 0.03, unadjusted (All SC AKB-9778 vs. SC placebo)

p = 0.006, adjusted for baseline UACR, HgbA1c, and systolic blood pressure (All SC AKB-9778 vs SC placebo)



AKB-9778:  
TIME-2b Study

# TIME-2b: Clinical trial design



- Phase 2b study in pts with moderate to severe non-proliferative diabetic retinopathy (NPDR) without DME
- 1° Endpoint:  $\geq 2$ -step improvement in DRSS at 48 weeks
- Key 2° Endpoints: development of DME/PDR, DR progression, renal function
- Enrollment commenced June 2017, enrollment closed February 2018 at 167 patients, data expected March 2019

DME – Diabetic macular edema  
DR – Diabetic retinopathy  
DRSS – Diabetic retinopathy severity score  
PDR – Proliferative diabetic retinopathy



AKB-9778:  
Primary Open-Angle Glaucoma

## Statistically significant reductions in intraocular pressure were observed in non-glaucoma patients in the TIME-2 study

	AKB-9778 Monotherapy		AKB-9778 + Lucentis®		Lucentis® monotherapy	
	SE	FE	SE	FE	SE	FE
Mean Baseline IOP (mmHG)	15.8	15.4	15.9	16.1	15.2	15.8
Mean Δ from BL (mmHG)	<b>-1.4</b>	<b>-1.4</b>	<b>-1.0</b>	<b>-1.5</b>	0.1	-0.1
t-test Δ BL-Mo 3 (p-value)	<b>&lt;0.01</b>	<b>&lt;0.01</b>	<b>&lt;0.05</b>	<b>&lt;0.01</b>	0.88	0.84

BL = baseline; SE = study eye; FE = Fellow eye

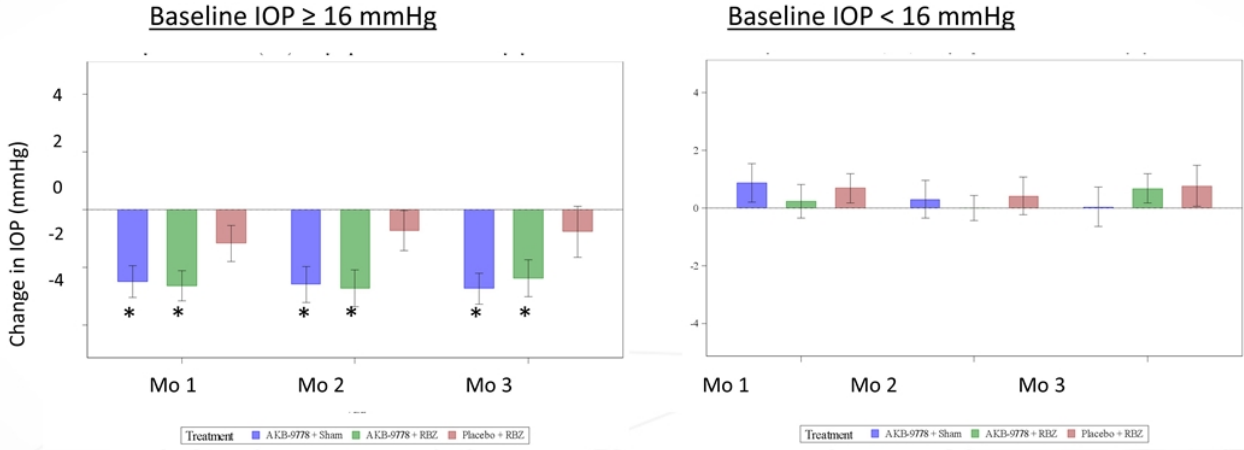
- Reduction of IOP increased to ~ 2-2.5 mm Hg in patients with baseline IOPs ≥ 16 mm Hg, similar to prostaglandin analogs in normotensive glaucoma

Dirks et al. Adv Ther. 23:3, 2006

Khawaja et al. Ophthalmology 121:1501, 2014

Stenkula and Wettrell, Graefe's Arch Clin Exp Ophthalmol 218:96, 1982

# Larger IOP changes seen in patients with higher baseline pressure



\* p<.01



# Loss of Tie2 function leads to increased IOP and glaucoma phenotype in mice and humans

The Journal of Clinical Investigation

RESEARCH ARTICLE

BRIEF REPORT

The Journal of Clinical Investigation

## Impaired angiopoietin/Tie2 signaling compromises Schlemm's canal integrity and induces glaucoma

Jaeryung Kim,<sup>1</sup> Dae-Young Park,<sup>1,2</sup> Hosung Bae,<sup>1</sup> Do Young Park,<sup>1</sup> Dongkyu Kim,<sup>2</sup> Choong-kun Lee,<sup>2</sup> Sukhyun Song,<sup>2</sup> Tae-Young Chung,<sup>3</sup> Dong Hui Lim,<sup>1,4</sup> Yoshiaki Kubota,<sup>5</sup> Young-Kwon Hong,<sup>4</sup> Yulong He,<sup>6</sup> Hellmut G. Augustin,<sup>6</sup> Guillermo Oliver,<sup>7</sup> and Gou Young Koh<sup>1,2</sup>

<sup>1</sup>Graduate School of Medical Science and Engineering, Korea Advanced Institute of Science and Technology (KAIST), Daejeon, Republic of Korea; <sup>2</sup>Center for Vascular Research, Institute for Basic Science, Daejeon, Republic of Korea; <sup>3</sup>Department of Ophthalmology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; <sup>4</sup>Department of Preventive Medicine, Catholic University School of Medicine, Seoul, Republic of Korea; <sup>5</sup>The Laboratory of Vascular Biology, School of Medicine, Keio University, Tokyo, Japan; <sup>6</sup>Department of Surgery, Department of Biochemistry and Molecular Biology, Norris Comprehensive Cancer Center, Beck School of Medicine, University of Southern California, Los Angeles, California, USA; <sup>7</sup>Yoon Sang Hematology Center, Collaborative Innovation Center of Hematology, Soochow University, Suzhou, China; <sup>8</sup>Division of Vascular Oncology and Metastasis, German Cancer Research Center Heidelberg (DKFZ) (DKFZ Alliance), Heidelberg, Germany; <sup>9</sup>Center for Vascular and Developmental Biology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

## A lymphatic defect causes ocular hypertension and glaucoma in mice

Benjamin R. Thomson,<sup>1</sup> Stefan Heinen,<sup>2</sup> Marie Jeansson,<sup>1</sup> Ashish K. Ghosh,<sup>1</sup> Anees Fatima,<sup>1</sup> Hoon-Ki Sung,<sup>2</sup> Tuncer Onay,<sup>1</sup> Hui Chen,<sup>4</sup> Shinji Yamaguchi,<sup>1</sup> Aris N. Economides,<sup>5</sup> Ann Flenniken,<sup>2</sup> Nicholas W. Gale,<sup>5</sup> Young-Kwon Hong,<sup>6</sup> Amani Fawzi,<sup>4</sup> Xiaorong Liu,<sup>4,7</sup> Tsutomu Kume,<sup>1</sup> and Susan E. Quaggin<sup>1,2</sup>

<sup>1</sup>Feinberg Cardiovascular Research Institute, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>2</sup>Lunenfeld-Tanenbaum Research Institute, Mt. Sinai Hospital, Toronto, Ontario, Canada; <sup>3</sup>Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden; <sup>4</sup>Department of Ophthalmology, Northwestern University, Chicago, Illinois, USA; <sup>5</sup>Regeneron Pharmaceuticals, Tarrytown, New York, USA; <sup>6</sup>Honoris Comprehensive Cancer Center, Keck School of Medicine, University of Southern California, Los Angeles, California, USA; <sup>7</sup>Department of Neurobiology, Northwestern University, Evanston, Illinois, USA

COMMENTARY

The Journal of

## All TIEd up: mechanisms of Schlemm's canal maintenance

Jeremiah Bernier-Latmani<sup>1</sup> and Tatiana V. Petrova<sup>1,2</sup>

<sup>1</sup>Department of Fundamental Oncology, Ludwig Cancer Research, Lausanne Branch, and Institute of Pathology, Centre Hospitalier Universitaire Vaudois and University of Lausanne, Lausanne, Switzerland; <sup>2</sup>Swiss Institute for Experimental Cancer Research (ISREC), School of Life Sciences, Swiss Federal Institute of Technology Lausanne (EPFL), Lausanne, Switzerland

**JCI** The Journal of Clinical Investigation  
Published by The American Society for Clinical Investigation | Founded 1908

J Clin Invest. 2016 Jul 1; 126(7): 2575–2587.

Published online 2016 Jun 6. doi: [10.1172/JCI85830](https://doi.org/10.1172/JCI85830)

PMCID: PMC4922711

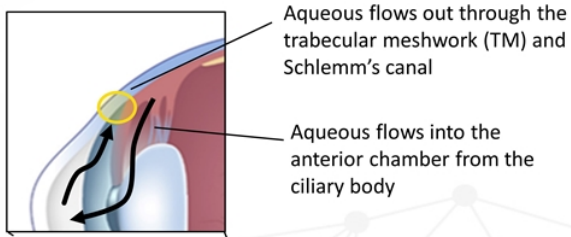
PMID: [27270174](https://pubmed.ncbi.nlm.nih.gov/27270174/)

## Angiopoietin receptor TEK mutations underlie primary congenital glaucoma with variable expressivity

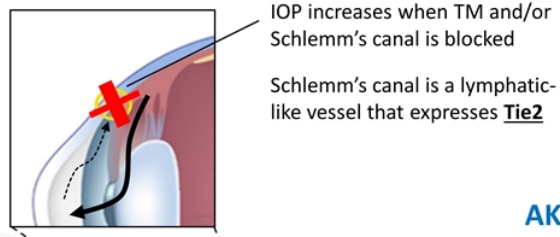
# Ocular hypertension and pathology of glaucoma:

*AKB-9778 presents a potentially new MOA that affects the main pathway in IOP reduction*

**Eye without glaucoma**

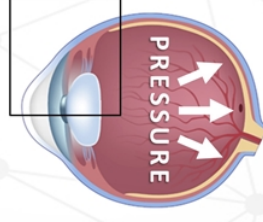
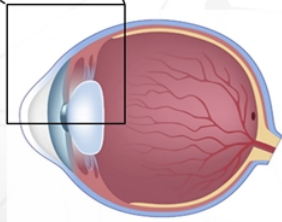


**Eye with glaucoma**



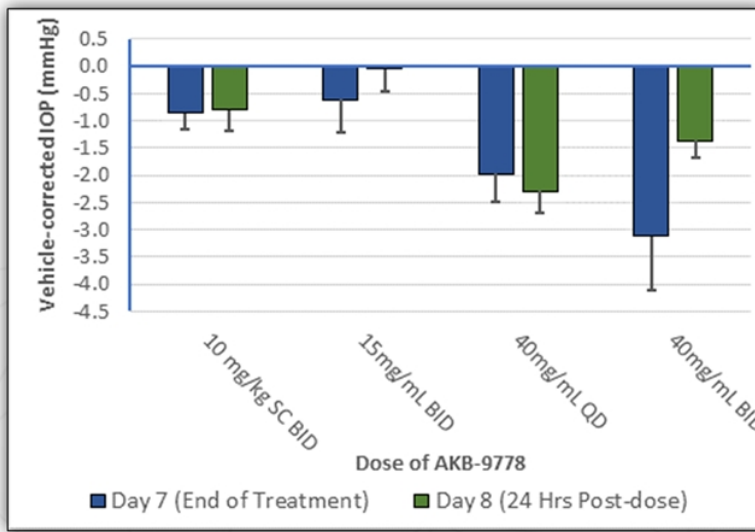
**AKB-9778: New MOA to affect outflow through the TM**

*Tie2 maintains vascular stability of Schlemm's canal*



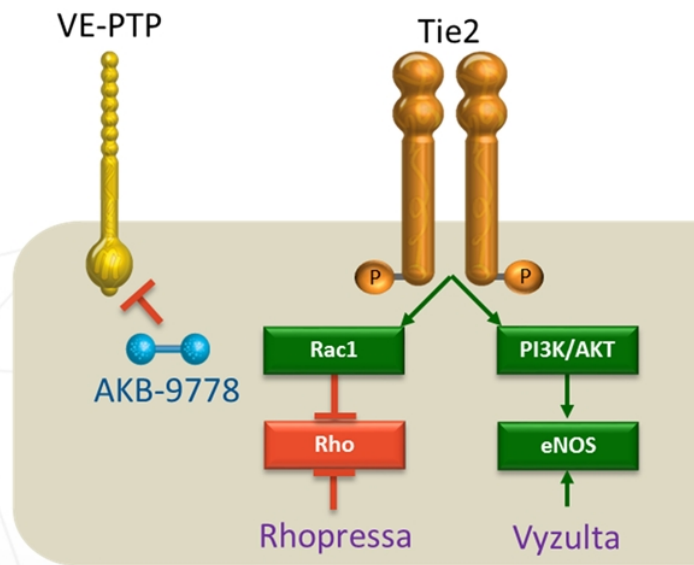
# Dose related IOP decrease observed after topical ocular administration of AKB-9778

## Normotensive New Zealand White Rabbits



# Inhibition of VE-PTP activates Tie2 & affects downstream Rho kinase and eNOS activity mechanistically

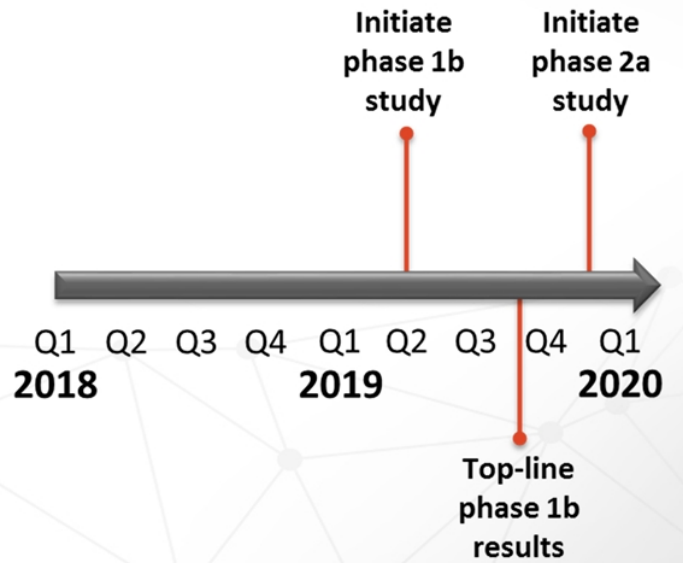
- AKB-9778 could act upstream from effects of recently approved glaucoma products Rhopressa and Vyzulta



# AKB-9778 in primary open-angle glaucoma

## AKB-9778 Target Product Profile

Primary Indication	Reduction of elevated intraocular pressure (IOP)
Target Pt. Population	Primary open angle glaucoma / ocular hypertension
Route of Administration	Self administered topical installation
Dosing Schedule	1 drop QD (blow fill seal, 0.3 ml, single-dose)
Efficacy	In adjunctive setting: Additive effect of at least 1.5 mm Hg when used as adjunct to first-line treatment
	In monotherapy setting: IOP reduction of at least 5 mm Hg (or 20%) OR at least 3 mm Hg compared to placebo
Safety/Tolerability	Lack of significant rate of systemic and ocular side effects seen with other classes of drugs (eg, Systemic: cardiovascular, respiratory, headache, drowsiness, depression, dry mouth, taste disturbance; Ocular: allergy, iris/skin discoloration, blurred vision, hyperemia).
	First-line therapy of choice in adjunctive setting
Positioning	First-line for patients where an alternative to prostaglandin analog (PGA) desired: PGA-intolerant or PGA-nonresponsive patients; concerns re PGA-associated cosmetic side effects

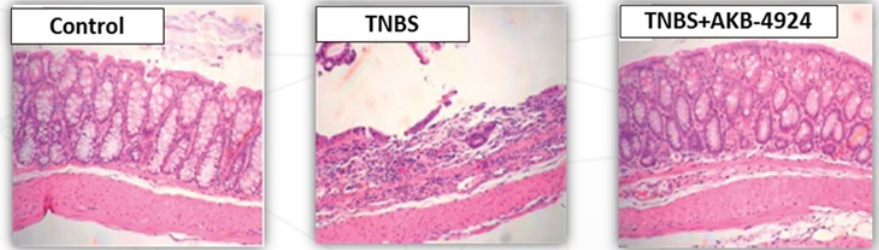




AKB-4924:  
Inflammatory Bowel Disease

# AKB-4924 efficacy demonstrated in multiple models of IBD

- Pre-clinical proof-of-concept across multiple models of IBD in both the induction and maintenance setting
  - TNBS-induced colitis
    - Wild type mice (below)
    - Chronic granulomatous disease mice
  - DSS-induced colitis
  - Genetic TNF $\alpha$  overexpression induced Crohn's Disease
  - Gut Graft Versus Host Disease



Normal Gut

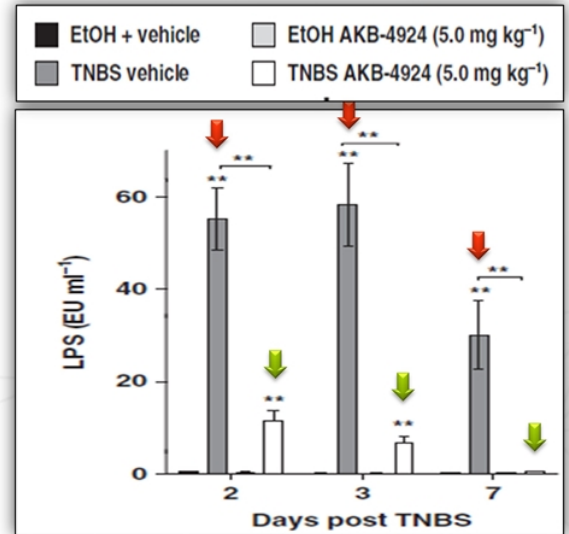
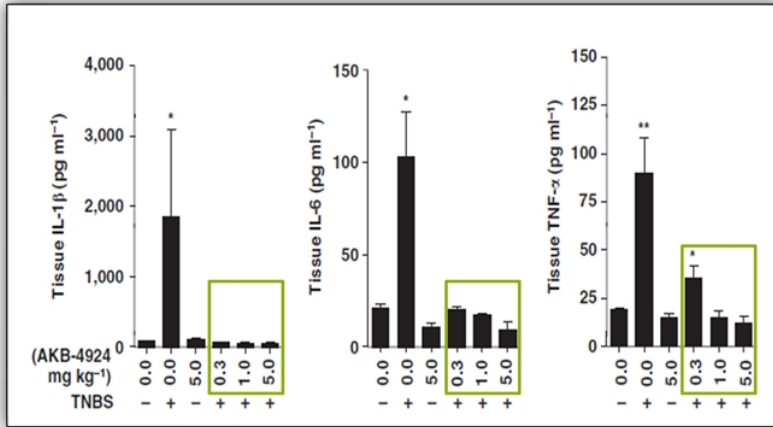
TNBS-Induced Colitis

AKB-4924 Prevention of TNBS Colitis

DSS – dextran sodium sulfate  
IBD – inflammatory bowel disease  
TNBS – trinitrobenzene sulphonic acid  
TNF $\alpha$  – tumor necrosis factor alpha

# AKB-4924 decreases colonic cytokine levels and enhances mucosal healing restoring gut wall integrity in preclinical models

AKB-4924 reduces levels of proinflammatory cytokines in target tissue (colon)

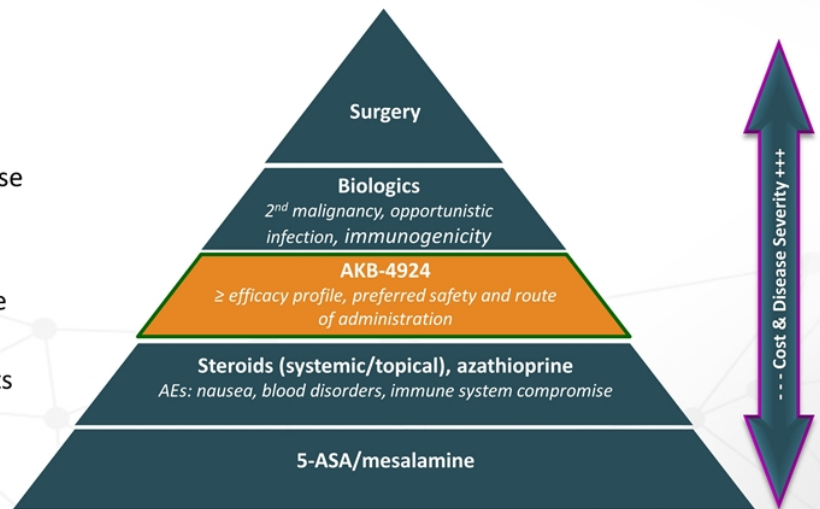


AKB-4924 reduces levels of circulating bacterial endotoxin (LPS) from the gut secondary to restoration of barrier function



# AKB-4924 in inflammatory bowel disease

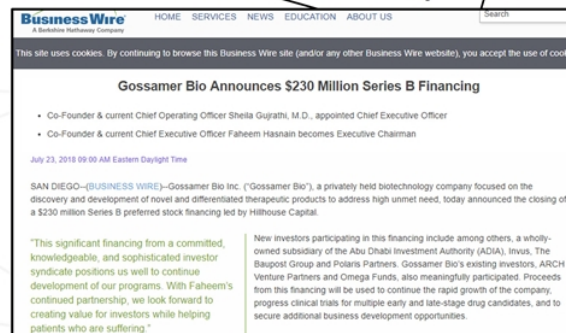
- First-in-class, HIF-1 $\alpha$  stabilizer for IBD
- Designed to address major unmet needs in IBD
- Efficacy and safety profile in preclinical models and early human studies support a preferred profile for moderate/severe and potentially earlier stage disease vs. current standard of care
- Oral, once-daily route of administration
- Completed Phase 1 SAD, currently performing Phase 1 MAD
  - Colon biopsies, drug concentration, local effects
  - Phase 1 MAD results expected Q4 2018
- Proof-of-concept data anticipated in Q3 2019



HIF-1 $\alpha$  – hypoxia inducible factor-1 alpha  
IBD – inflammatory bowel disease  
SAD – single ascending dose; MAD – multiple ascending dose

# AKB-4924 Partnered with Gossamer Bio

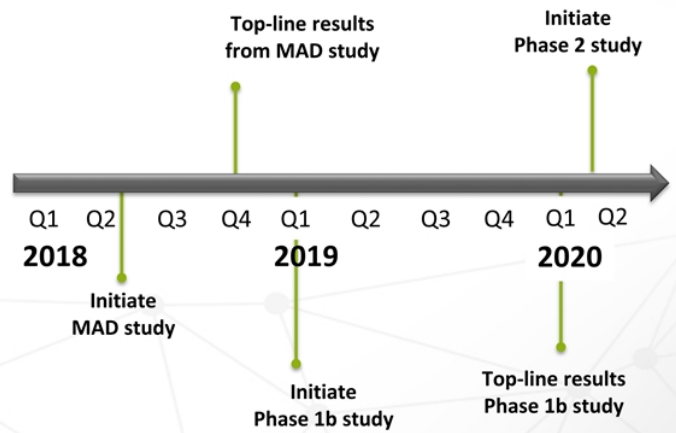
- Gossamer Bio founded by former Receptos team of Faheem Hasnain and Sheila Gujrathi, MD
  - Receptos sold to Celgene in 2015 for \$7.2 billion after Phase 2 IBD and MS trials
- \$20 million upfront payment for exclusive worldwide rights to AKB-4924 (now named GB004)
- \$400 million in potential development and commercial milestones
- Tiered royalties ranging from high single-digit to mid-teen percentages on annual sales
- Potential option to participate in sale of GB004 or the company in exchange for relinquishing existing royalty and milestones



# AKB-4924 in inflammatory bowel disease

## AKB-4924 Target Product Profile

Primary Indication	<ul style="list-style-type: none"> <li>- Inducing and maintaining clinical response &amp; remission</li> <li>- Improving endoscopic appearance of the mucosa</li> <li>- Achieving corticosteroid-free remission</li> </ul>
Target Pt. Population	Moderate/Severe Ulcerative Colitis
Route of Administration	PO (enteric-coated tablet)
Dosing Schedule	Once daily
Efficacy	Non-inferior to infliximab
Safety/ Tolerability	Lack of secondary malignancy, opportunistic infection, or immunogenicity reactions
Positioning	First-line therapy of choice in moderate to severe ulcerative colitis

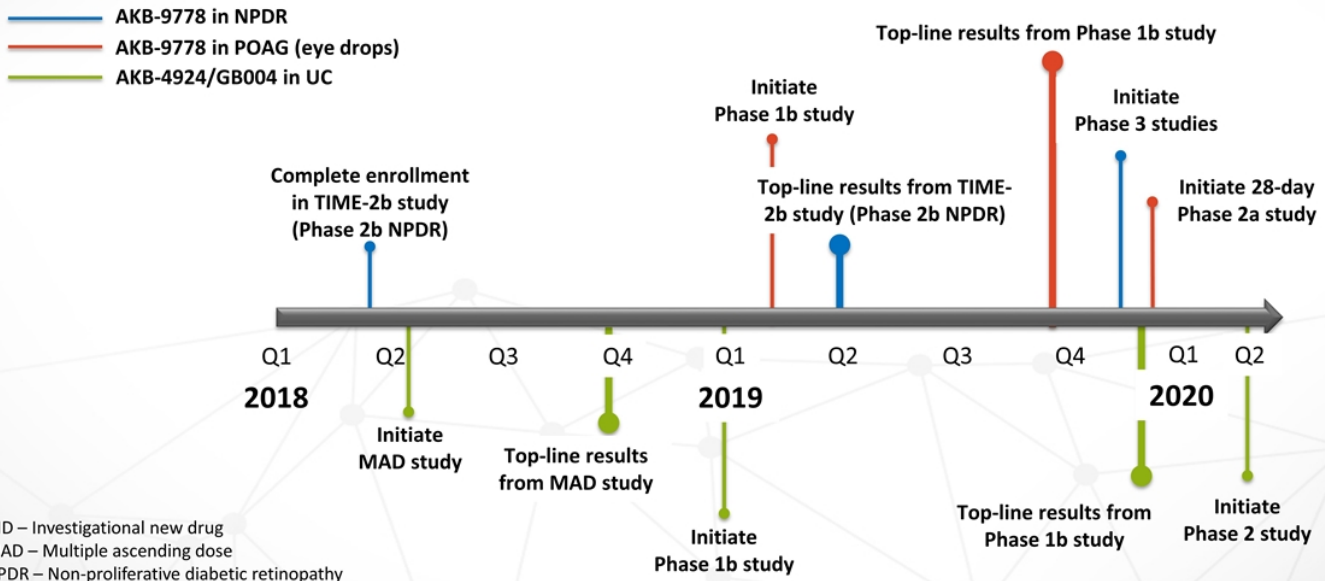


IND – investigational new drug  
MAD – multiple ascending dose  
PO – Oral



## Milestones and Summary

# Milestone rich timeline over next 18 months



IND – Investigational new drug  
MAD – Multiple ascending dose  
NPDR – Non-proliferative diabetic retinopathy  
POAG – Primary open angle glaucoma  
UC – Ulcerative colitis

# Aerpio corporate highlights

- Tie2 pathway validated in the treatment of diabetic microvascular disease
  - Preclinical evidence suggests AKB-9778 seals vascular leak models of diabetic retinopathy and nephropathy
  - AKB-9778 TIME-2 data demonstrates clinical activity 4 ways: DRSS improvement in study and fellow eyes, DME in combination w Lucentis, decrease IOP and improvement in UACR
  - Further validation of Tie2 activation with Regeneron and Roche diabetic retinopathy data
  - Large commercial opportunity
- TIME-2b Phase 2b study in non-proliferative diabetic retinopathy (NPDR), fully enrolled 3 months ahead of projection and increased to 167 patients – Data expected March 2019
  - Treat both eyes and possibly kidney without treatment burden of intravitreal injection
- Advancing distinct development program in primary open-angle glaucoma
- AKB-4924 new, differentiated mechanism to treat IBD with premier corporate partner, Gossamer Bio
- Strong balance sheet after \$50 million follow-on financing, uplisting to NASDAQ and Gossamer partnership
- Multiple potential clinical catalysts starting in Q4 2018



[www.aerpio.com](http://www.aerpio.com)