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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): April 10, 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 April 10, 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: April 10, 2019

**AERPIO PHARMACEUTICALS, INC.**

By: /s/ Stephen Hoffman

Stephen Hoffman

Chief Executive Officer



# Corporate Presentation

April 10, 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

- Developing first-in-class treatments for ocular diseases and complications of diabetes
- Lead asset: AKB-9778, a Tie2 activator, which is a key regulator of vascular stability
- TIME-2b Phase 2 clinical trial in patients with non-proliferative diabetic retinopathy missed its primary endpoint but:
  - Reproduced evidence of improved kidney function (UACR) in patients early diabetic nephropathy
  - Reproduced reduction in IOP seen in TIME-2; data to be presented at ARVO April 28 – May 2, 2019
  - Full data analysis at an upcoming medical conference
- Pipeline opportunities
  - Phase 1b of topical ocular AKB-9778 for evaluation in open-angle glaucoma expected to begin Q2 2019
  - Will seek pharma partner to further study slowing diabetic nephropathy of subcutaneous AKB-9778
  - Gossamer partnership on GB004: up to \$400M in milestones, tiered royalties to mid-teens, option to participate in sale of GB-004
  - ARP-1536: humanized Mab that activates Tie2
- Strong balance sheet (\$62.6 million end of 2018), expense reduction, cash to mid-2021



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

# Active Tie2 is essential for vascular stability

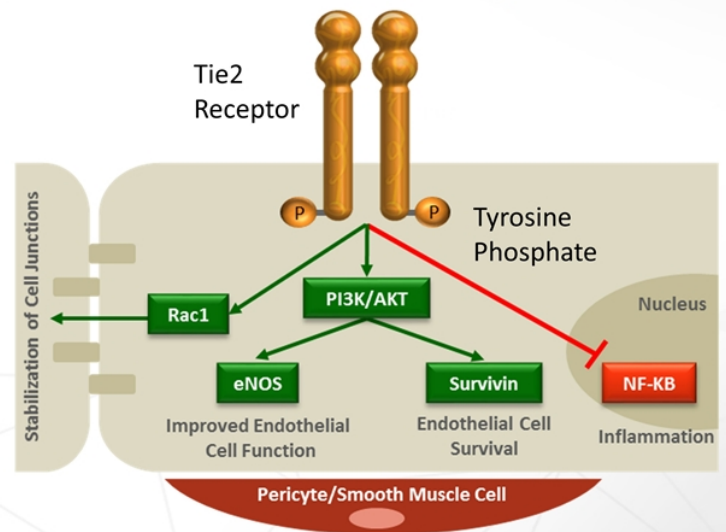
**Tie2** is a transmembrane receptor found on endothelial cells, the foundation for vascular stability, and for formation and maintenance of Schlemm's canal and the conventional outflow tract in the eye

## **Tie2** activity...

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

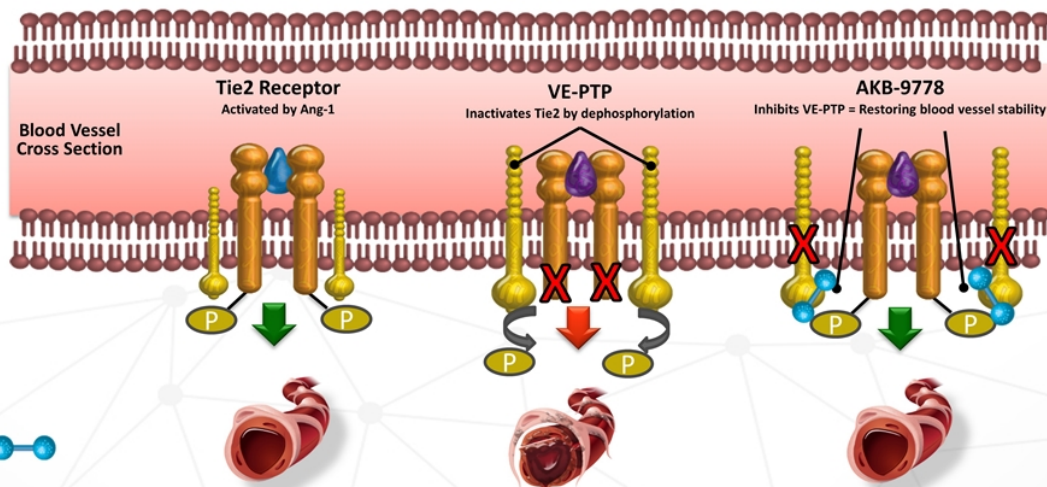
## **Inactive Tie2 = Vascular Destabilization**

- Promotes pathologic vascular leak, neovascularization and elevated intra-ocular pressure





# Inhibiting VE-PTP with AKB-9778 restores Tie2 activation and endothelial cell stability even in absence of Ang1

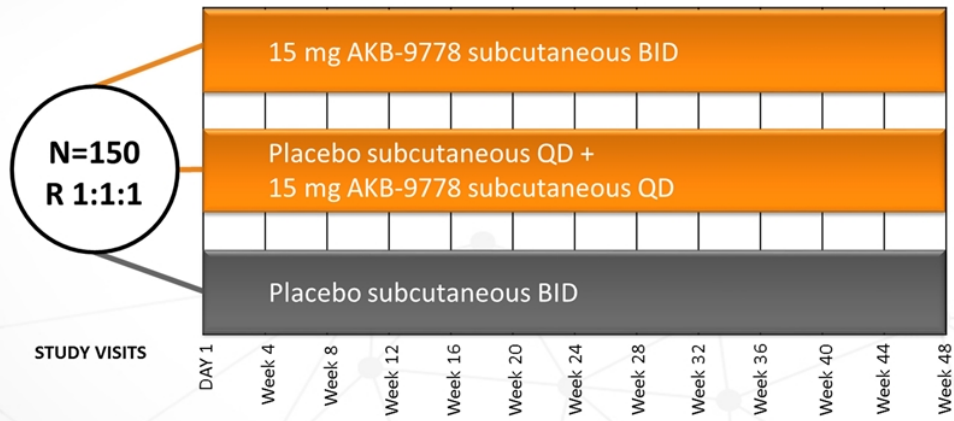


Ang-1 – Angiotensin 1  
Ang-2 – Angiotensin 2  
VE-PTP – Vascular endothelial protein tyrosine phosphatase



TIME-2b Clinical Trial:  
AKB-9778 in Non-Proliferative Diabetic  
Retinopathy

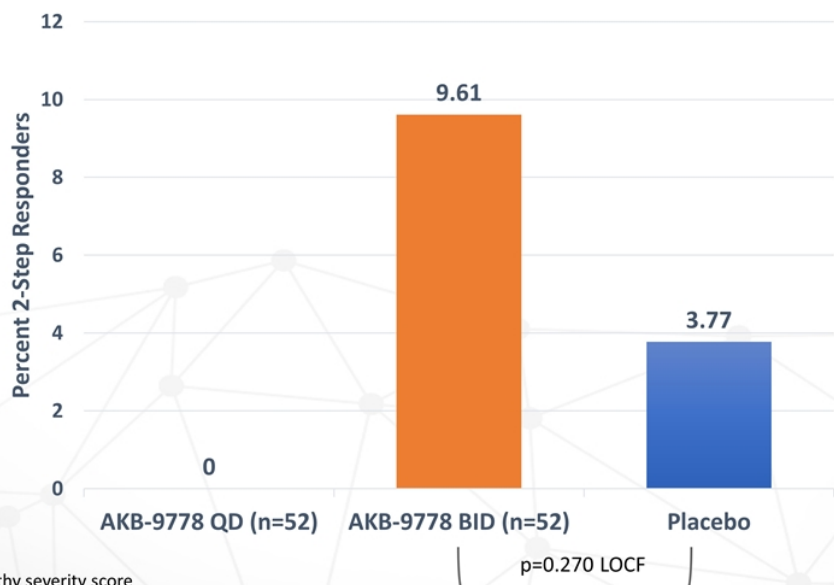
# TIME-2b: Clinical trial design



- 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
- Top-line data announced March 18, 2019

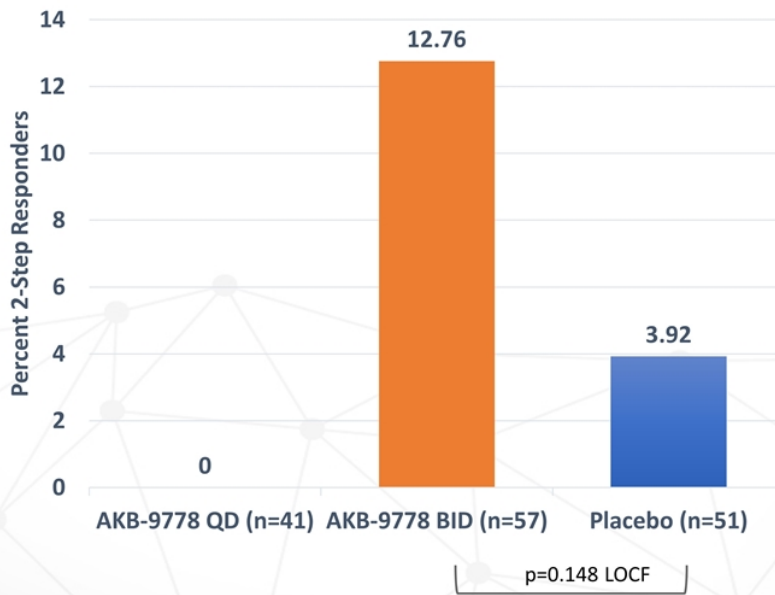
DME – Diabetic macular edema  
DR – Diabetic retinopathy  
DRSS – Diabetic retinopathy severity score  
PDR – Proliferative diabetic retinopathy

# TIME-2b Primary Endpoint: $\geq 2$ -step Improvement in DRSS in Study Eye

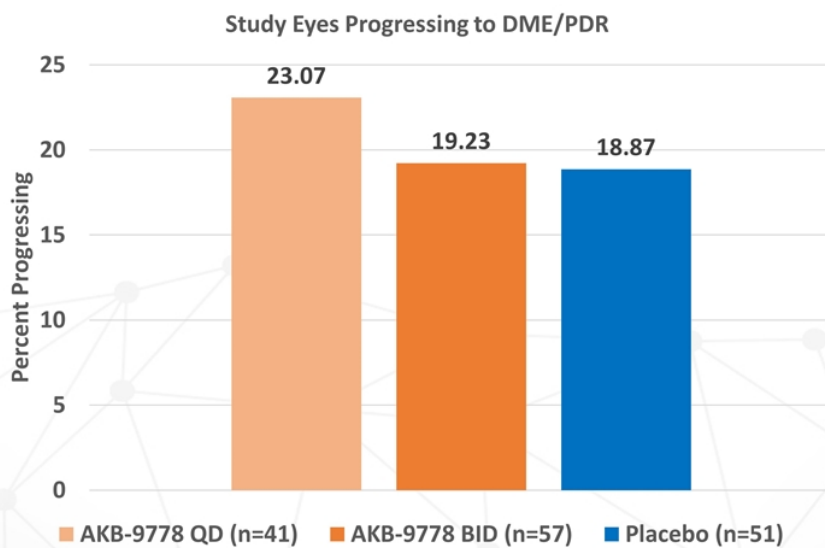


DRSS – Diabetic retinopathy severity score

# TIME-2b Primary Endpoint in All Qualified Eyes with Baseline DRSS 5 or 6 (moderately severe & severe NPDR)



# Progression to Vision-Threatening Complications (DME and/or PDR)



## TIME-2b: Safety and Tolerability

- Generally safe and well tolerated
- One death in subject receiving placebo
- Dizziness AE 10.9% in AKB-9778 BID vs 7.0% in the placebo arm (vast majority rated as mild, and none rated as severe)
- Headache of 10.9% in AKB-9778 BID vs 3.5% in the placebo arm (all rated as mild)
- Withdrawals due to AE and SAEs were balanced between AKB-9778 BID and placebo groups



AKB-9778: Kidney Function  
TIME-2 and TIME-2b Data



# Diabetic kidney disease is a major problem

## ~30 million diabetics in the United States

Approximately 40% have kidney disease

- The overall prevalence of CKD in the general population is approximately 14 percent
- More than 661,000 Americans have kidney failure
- 468,000 individuals are on dialysis
  - \$89,000 per year
  - \$42 billion per year in the US
- 193,000 live with a functioning kidney transplant
- Each year, kidney disease kills more people than breast or prostate cancer



**Diabetic  
Nephropathy  
12 M**

# 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)

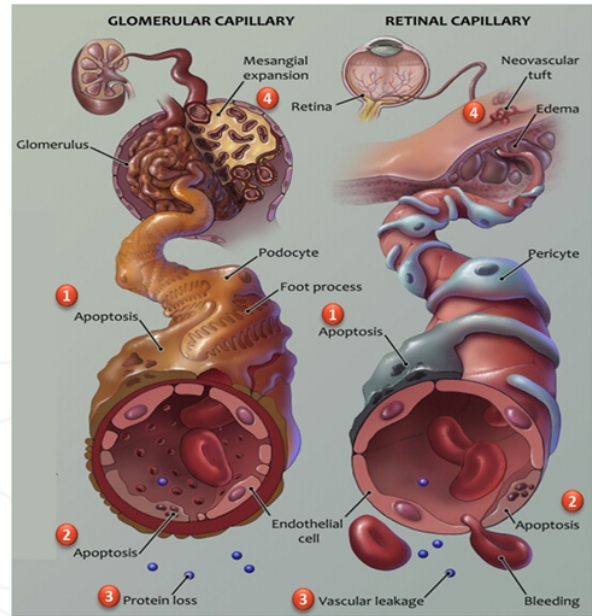
**Vascular Destabilization**  
(support cell loss/endothelial dysfunction) 1

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

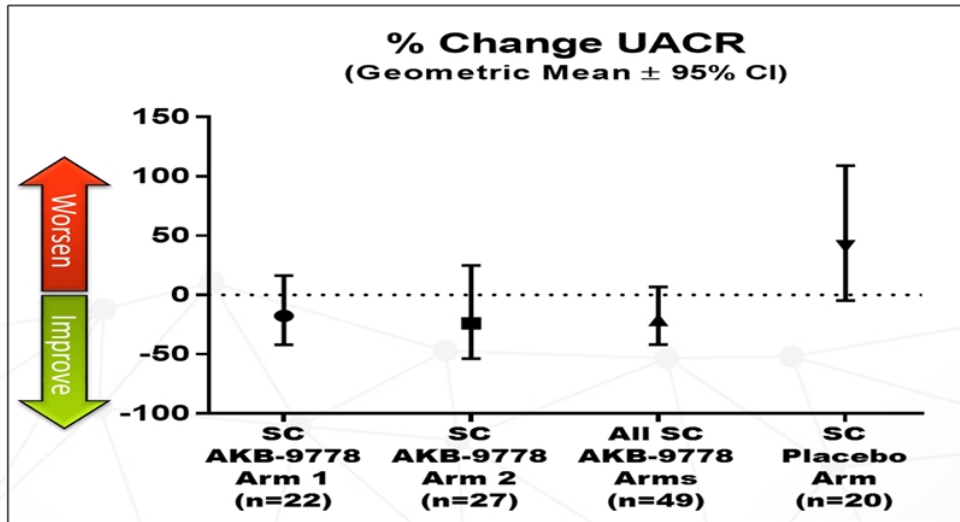
↑ Ischemia

↓ 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)

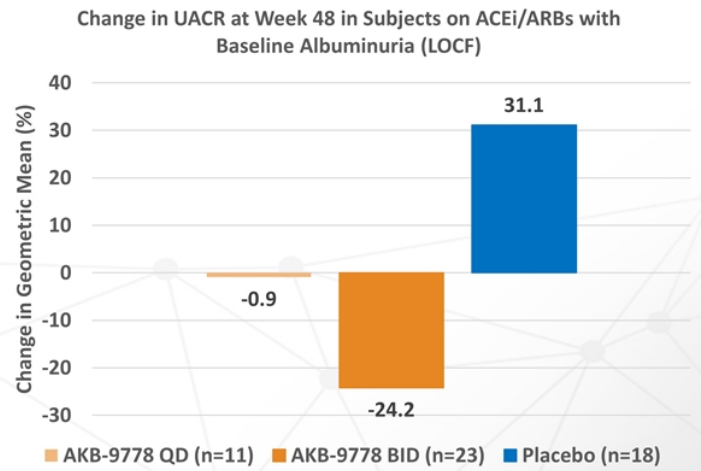
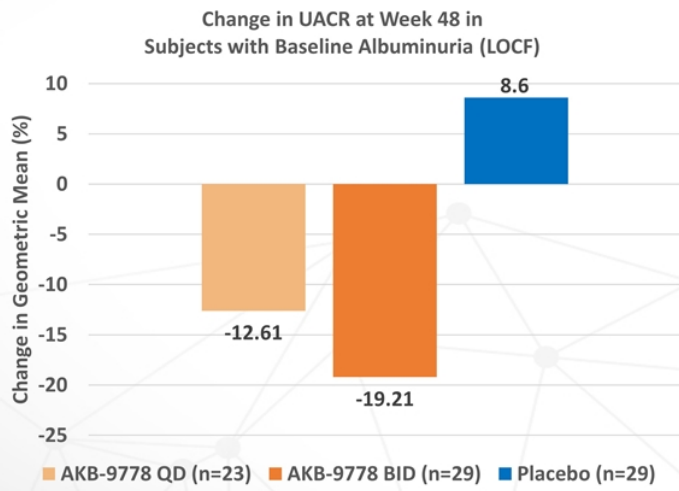
p = 0.006, adjusted for baseline UACR, HgbA1c, and systolic blood pressure (All SC AKB-9778 vs SC placebo)

## TIME-2b: Baseline UACR Status

	AKB-9778 QD (N=55)	AKB-9778 BID (N=55)	Placebo (N=57)	Overall (N=167)
Median UACR	29.65	37.90	37.55	37.55
UACR Category				
Normalalbuminuria (<30mg/g)	28	24	24	75
Albuminuria (≥30mg/g)	26	31	33	90
Microalbuminuria (30-299mg/g)	20	16	22	58
Macroalbuminuria (≥300mg/g)	6	15	11	32
Not Available	1	0	0	1

# TIME-2b Data – Prespecified Endpoint

Prespecified Endpoint: Percent Change in UACR for Patients with Baseline Proteinuria ( $\geq 30$  mg/g)  
– All Patients and Patients On ACEi/ARB Therapy



% Change in Geometric Mean  
UACR – Urine albumin/creatinine ratio



## 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

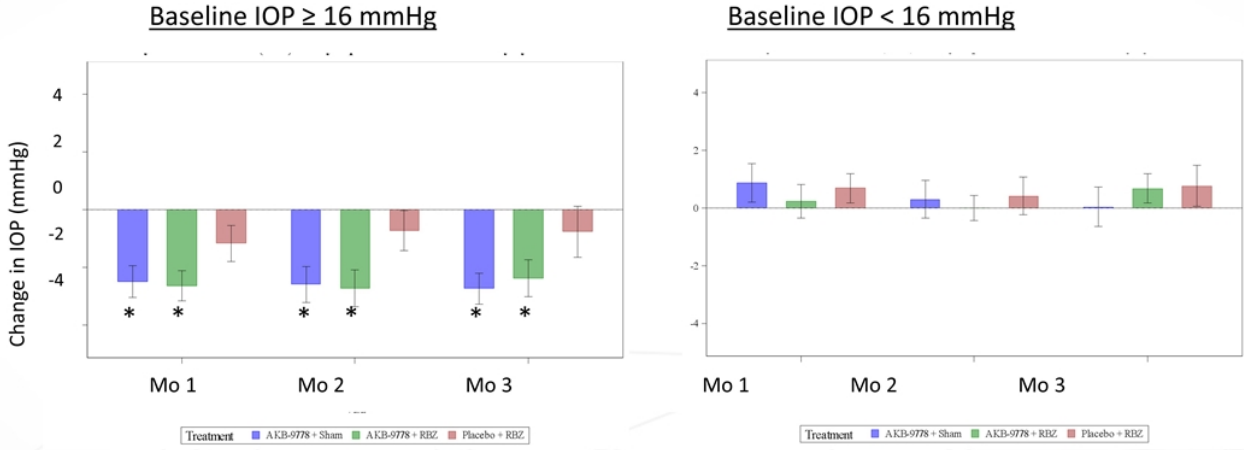
- Reduction of IOP increased to ~ 2-2.5 mm Hg in patients with baseline IOPs ≥ 16 mm Hg, similar to prostaglandin analogs in normotensive glaucoma

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



# Tie2 Pathway Activation is Critical for Development and Maintenance of Schlemm's Canal and Conventional Outflow: Mouse and Human Genetic Data

BRIEF REPORT

The Journal of Clinical Investigation

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

Benjamin R. Thomson,<sup>1</sup> Stefan Heinen,<sup>2</sup> Marie Jeansson,<sup>3</sup> Asish K. Ghosh,<sup>4</sup> Anees Fatima,<sup>5</sup> Hoon-Ki Sung,<sup>6</sup> Tuncer Onay,<sup>7</sup> Hui Chen,<sup>8</sup> Shinji Yamaguchi,<sup>9</sup> Aris N. Economides,<sup>10</sup> Ann Flenniken,<sup>11</sup> Nicholas W. Gale,<sup>12</sup> Young-Kwon Hong,<sup>13</sup> Amani Fawzi,<sup>14</sup> Xiaorong Liu,<sup>15</sup> Tsutomu Kume,<sup>16</sup> and Susan E. Quaggin<sup>17</sup>

<sup>1</sup>Feiberg 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>Department of Ophthalmology, Northwestern University, Chicago, Illinois, USA; <sup>6</sup>Department of Ophthalmology, Northwestern University, Chicago, Illinois, USA; <sup>7</sup>Department of Ophthalmology, Northwestern University, Chicago, Illinois, USA; <sup>8</sup>Department of Ophthalmology, Northwestern University, Chicago, Illinois, USA; <sup>9</sup>Department of Ophthalmology, Northwestern University, Chicago, Illinois, USA; <sup>10</sup>Department of Ophthalmology, Northwestern University, Chicago, Illinois, USA; <sup>11</sup>Department of Ophthalmology, Northwestern University, Chicago, Illinois, USA; <sup>12</sup>Department of Ophthalmology, Northwestern University, Chicago, Illinois, USA; <sup>13</sup>Department of Ophthalmology, Northwestern University, Chicago, Illinois, USA; <sup>14</sup>Department of Ophthalmology, Northwestern University, Chicago, Illinois, USA; <sup>15</sup>Department of Ophthalmology, Northwestern University, Chicago, Illinois, USA; <sup>16</sup>Department of Ophthalmology, Northwestern University, Chicago, Illinois, USA; <sup>17</sup>Department of Ophthalmology, Northwestern University, Chicago, Illinois, USA

Tie2 KO or Angpt-1/2 KO in mice results in congenital glaucoma due failed Schlemm's canal development

The Journal of Clinical Investigation

## Angiopoietin-1 is required for Schlemm's canal development in mice and humans

Benjamin R. Thomson,<sup>1,2</sup> Tomokazu Souma,<sup>3</sup> Stuart W. Tompson,<sup>4</sup> Tuncer Onay,<sup>5</sup> Krishnakumar Kizhathil,<sup>6</sup> Owen M. Siggs,<sup>7</sup> Liang Feng,<sup>8</sup> Kristina N. Whisenand,<sup>9</sup> Tammy L. Yanovitch,<sup>10</sup> Luba Kalaydjieva,<sup>11</sup> Dimitar N. Azmanov,<sup>12</sup> Simone Finzi,<sup>13</sup> Christine E. Tanna,<sup>14</sup> Alex W. Hewitt,<sup>15,16</sup> David A. Mackey,<sup>17,18</sup> Yasmin S. Bradfield,<sup>19</sup> Emmanuelle Souzeau,<sup>20</sup> Shari Javadpour,<sup>21</sup> Janey L. Wiggs,<sup>22</sup> Francesca Pasutto,<sup>23</sup> Xiaorong Liu,<sup>24</sup> Simon W.M. John,<sup>25</sup> Jamie E. Craig,<sup>26</sup> Jing Jin,<sup>27</sup> Terri L. Young,<sup>28</sup> and Susan E. Quaggin<sup>29</sup>

<sup>1</sup>Feiberg Cardiovascular Research Institute and Division of Nephrology/Hypertension, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>2</sup>Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, USA; <sup>3</sup>Howard Hughes Medical Institute and The Jackson Laboratory, Bar Harbor, Maine, USA; <sup>4</sup>Department of Ophthalmology, Flinders University, Adelaide, South Australia, Australia; <sup>5</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>6</sup>Department of Ophthalmology, Flinders University, Adelaide, South Australia, Australia; <sup>7</sup>Department of Ophthalmology, Flinders University, Adelaide, South Australia, Australia; <sup>8</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>9</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>10</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>11</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>12</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>13</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>14</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>15</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>16</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>17</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>18</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>19</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>20</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>21</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>22</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>23</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>24</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>25</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>26</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>27</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>28</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>29</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

Mice and humans with LOF Angpt-1 mutations associated with congenital glaucoma

The Journal of Clinical Investigation

RESEARCH ARTICLE

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

Tomokazu Souma,<sup>1</sup> Stuart W. Tompson,<sup>2</sup> Benjamin R. Thomson,<sup>3</sup> Owen M. Siggs,<sup>4</sup> Krishnakumar Kizhathil,<sup>5</sup> Shinji Yamaguchi,<sup>6</sup> Liang Feng,<sup>7</sup> Yuchuanan Lin-Whighouath,<sup>8</sup> Kristina N. Whisenand,<sup>9</sup> Sebastian Maier-Stroh,<sup>10</sup> Tammy L. Yanovitch,<sup>11</sup> Luba Kalaydjieva,<sup>12</sup> Dimitar N. Azmanov,<sup>13</sup> Simone Finzi,<sup>14</sup> Lucia Mauli,<sup>15</sup> Shahbanou Javadpour,<sup>16</sup> Emmanuelle Souzeau,<sup>17</sup> Tiger Zhou,<sup>18</sup> Alex W. Hewitt,<sup>19,20</sup> Bethany Kloss,<sup>21</sup> Kathryn R. Burdon,<sup>22</sup> David A. Mackey,<sup>23,24</sup> Kerri F. Allen,<sup>25</sup> Jonathan B. Ruddle,<sup>26</sup> Sing-Hui Lim,<sup>27</sup> Steve Rozza,<sup>28</sup> Khanh-Nhat Tran-Viet,<sup>29</sup> Xiaorong Liu,<sup>30</sup> Simon John,<sup>31</sup> Janey L. Wiggs,<sup>32</sup> Francesca Pasutto,<sup>33</sup> Jamie E. Craig,<sup>34</sup> Jing Jin,<sup>35</sup> Susan E. Quaggin,<sup>36</sup> and Terri L. Young<sup>37</sup>

<sup>1</sup>Feiberg Cardiovascular Research Institute and Division of Nephrology/Hypertension, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>2</sup>Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, USA; <sup>3</sup>Howard Hughes Medical Institute and The Jackson Laboratory, Bar Harbor, Maine, USA; <sup>4</sup>Department of Ophthalmology, Flinders University, Adelaide, South Australia, Australia; <sup>5</sup>Department of Ophthalmology, Flinders University, Adelaide, South Australia, Australia; <sup>6</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>7</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>8</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>9</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>10</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>11</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>12</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>13</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>14</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>15</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>16</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>17</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>18</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>19</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>20</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>21</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>22</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>23</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>24</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>25</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>26</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>27</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>28</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>29</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>30</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>31</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>32</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>33</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>34</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>35</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>36</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>37</sup>Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

Families with Tie2 LOF mutations associated with congenital glaucoma

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LETTERS

<https://doi.org/10.1038/415589-018-0126-8>

nature  
gene

## Genome-wide analyses identify 68 new loci associated with intraocular pressure and improve risk prediction for primary open-angle glaucoma

Anthony P. Khawaja<sup>1,2,3,4</sup>, Jessica N. Cooke Bailey<sup>5,6,7</sup>, Nicholas J. Wareham<sup>8</sup>, Robert A. Scott<sup>9</sup>, Mark Simcoe<sup>10,11</sup>, Robert P. Igo Jr<sup>12</sup>, Yunjoo E. Song<sup>13</sup>, Robert Wojcicki<sup>14,15</sup>, Ching-Yu Cheng<sup>16,17</sup>, Peng T. Khaw<sup>18</sup>, Louis R. Pasquale<sup>19</sup>, Jonathan L. Haines<sup>20</sup>, Paul J. Foster<sup>21,22</sup>, Janey L. Wiggs<sup>23,24</sup>, Chris J. Hammond<sup>25,26</sup>, Pirro G. Hysi<sup>27,28</sup>, UK Biobank Eye and Vision Consortium<sup>29</sup> and NEIGHBORHOOD Co

Several loci support an important role of Tie2/ANGPT signaling in IOP regulation.

RESEARCH ARTICLE

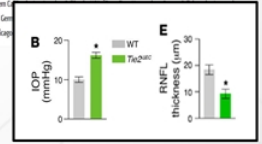
The Journal of Clinical Investigation

RESEARCH ARTICLE

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

Jaeryung Kim,<sup>1</sup> Dae-Young Park,<sup>1,2</sup> Hossung Bae,<sup>3</sup> Do Young Park,<sup>4</sup> Dongkyu Kim,<sup>5</sup> Choong-kun Lee,<sup>6</sup> Sukhyun Song,<sup>7</sup> Tae-Young Chung,<sup>8</sup> Dong Hui Lim,<sup>9</sup> Yoshiaki Kubota,<sup>10</sup> Young-Kwon Hong,<sup>11</sup> Yulong He,<sup>12</sup> Hellmut C. Augustin,<sup>13</sup> Guillermo Oliver,<sup>14</sup> and Gou Young Koh<sup>1,2</sup>

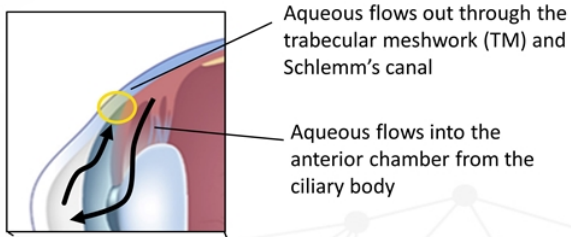
<sup>1</sup>Graduate School of Medical Science and Engineering, Korea Advanced Institute of Science and Technology (KAIST), Daejeon, Republic of Korea; <sup>2</sup>Center for Molecular Research, KAIST, Daejeon, Republic of Korea; <sup>3</sup>Department of Preventive Medicine, Catholic University School of Medicine, Seoul, Republic of Korea; <sup>4</sup>The Laboratory of Vascular Biology, School of Medicine, Keio University, Tokyo, Japan; <sup>5</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>6</sup>Department of Ophthalmology, Samsung Medical Center, Samsung Biomedical Research Institute, Seoul, Republic of Korea; <sup>7</sup>Department of Ophthalmology, Seoul National University School of Medicine, Seoul, Republic of Korea; <sup>8</sup>Department of Ophthalmology, Seoul National University School of Medicine, Seoul, Republic of Korea; <sup>9</sup>Department of Ophthalmology, Seoul National University School of Medicine, Seoul, Republic of Korea; <sup>10</sup>Department of Ophthalmology, Seoul National University School of Medicine, Seoul, Republic of Korea; <sup>11</sup>Department of Ophthalmology, Seoul National University School of Medicine, Seoul, Republic of Korea; <sup>12</sup>Department of Ophthalmology, Seoul National University School of Medicine, Seoul, Republic of Korea; <sup>13</sup>Department of Ophthalmology, University of Southern California, Los Angeles, California, USA; <sup>14</sup>Department of Ophthalmology, University of Southern California, Los Angeles, California, USA



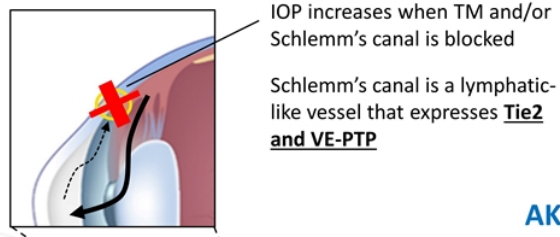
# Ocular hypertension and pathology of glaucoma:

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

**Eye without glaucoma**

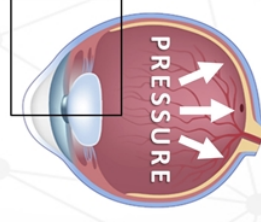
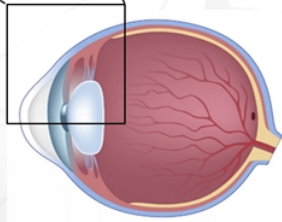


**Eye with glaucoma**



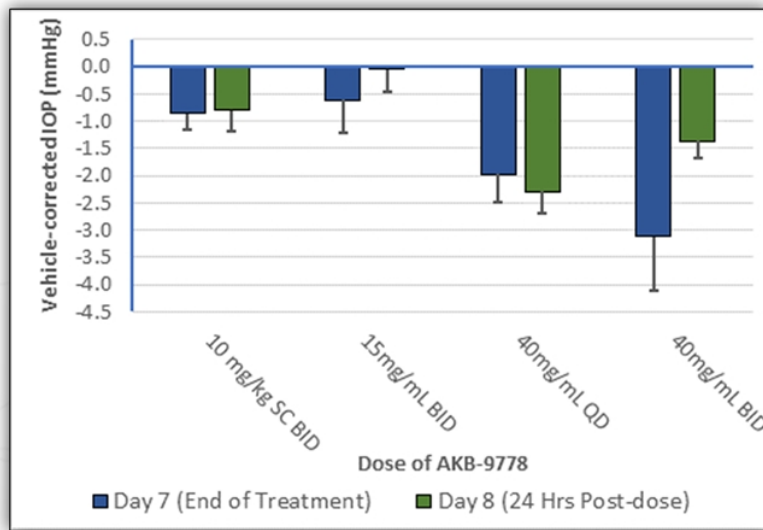
**AKB-9778: New MOA to affect outflow through the TM**

*Tie2 maintains vascular stability of Schlemm's canal*



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

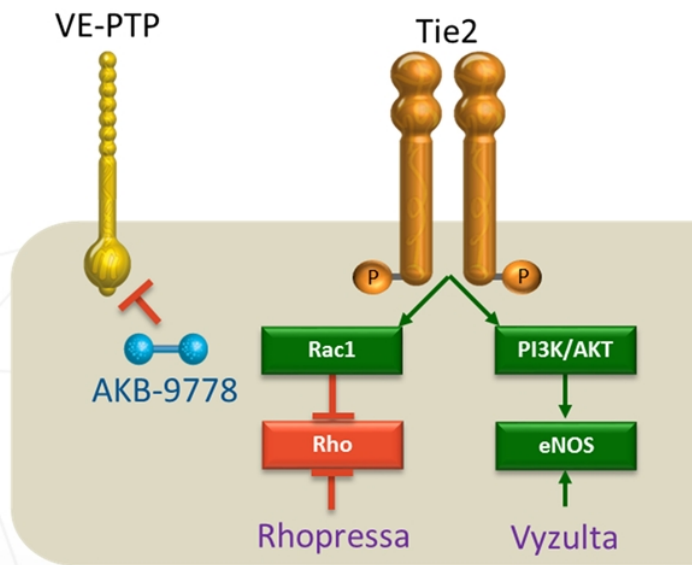
## Normotensive New Zealand White Rabbits



- IOP lowering is dose dependent (40 mg/ml > 15 mg/ml) and is persistent 24 hours post-dose (Day 8)
- IOP lowering by topical dosing (40 mg/ml group) was greater than SC dosing (10 mg/kg)

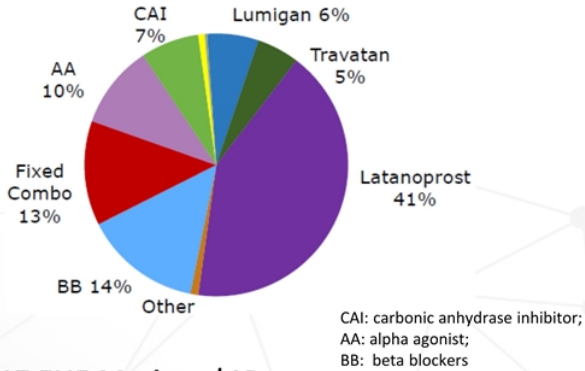
# Inhibition of VE-PTP activates Tie2 & affects downstream Rho kinase and eNOS activity mechanistically

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



# Commercial Opportunity in Glaucoma

- **2018 US Market: \$3B**
- Half of volume is first-line prostaglandins (mostly generics)
- Half of volume is 2-3X/day adjuncts



- **2017 EU5 Market: \$1B**
- **2017 JP Market: \$0.8 B**

Sources: Aerie Corporate Presentation – March 2019

Source: Cowen and Company 2018 Therapeutics Conference

## Novel, Additive IOP-Lowering Agents For Glaucoma Are Badly Needed

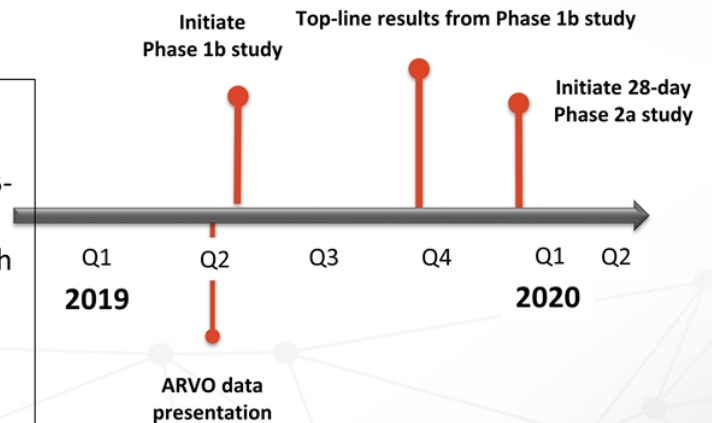
The vast majority of our surveyed physicians believe that approximately 20-40% of patients are treated with second-line or two concurrent IOP-lowering agents. Yet, physicians are still unsatisfied with available options and are demanding agents with new, safe, mechanisms of action.

- AKB-9778 could be the first drug targeting the site of pathology – Schlemm's Canal

# AKB-9778 in primary open-angle glaucoma

## TIME-2b IOP data to be presented at ARVO:

- “By targeting Tie2/VE-PTP in Schlemm’s canal, AKB-9778 lowers intraocular pressure via increasing outflow facility in mice” – Dr. Daniel Stamer, Joseph A. C. Wadworth Professor of Ophthalmology, Duke University, and incoming President of ARVO, April 29, 2019
- ARVO Special Session “The Role of Tie2 Pathway in Ocular Disease”, May 1, 2019

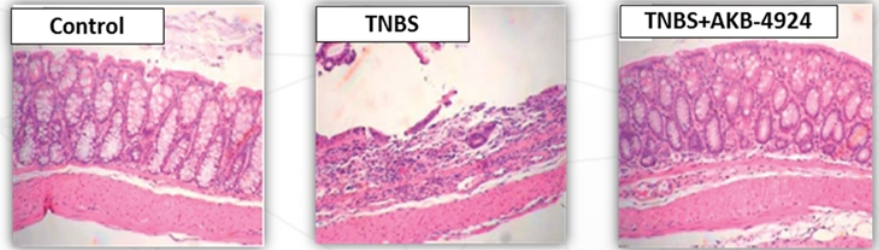




GB004 (formerly AKB-4924):  
Inflammatory Bowel Disease

# GB004 (formerly 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

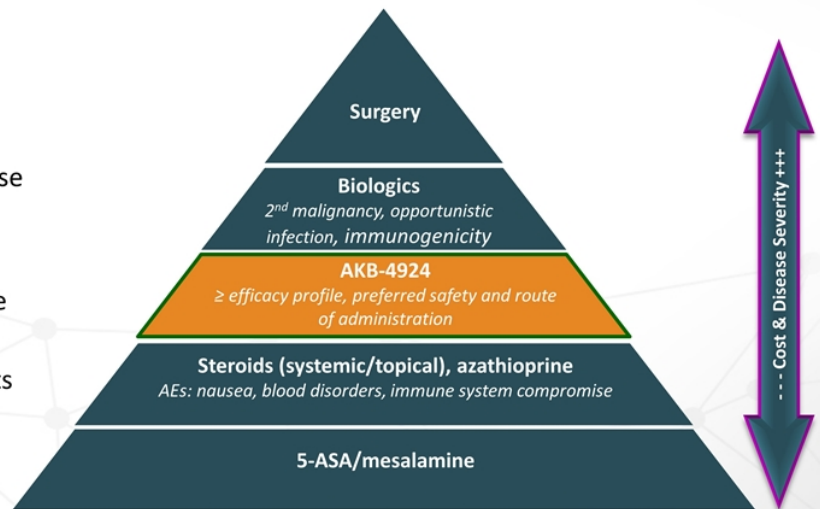
AKB-4924 Prevention of TNBS Colitis

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



# AKB-4924 in inflammatory bowel disease

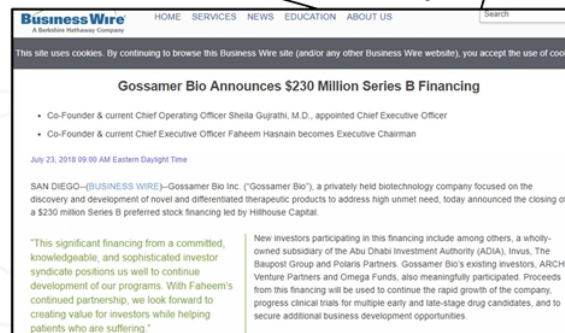
- First-in-class, HIF-1 $\alpha$  stabilizer for IBD
- Designed to address major unmet needs in IBD
- Efficacy and safety profile in preclinical models and early human studies support a preferred profile for moderate/severe and potentially earlier stage disease vs. current standard of care
- Oral, once-daily 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

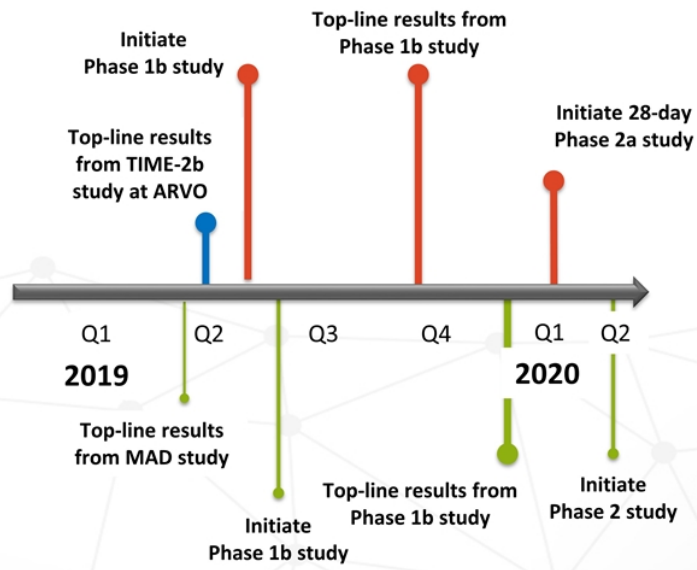




## Milestones and Summary

# Milestone rich timeline over next 18 months

- AKB-9778 TIME-2b Study
- AKB-9778 in POAG (eye drops)
- AKB-4924/GB004 in IBD\*\*



MAD – Multiple ascending dose  
POAG – Primary open angle glaucoma  
UC – Ulcerative colitis  
\*\*disclosure at discretion of Gossamer Bio

# Overview of Aerpio

- Developing first-in-class treatments for ocular diseases and complications of diabetes
- Lead asset: AKB-9778, a Tie2 activator, which is a key regulator of vascular stability
- TIME-2b Phase 2 clinical trial in patients with non-proliferative diabetic retinopathy missed its primary endpoint but:
  - Reproduced evidence of improved kidney function (UACR) in patients early diabetic nephropathy
  - Reproduced reduction in IOP seen in TIME-2; data to be presented at ARVO April 28 – May 2, 2019
  - Full data analysis at an upcoming medical conference
- Pipeline opportunities
  - Phase 1b of topical ocular AKB-9778 for evaluation in open-angle glaucoma expected to begin Q2 2019
  - Will seek pharma partner to further study slowing diabetic nephropathy of subcutaneous AKB-9778
  - Gossamer partnership on GB004: up to \$400M in milestones, tiered royalties to mid-teens, option to participate in sale of GB-004
  - ARP-1536: humanized Mab that activates Tie2
- Strong balance sheet (\$62.6 million end of 2018), expense reduction, cash to mid-2021



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