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

# FORM 8-K

**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 8, 2018**

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

| DELAWARE | 000-53057 | 61-1547850 |
|---|---|---|
| (State or other jurisdiction of incorporation) | (Commission File Number) | (I.R.S. Employer Identification No.) |

| 9987 Carver Road<br>Cincinnati, OH | 45242 |
|---|---|
| (Address of principal executive offices) | (Zip Code) |

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

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

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. ☒

**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 8, 2018. 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

| Exhibit No. | Description |
|---|---|
| 99.1 | Aerpio Pharmaceuticals, Inc., corporate presentation. |

**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 8, 2018

**AERPIO PHARMACEUTICALS, INC.**

By: /s/ Stephen Hoffman
Stephen Hoffman
Chief Executive Officer


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# Forward looking statement

- This presentation has been prepared by Aerpio Pharmaceuticals ("we", "us" or, the "Company"), solely for information purposes and is for the recipient to familiarize itself with the Company, and the fact that this meeting has taken place and anything you hear or learn during this meeting are strictly confidential. By agreeing to attend this meeting, you agree to keep all such information confidential. Except for internal use, this information may not be excerpted from, summarized, distributed, reproduced or used without the prior written consent of the Company. This presentation does not constitute an offer or invitation for the sale or purchase of securities. The Company does not make any representation or warranty, express or implied, as to the accuracy or completeness of the information contained herein and shall not have any liability for such information. Interested parties should conduct their own investigation and analysis of the Company, its business, prospects, results of operations and financial condition.
- This presentation 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. By attending or receiving this presentation you acknowledge that you will be solely responsible for your own assessment of the market and our market position and that you will conduct your own analysis and are solely responsible for forming your own view of the potential future performance of our business.

# Corporate highlights

- Advancing first-in-class treatments for ophthalmic disease
  - Non-proliferative diabetic retinopathy (NPDR)
  - Primary open angle glaucoma (POAG)
- AKB-9778 is the most potent activator of the Tie2 pathway, proven essential for vascular stability
  - Phase 2b DR data expected Q2 2019
  - Proof-of-concept in DR demonstrated in Phase 2a DME study
  - Approximately 13 million DR patients in the US and 20 million in EU
    - Multi-billion dollar market potential
  - Strong rationale for efficacy in primary open angle glaucoma
    - Phase 1b demonstration of intra-ocular pressure lowering Q3 2019
  - Potential for activity in systemic vascular complications of diabetes
- AKB-4924, a HIF-1$\alpha$ stabilizer in development for inflammatory bowel disease
  - Proof-of-concept target engagement data expected Q4 2018
- Aerpio holds global rights to all intellectual property

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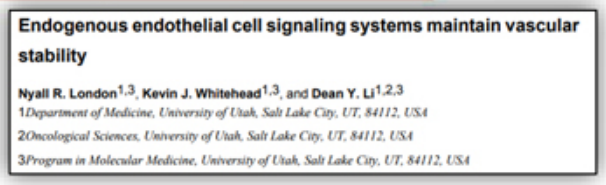
# The Tie2 Pathway & Diabetic Eye Disease

# The Tie2 pathway is validated as the major axis for vascular stability and quiescence

**Tie2** is a transmembrane receptor found on endothelial cells

**Tie2** activity
- Maintains integrity of endothelial cell junctions (blocks vessel leak)
- Enhances endothelial cell function and viability
- Inhibits vascular inflammation

**Active Tie2 = Vascular Stability**



Endogenous endothelial cell signaling systems maintain vascular stability

Nyall R. London[1,3], Kevin J. Whitehead[1,3], and Dean Y. Li[1,2,3]

1*Department of Medicine, University of Utah, Salt Lake City, UT, 84112, USA*

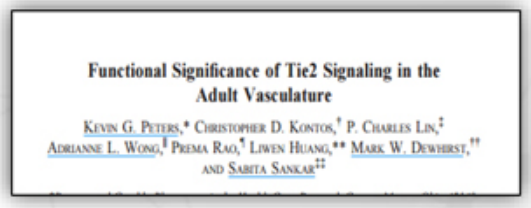
2*Oncological Sciences, University of Utah, Salt Lake City, UT, 84112, USA*

3*Program in Molecular Medicine, University of Utah, Salt Lake City, UT, 84112, USA*

Angiopoietin-1/Tie2 receptor signaling in vascular quiescence and angiogenesis

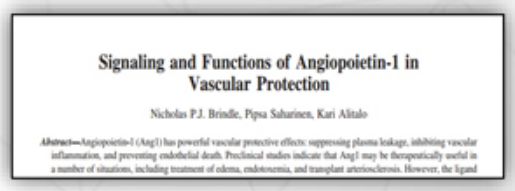
Shigetomo Fukuhara, Keisuke Sako, Kazuomi Noda, Jianghui Zhang, Masayoshi Minami and Naoki Mochizuki

Department of Structural Analysis, National Cardiovascular Center Research Institute, Suita, Osaka, Japan



Functional Significance of Tie2 Signaling in the Adult Vasculature

Kevin G. Peters,* Christopher D. Kontos,† P. Charles Lin,‡ Adrianne L. Wong,§ Prema Rao,¶ Liwen Huang,** Mark W. Dewhirst,†† and Sabita Sankar‡‡



Signaling and Functions of Angiopoietin-1 in Vascular Protection

Nicholas P.J. Brindle, Pipsa Saharinen, Kari Alitalo

*Abstract*—Angiopoietin-1 (Ang1) has powerful vascular protective effects: suppressing plasma leakage, inhibiting vascular inflammation, and preventing endothelial death. Preclinical studies indicate that Ang1 may be therapeutically useful in a number of situations, including treatment of edema, endotoxemia, and transplant arteriosclerosis. However, the ligand

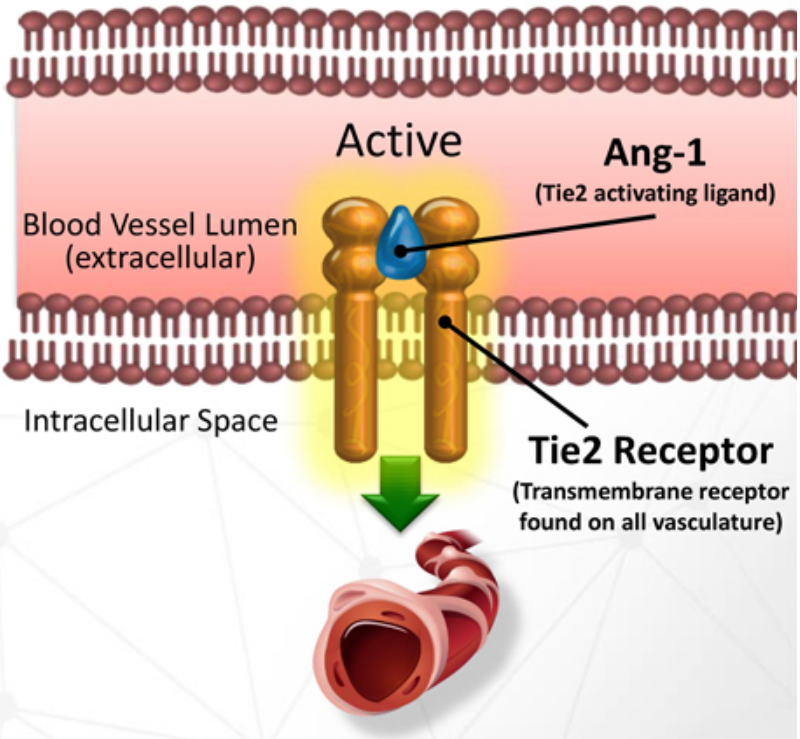
# Activation of the Tie2 receptor is the goal of all the therapeutics in development

**Ang-2 Antibody**

**Ang-2/VEGF Antibody**

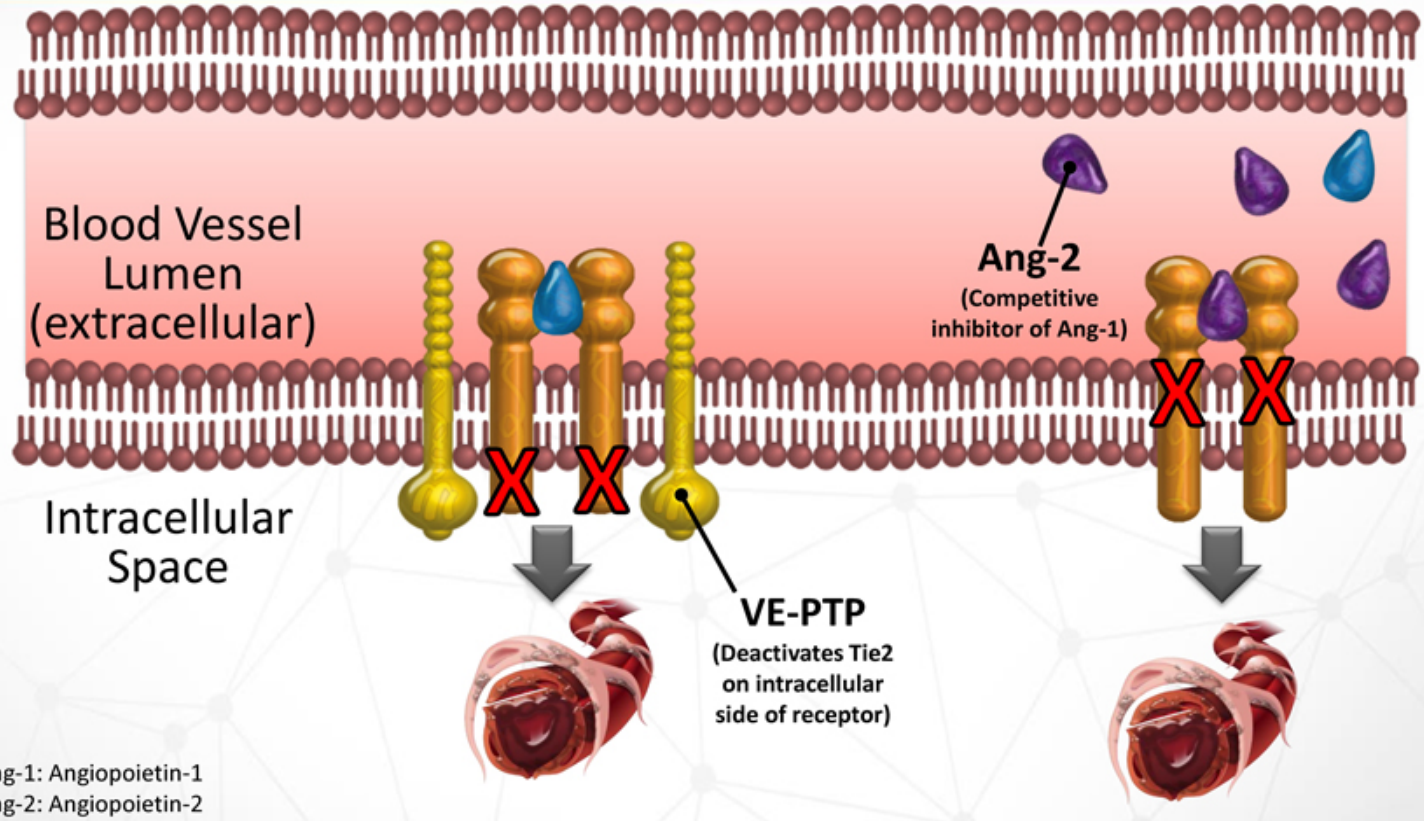
**VE-PTP Small Molecule**

AKB-9778 – Aerpio



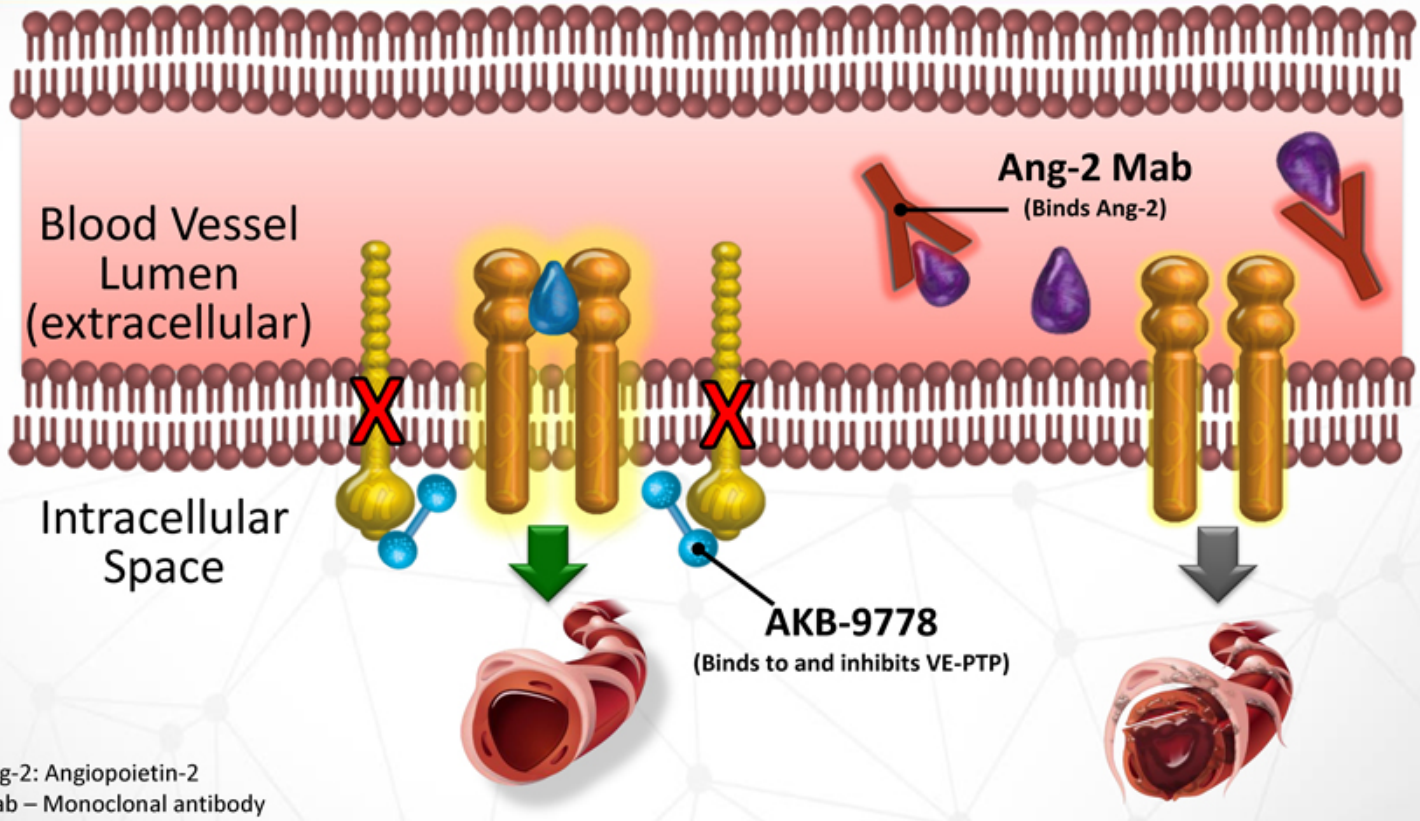

Ang-2: Angiopoietin-2
VEGF: Vascular endothelial growth factor
VE-PTP: Vascular endothelial protein tyrosine phosphatase

# In diabetic eye disease, VE-PTP and Ang-2 upregulation turns off Tie2



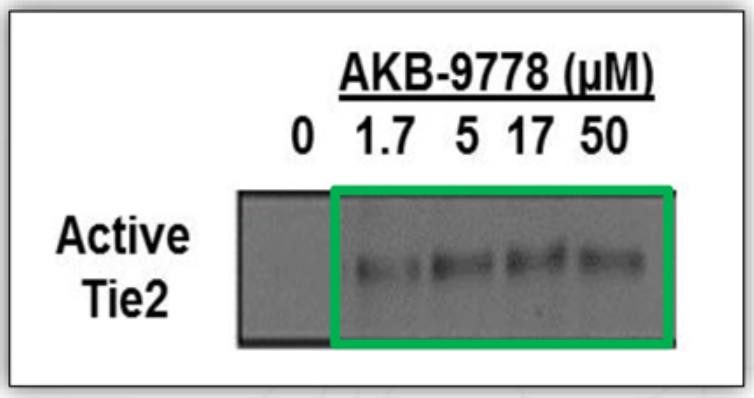

Ang-1: Angiopoietin-1
Ang-2: Angiopoietin-2
VE-PTP: Vascular endothelial protein tyrosine phosphatase

# VE-PTP inhibition activates Tie2 more robustly than Ang-2 inhibition

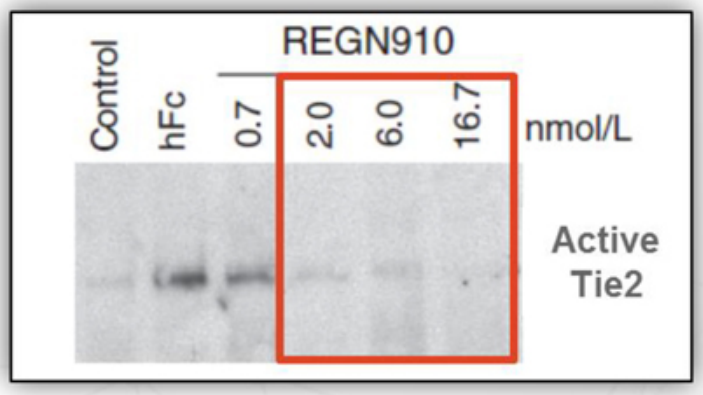



Ang-2: Angiopoietin-2
Mab – Monoclonal antibody
VE-PTP – Vascular endothelial protein tyrosine phosphatase

# VE-PTP inhibition is the optimal approach to activating Tie2



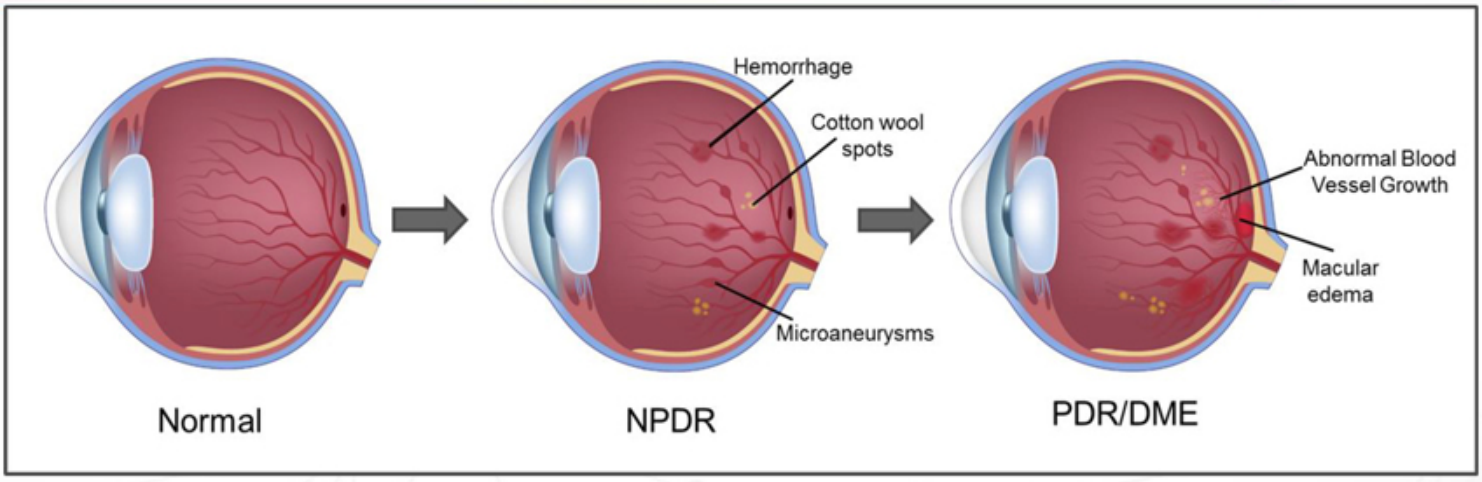

AKB-9778
robustly activates Tie2
in human endothelial cells




Nesvacumab (REGN910)
minimally activates Tie2
in human endothelial cells

Shen et al. JCI 124:4564-76, 2014
Daly et al. Cancer Research 73:108-18, 2012

# Vascular changes seen in early diabetic eye disease are caused by loss of Tie2 function




- 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 is severe enough to cause significant vision loss and potentially blindness

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

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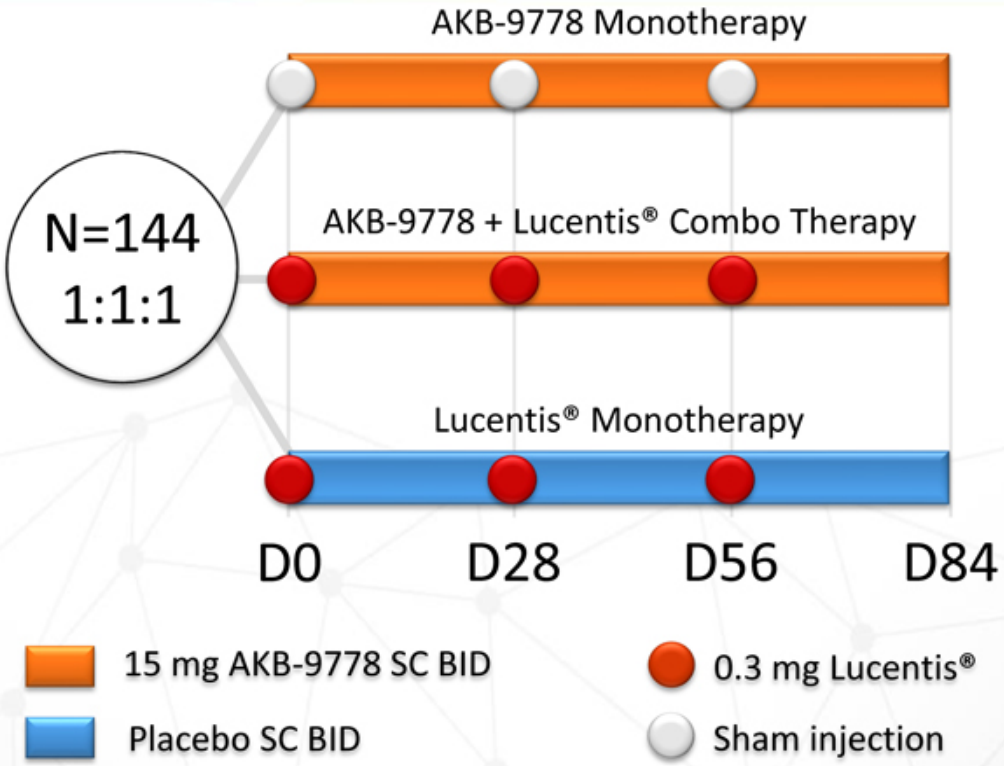
# AKB-9778 TIME-2 Clinical Data: Diabetic Macular Edema

# TIME-2 tested AKB-9778 alone and with Lucentis® in a randomized, phase 2a study



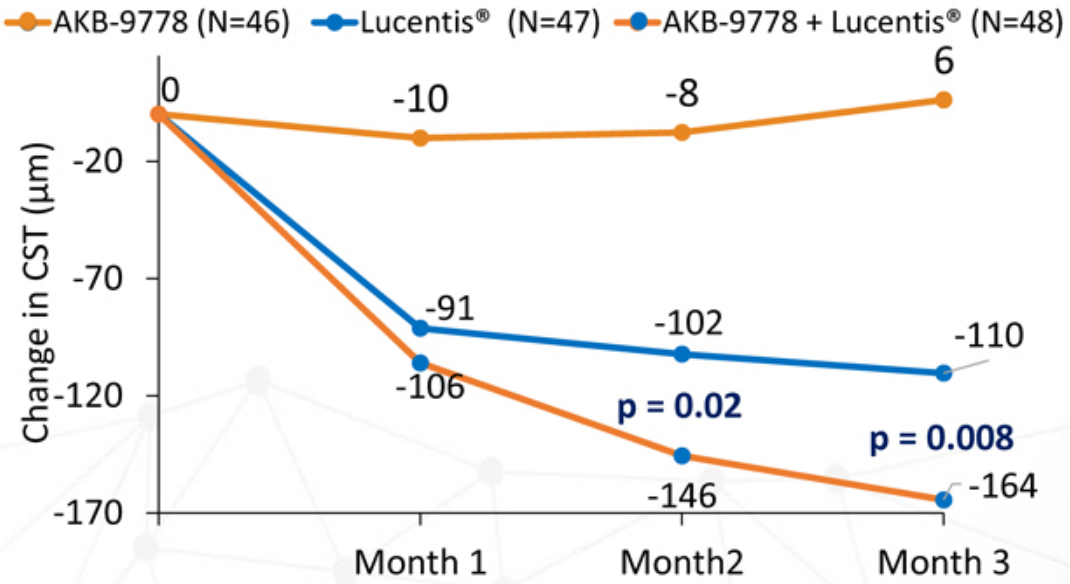

15 mg AKB-9778 SC BID

Placebo SC BID

0.3 mg Lucentis®

Sham injection

# TIME-2: Change in retinal thickness over time




- P1 data showed efficacy as monotherapy in DME prompting testing of monotherapy in P2
- No efficacy seen as monotherapy in primarily VEGF-driven disease (DME)
- Vascular stabilizing effect of combination therapy significantly greater than either agent alone

Campochiaro P, et al. *Ophthalmology*, Aug. 2016; Vol. 123.

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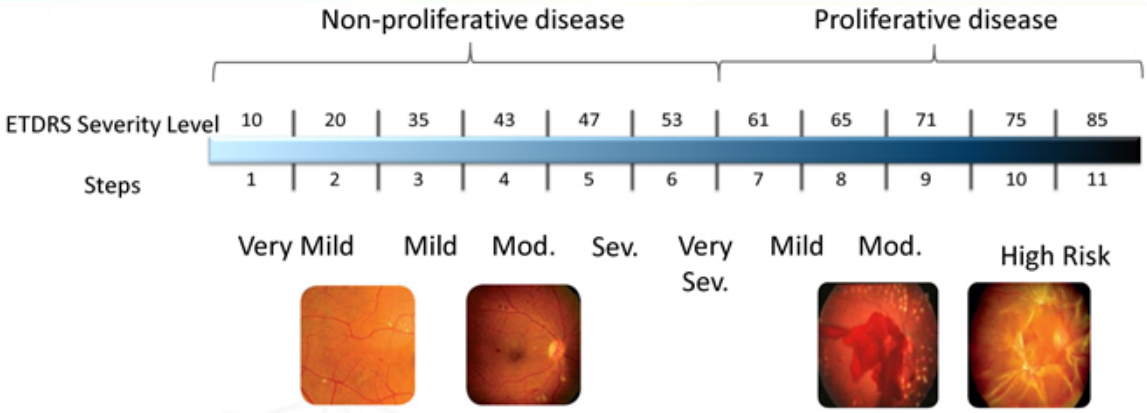
# AKB-9778 TIME-2 Clinical Data: Diabetic Retinopathy

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

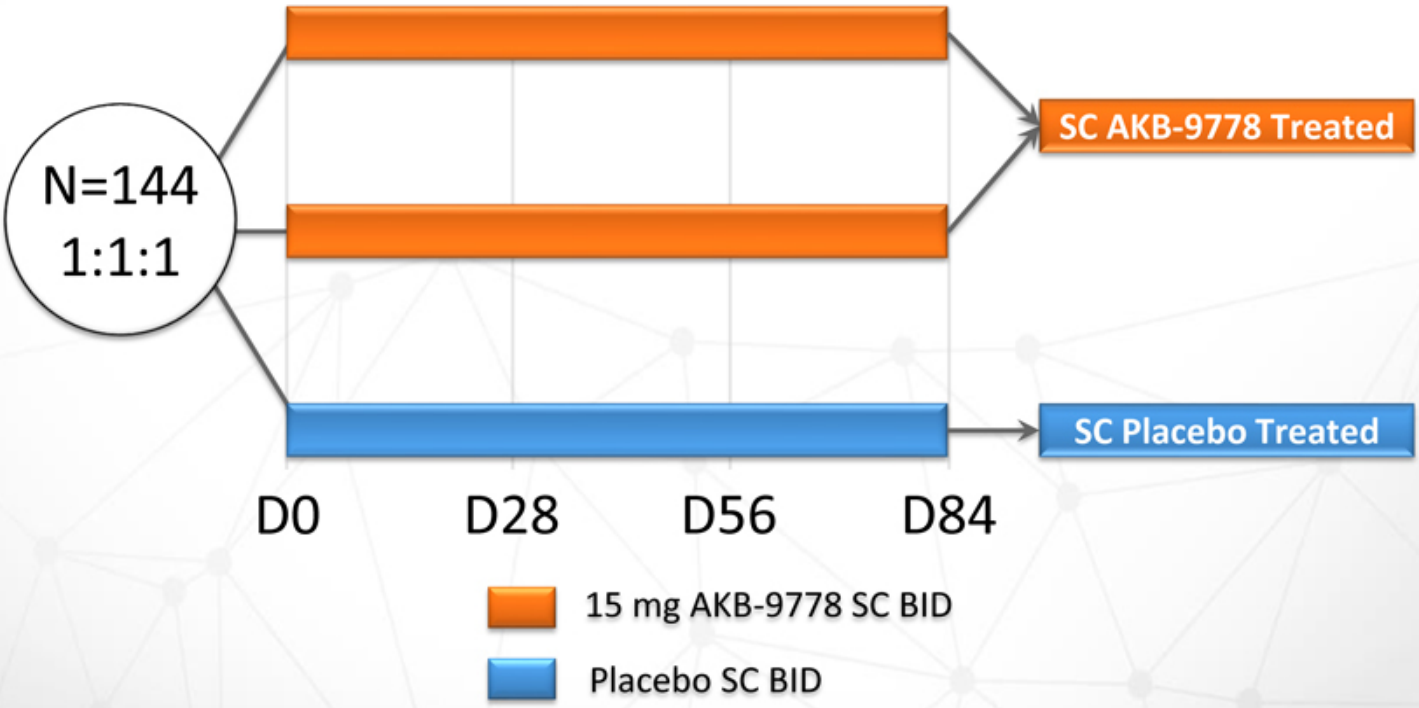



- 2-step improvement in DRSS at one year is a FDA-accepted endpoint for approval
- Risk of vision-threatening events (diabetic macular edema, hemorrhage, retinal detachment, etc.) increases with worsening step progression
- Treatment of diabetic retinopathy is generally not initiated until later in disease due to the drawbacks of currently available interventions (e.g. laser, intraocular injection)
- Early intervention with AKB-9778 could slow or prevent disease progression and represents a potential paradigm change in the treatment of diabetic eye disease globally

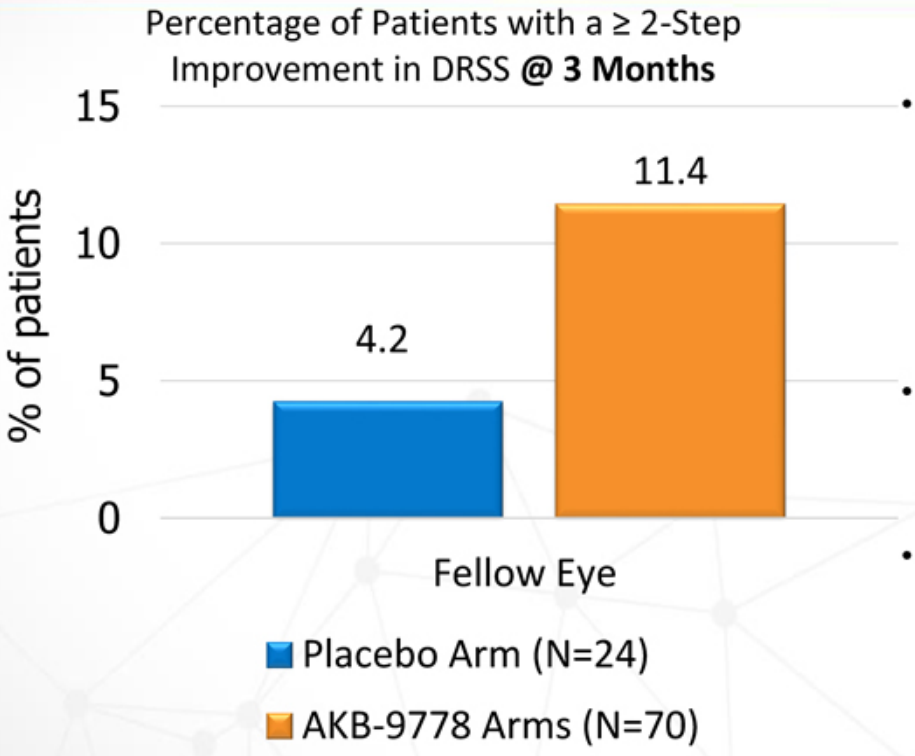
Klein R et al., *Arch Ophthalmol.*, 2001, Vol. 119.

# Assessment of AKB-9778 on DRSS from the TIME-2 study

- Pre-specified, planned analysis comparing effect of AKB-9778 on DRSS in fellow eyes without DME



# Assessment of AKB-9778 on diabetic retinopathy severity score from the TIME-2 study




- 2-step improvement expected to increase at one-year timepoint (on-going TIME-2b study)
  - Lucentis 2-step improvement from RISE/RIDE studies at M3 (16-18%), M6 (27%), M12 (31-34%)
- Placebo rate of improvement consistent with sham control in 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

DRSS – Diabetic retinopathy severity score

Campochiaro P, et al. *Ophthalmology*, Aug. 2016; Vol. 123.

# TIME-2 safety results

| | AKB-9778 (N=48) | Lucentis® (N=47) | AKB-9778 + Lucentis® (N=49) |
|---|---|---|---|
| Number of Ocular AEs | 17 | 45 | 48 |
| Subjects w/ Ocular AEs, n (%) | 10 (20.8) | 19 (40.4) | 23 (46.9) |
| Number of Non-Ocular AEs | 76 | 89 | 108 |
| Subjects w/ Non-Ocular AEs, n (%) | 28 (58.3) | 30 (63.8) | 33 (67.3) |
| Number of Serious AEs* | 2 | 0 | 2 |
| Subjects w/ Serious AEs, n (%) | 2 (4.2) | 0 | 2 (4.1) |

* No serious AEs were considered drug-related by investigators

Campochiaro P, et al. *Ophthalmology*, Aug. 2016; Vol. 123.

# AKB-9778 development: DR vs. DME

- Emergence of approval pathway for DR (2015 Lucentis & Eylea approvals) led us to pre-specify a DRSS analysis in the TIME-2 study
- 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
  - No increase in frequency of visits to ophthalmologist
  - Treats both eyes via systemic delivery (70% have bilateral disease)
  - Potential to prevent vision threatening DME and PDR
  - May improve diabetes-induced compromise of other vascular beds
- Commercial considerations

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

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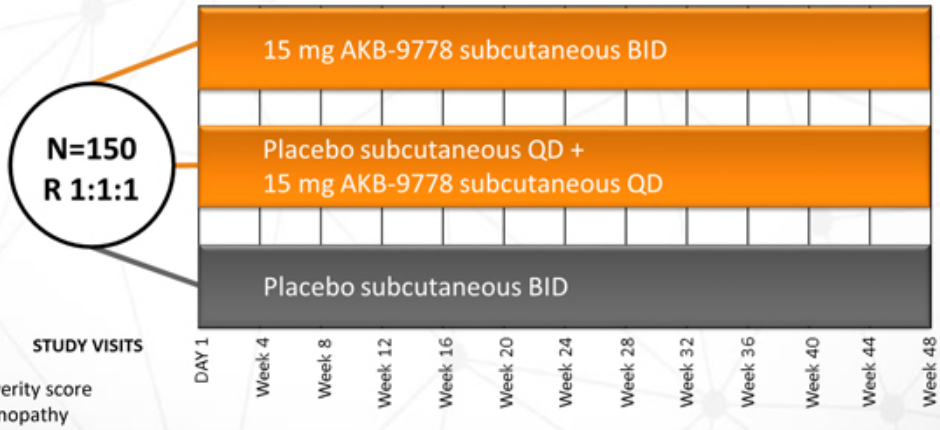
# TIME-2b Study

# TIME-2b: Clinical trial design

- Prospective, randomized, placebo-controlled study in pts with moderate to severe Non-Proliferative Diabetic Retinopathy (NPDR) without DME
- 150 patients: 15mg AKB-9778 once or twice/day vs. placebo
- 48 week treatment period
- 50 sites in United States
- 1º Endpoint: ≥ 2-step improvement in DRSS at 48 weeks
- Key 2º Endpoints: development of DME/PDR, DR progression, renal function
- Enrollment commenced June 2017, data expected Q2 2019




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

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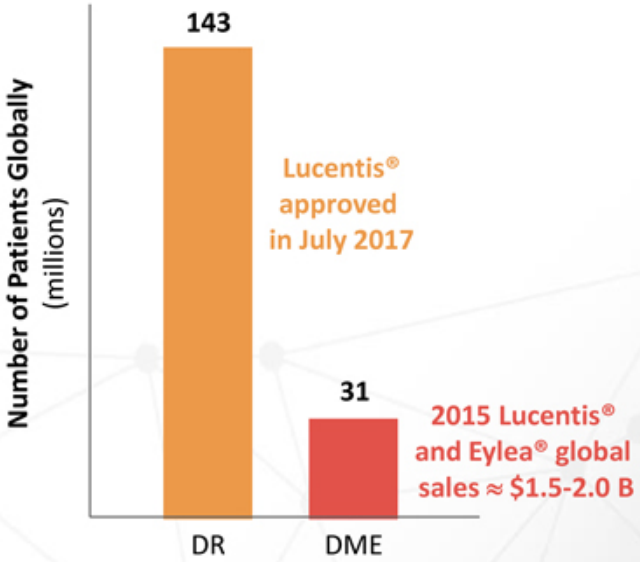
# Commercial Opportunity: AKB-9778 in Diabetic Retinopathy

# DR represents a large unmet medical need with significant market potential

- Diabetes affects over **400M patients worldwide**
  - Over 40M patients in North America and 60M in Europe

**1 in 3 diabetics have DR**

**1 in 15 diabetics have DME**




DR – diabetic retinopathy
DME – diabetic macular edema

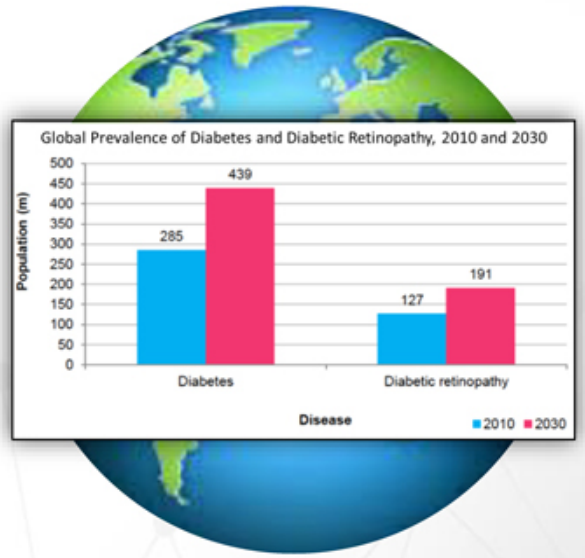
Yau J. et al. *Diabetes Care*, March 2012, Vol 35.
International Diabetes Federation. *2015 IDF Diabetes Atlas*. Retrieved from http://www.diabetesatlas.org/
Cowen and Company. *2016 Therapeutic Categories Outlook*. New York.

# Unmet need for the treatment of early diabetic eye disease is clear

Lloyd Paul Aiello, MD, PhD
Beetham Eye Institute, Joslin Diabetes Center
**2015 FDA/NEI Workshop on Diabetic Retinopathy**

## Need for Earlier Interventions

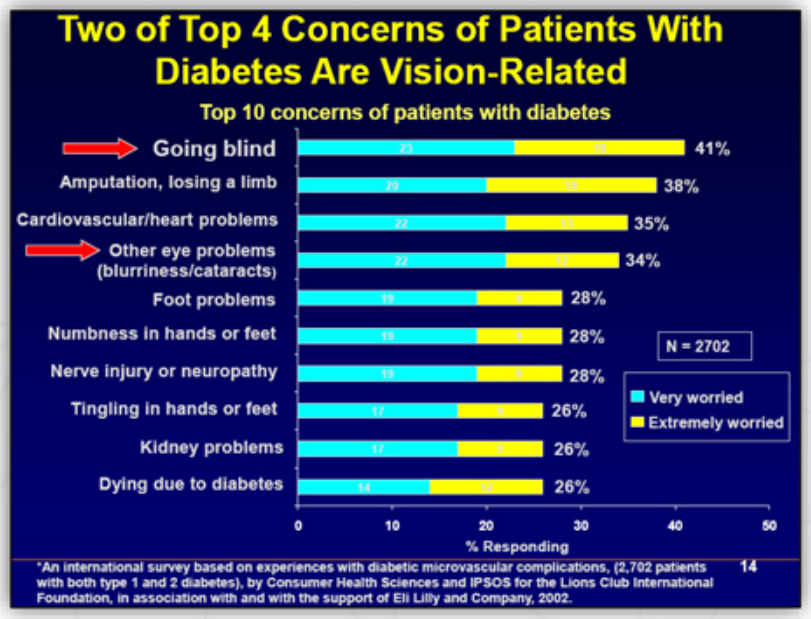
- Our current antiVEGF approaches to DME, and DR with DME, although more effective, are no more an ultimate worldwide therapeutic solution than was laser given the current barriers to access, treatment burden, required expertise, risks, etc.
- To be truly successful we will need low risk, low cost, effective early treatments with the ability for mass distribution
  - Similar to polio, smallpox, vitamin A, trachoma
- Requires new and ongoing research, assessments of new endpoints and evolution of clinical trial approaches




DME- Diabetic macular edema
DR – diabetic retinopathy
FDA – Food and Drug Administration
NEI – National Eye Institute
VEGF – Vascular endothelial growth factor
Visiongain: Global Ophthalmic Drugs Market Forecast 2017-2027.

# Opportunity to treat earlier stage disease

- Treating patients earlier in the disease process represents a large market opportunity with significant unmet need

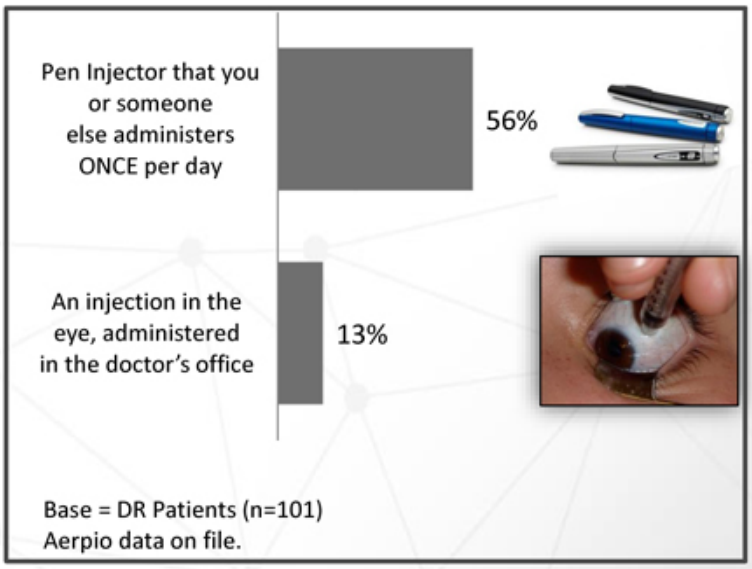



- Vision-related concerns are the greatest health concern of patients with diabetes and a strong motivator

# Patient preferred treatment modality

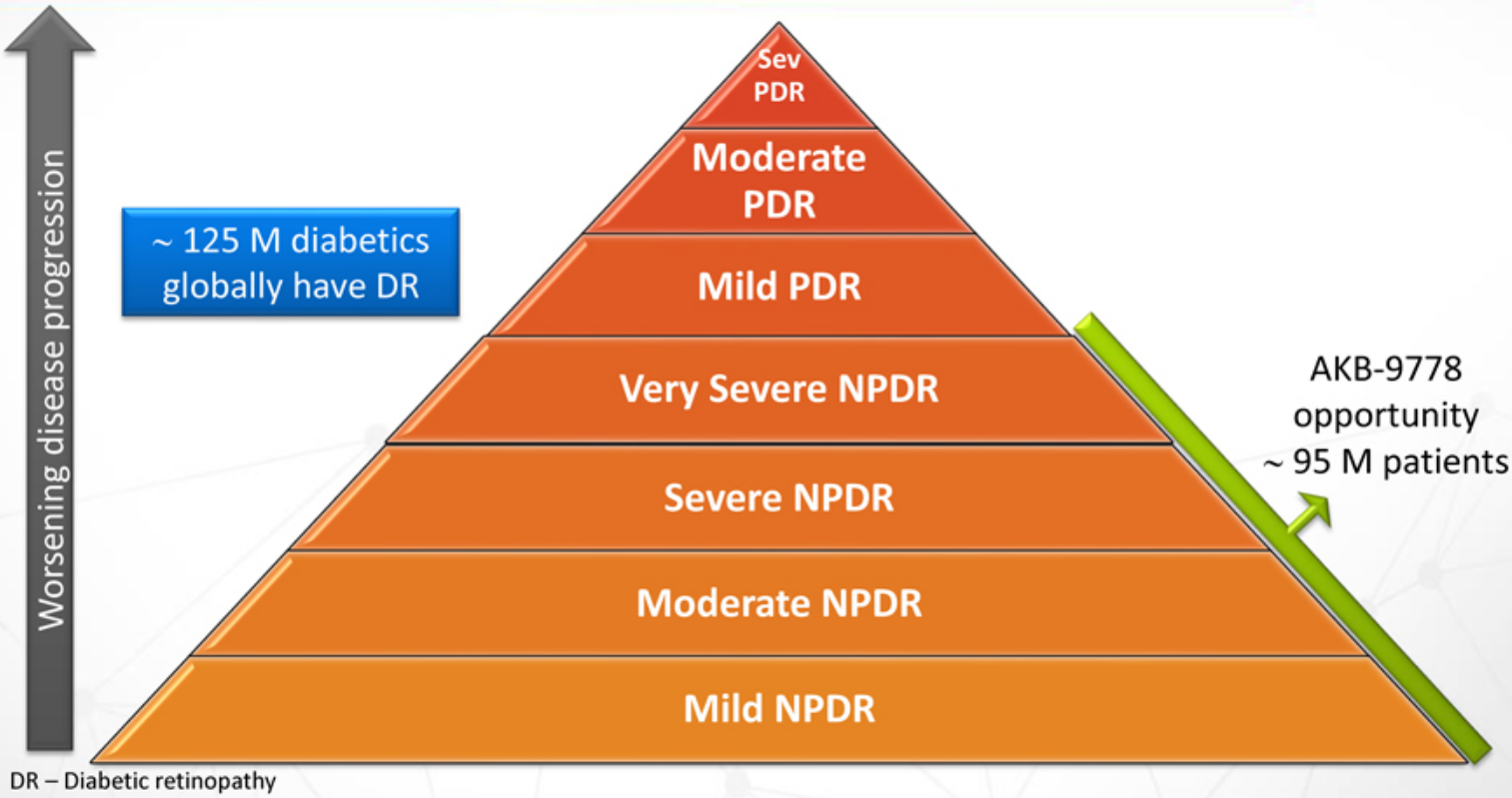
- Monthly intraocular injections of anti-VEGF for DR is not a sustainable treatment strategy


- In contrast, AKB-9778 is patient-administered via daily SC injection
  - Reduces treatment and visit burden
  - More acceptable treatment delivery, avoiding eye injections, for less symptomatic patients
  - Exposure to systemic vasculature may effectively treat both eyes and other vascular complications of diabetes



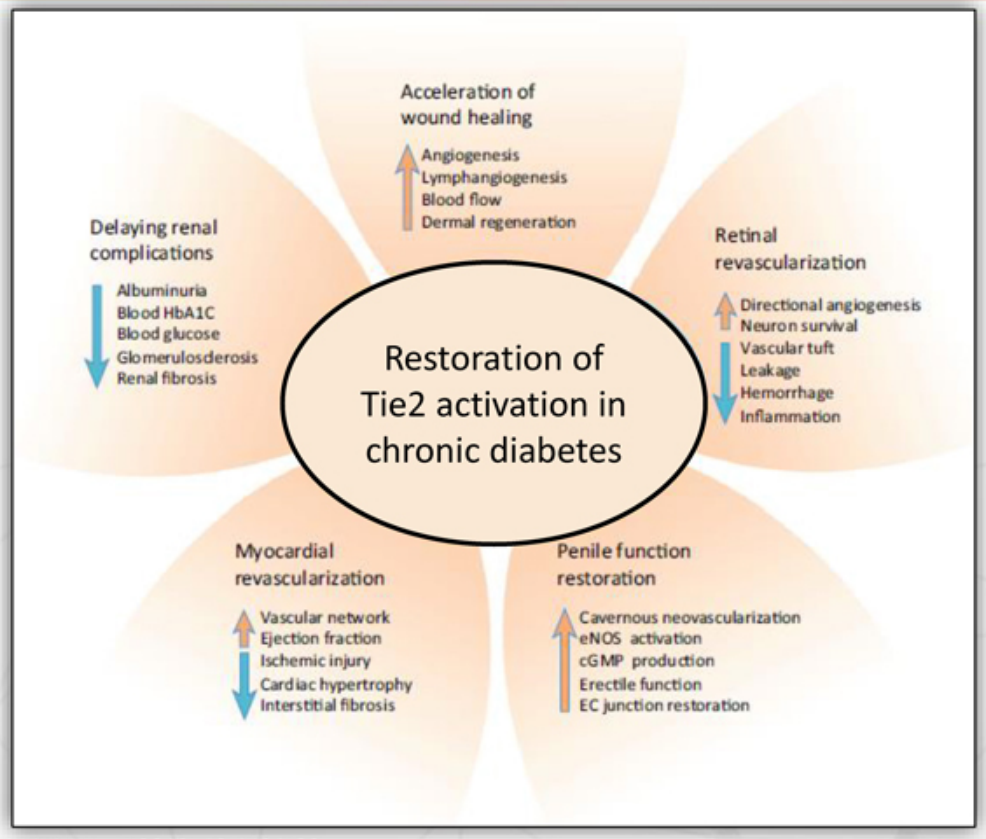

SC – Subcutaneous
VEGF – Vascular endothelial growth factor
Lucentis® package insert
Kiss S, et al. *Clin Ophthalmol.* 2014;8:1611-1621.

# AKB-9778 market opportunity includes the largest segment of diabetic eye disease




DR – Diabetic retinopathy
NPDR – Non-proliferative diabetic retinopathy
PDR – Proliferative diabetic retinopathy

# Systemic Tie2 stabilization may have implications for other diabetic complications




Koh, G. Trends in Molec Med. January 2013, 19:1. 31-39.

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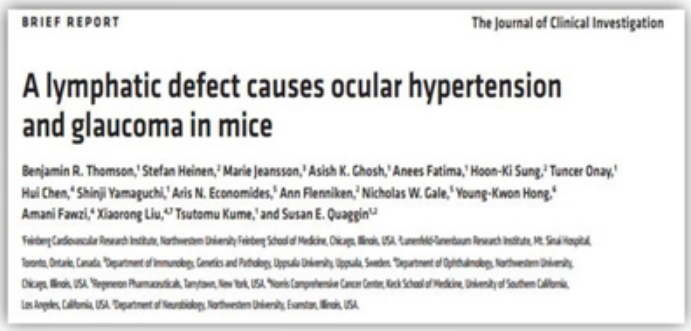
# AKB-9778:
# Primary Open-Angle Glaucoma

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



BRIEF REPORT

The Journal of Clinical Investigation

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

Benjamin R. Thomson,[1] Stefan Heinen,[2] Marie Jeansson,[3] Asish K. Ghosh,[1] Anees Fatima,[1] Hoon-Ki Sung,[2] Tuncer Onay,[1] Hui Chen,[4] Shinji Yamaguchi,[1] Aris N. Economides,[5] Ann Flenniken,[2] Nicholas W. Gale,[5] Young-Kwon Hong,[6] Amani Fawzi,[4] Xiaorong Liu,[4,7] Tsutomu Kume,[1] and Susan E. Quaggin[1,2]

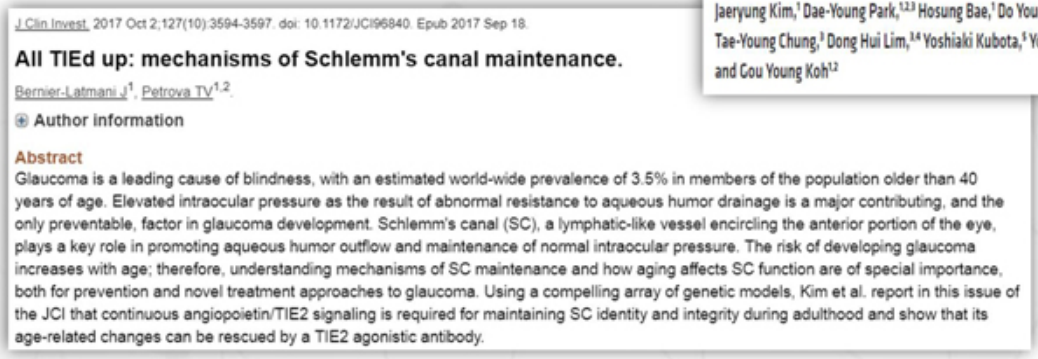
[1]Feinberg Cardiovascular Research Institute, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA. [2]Lunenfeld-Tanenbaum Research Institute, Mt. Sinai Hospital, Toronto, Ontario, Canada. [3]Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden.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

The Journal of Clinical Investigation

RESEARCH ARTICLE

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

Jaeryung Kim,[1] Dae-Young Park,[1,2,3] Hosung Bae,[1] Do Young Park,[1] Dongkyu Kim,[2] Choong-kun Lee,[1] Sukhyun Song,[2] Tae-Young Chung,[3] Dong Hui Lim,[3,4] Yoshiaki Kubota,[5] Young-Kwon Hong,[6] Yulong He,[7] Hellmut G. Augustin,[8] Guillermo Oliver,[9] and Gou Young Koh[1,2]



J Clin Invest. 2017 Oct 2;127(10):3594-3597. doi: 10.1172/JCI96840. Epub 2017 Sep 18.

**All TIEd up: mechanisms of Schlemm's canal maintenance.**

Bernier-Latmani J[1], Petrova TV[1,2].

Author information

Abstract

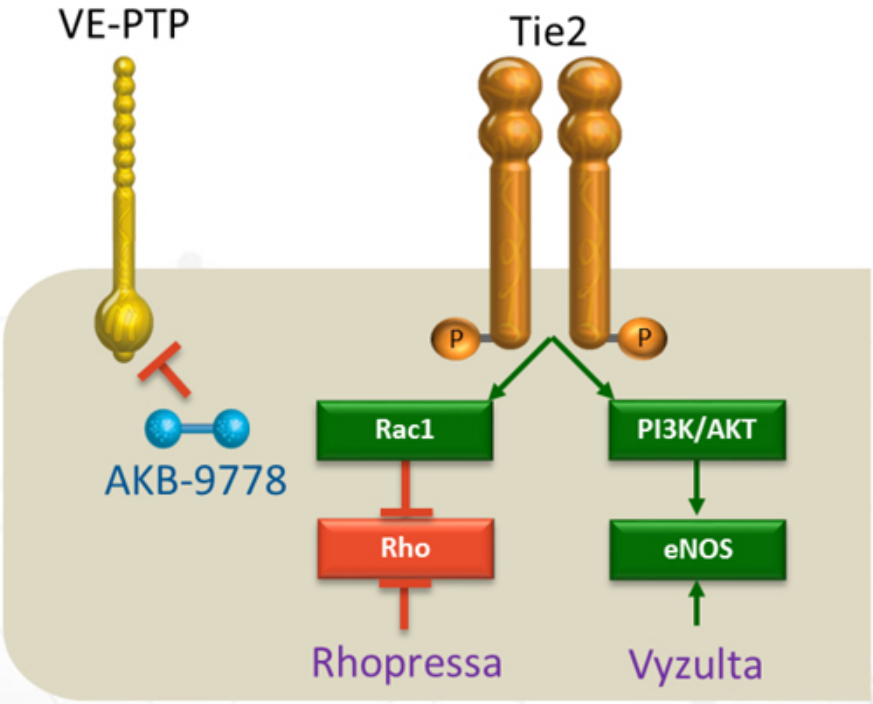
Glaucoma is a leading cause of blindness, with an estimated world-wide prevalence of 3.5% in members of the population older than 40 years of age. Elevated intraocular pressure as the result of abnormal resistance to aqueous humor drainage is a major contributing, and the only preventable, factor in glaucoma development. Schlemm's canal (SC), a lymphatic-like vessel encircling the anterior portion of the eye, plays a key role in promoting aqueous humor outflow and maintenance of normal intraocular pressure. The risk of developing glaucoma increases with age; therefore, understanding mechanisms of SC maintenance and how aging affects SC function are of special importance, both for prevention and novel treatment approaches to glaucoma. Using a compelling array of genetic models, Kim et al. report in this issue of the JCI that continuous angiopoietin/TIE2 signaling is required for maintaining SC identity and integrity during adulthood and show that its age-related changes can be rescued by a TIE2 agonistic antibody.

# Glaucoma is the leading cause of blindness in the world


Weinreb, R. N. *et al.* (2016) Primary open-angle glaucoma. *Nat. Rev. Dis. Primers* doi:10.1038/nrdp.2016.67
Tham, Y.-C. et al. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology* 121, 2081–2090 (2014).
Kapetanakis, V. V. et al. Global variations and time trends in the prevalence of primary open angle glaucoma (POAG): a systematic review and meta-analysis. *Br. J. Ophthalmol.* **100**, 86–93 (2016).

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

- AKB-9778 could achieve effects of both of the recently approved glaucoma products



# Stat sig reductions in IOP were observed in the TIME-2 study at every time point

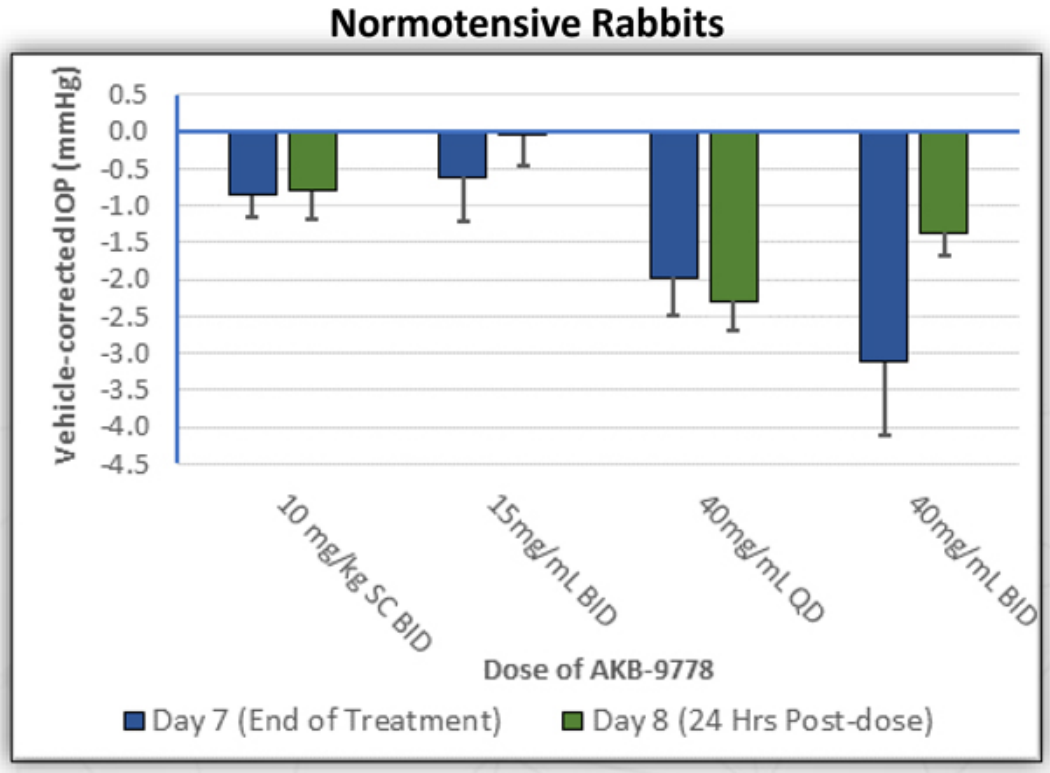
| | AKB-9778 Monotherapy | | AKB-9778 + Lucentis® | | Lucentis® monotherapy | |
|---|---|---|---|---|---|---|
| | SE | FE | SE | FE | SE | FE |
| Mean Baseline IOP (mmHG) | 15.8 | 15.4 | 15.9 | 16.1 | 15.2 | 15.8 |
| Mean Δ from BL (mmHG) | **-1.4** | **-1.4** | **-1.0** | **-1.5** | 0.1 | -0.1 |
| t-test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

BL = baseline; SE = study eye; FE = Fellow eye; SD = standard deviation

- 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
- Systemically administered β-blockers and nitrates, drugs used in glaucoma as topical drops, have shown a similar stat sig reductions in IOP when administered systemically, ~ 1 mm Hg

Dirks et al. Adv Ther. 23:3, 2006
Khawaja et al. Ophthalmology 121:1501, 2014
Stenkula and Wettrell, Graefe's Arch Clin Exp Ophthalomol 218:96, 1982

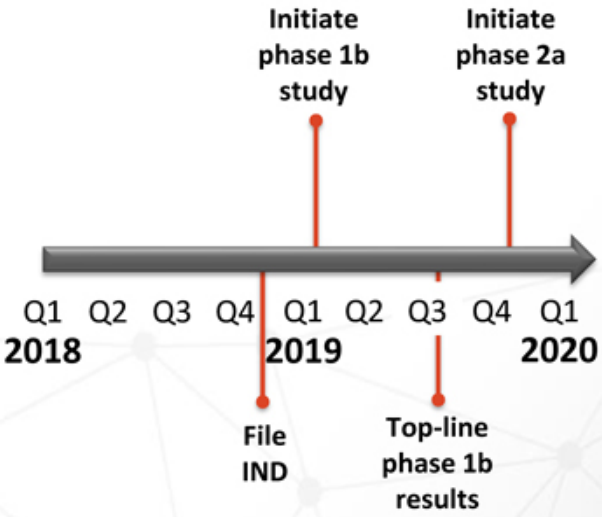
# Dose related IOP decrease observed after topical ocular administration of AKB-9778



# 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 | 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<br>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). |
| Positioning | First-line therapy of choice in adjunctive setting<br>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 |

IND – investigational new drug



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# AKB-4924:
# Inflammatory Bowel Disease

# AKB-4924 in inflammatory bowel disease

- First-in-class, HIF-1α stabilizer for IBD
- Addresses major unmet needs in IBD
- Efficacy and safety 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
- Proof-of-concept data in Q3 2019

AE – adverse event
HIF-1α– hypoxia inducible factor-1 alpha
IBD – inflammatory bowel disease

# AKB-4924 in Inflammatory Bowel Disease: Novel Mechanism of Action

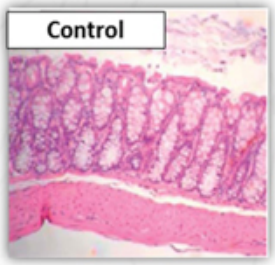
- AKB-4924 is a HIF-1α stabilizer that represents a new therapeutic class of potentially transformative therapeutics in IBD
- MOA enhances both mucosal wound healing and the resolution of inflammation
  - HIF-1α regulates innate immune responses by supporting broad-spectrum bactericidal and phagocytic activities of epithelial cells, neutrophils and macrophages important for the resolution of inflammation[1]
  - HIF-1α elicits a protective barrier function in intestinal epithelia during tissue injury and inflammation supporting resolution of inflammation and restoration of normal gut homeostasis[2-5]

HIF-1α – hypoxia inducible-1 alpha
IBD – inflammatory bowel disease
MOA – mechanism of action

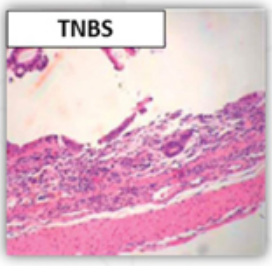
1. Nizet and Johnson, Nature Reviews Immunol. 9:609,2009; 2. Furuta GT, Turner JR, Taylor CT, et al. J. Ex. Med. 2001;193:1027-1034; 3. Comerford KM, Wallace TJ, Karhausen J, et al. Cancer Res 2002;62:3387-94; 4. Synnestvedt K, Furuta GT, Comerford KM, et al. J. Clin. Invest. 2002;110:993-1002; 5. Eltzschig HK, Ibla JC, Furuta Gt, et al. J. Ex. Med. 2003;198:783-796; 6. Karhausen JO, Furuta GT, Tomaszewski JE, et al. J Clin Invest 2004;114:1098-1106; 7. Robinson A, Keely S, Karhausen J, et al. Gastroenterology 2008;134:145-55.

# AKB-4924 efficacy demonstrated in multiple models of IBD

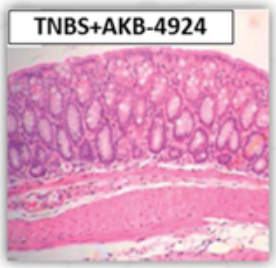
- Pre-clinical proof-of-concept across multiple models of IBD in both the induction and maintenance setting
  - TNBS-induced colitis
    - Wild type mice (below)
    - Chronic granulomatous disease mice
  - DSS-induced colitis
  - Genetic TNFα overexpression induced Crohn's Disease
  - Gut Graft Versus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




Normal Gut




TNBS-Induced Colitis

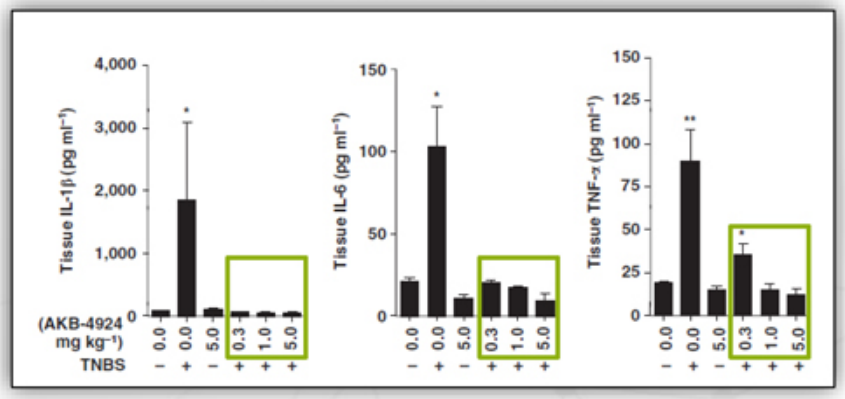


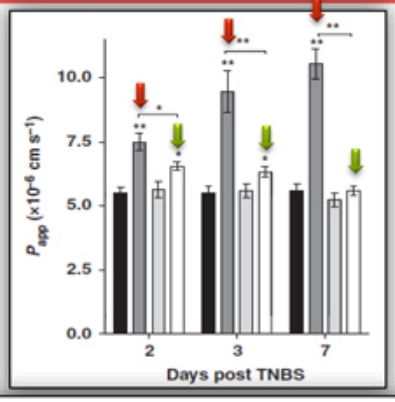

AKB-4924 Prevention of TNBS Colitis

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

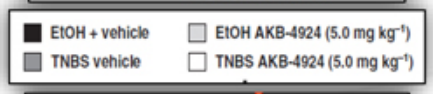
# AKB-4924 decreases colonic cytokine levels and enhances mucosal healing

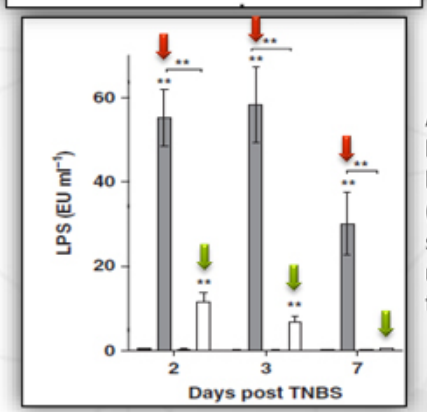
AKB-4924 reduces levels of proinflammatory cytokines in target tissue (colon)




AKB-4924 significantly reduces TNBS-induced leak of fluorescent dextran from colon over 7 days

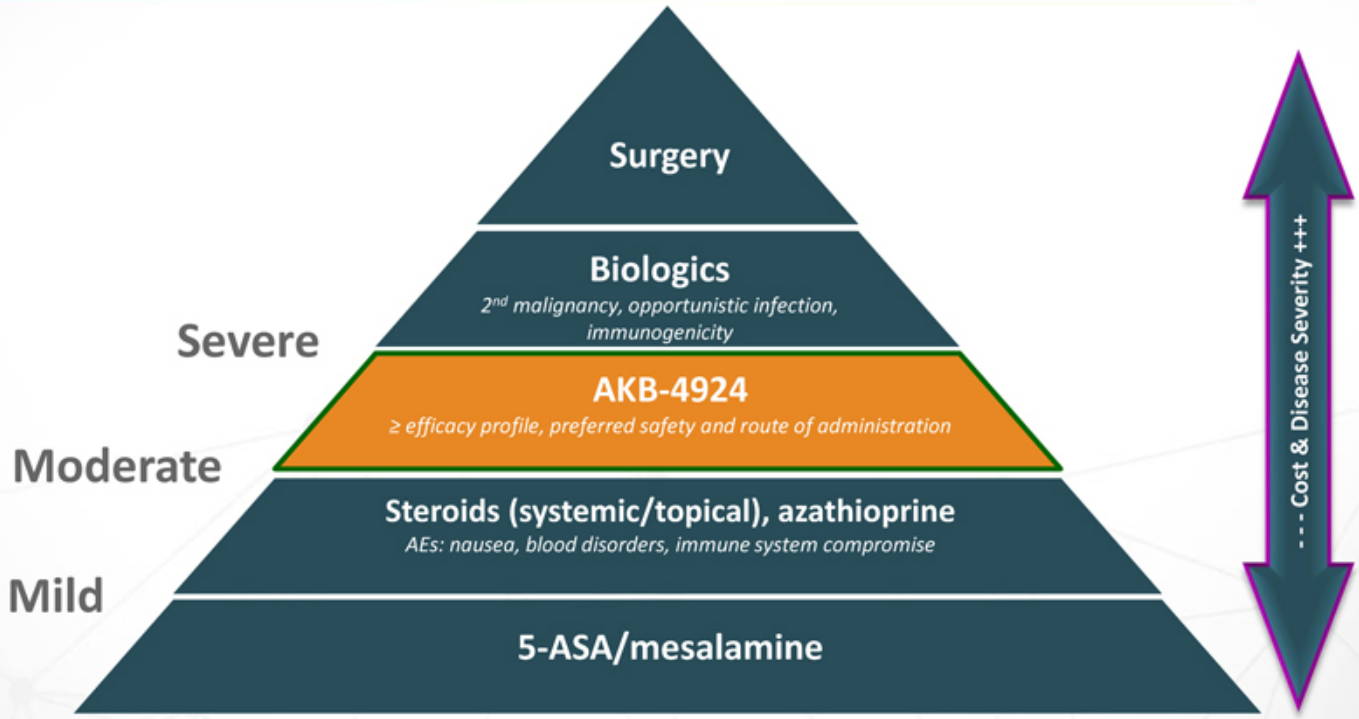



AKB-4924 reduces levels of circulating bacterial endotoxin (LPS) from the gut secondary to restoration of barrier function

Keely et al. Immunology 2014;7:114-123.

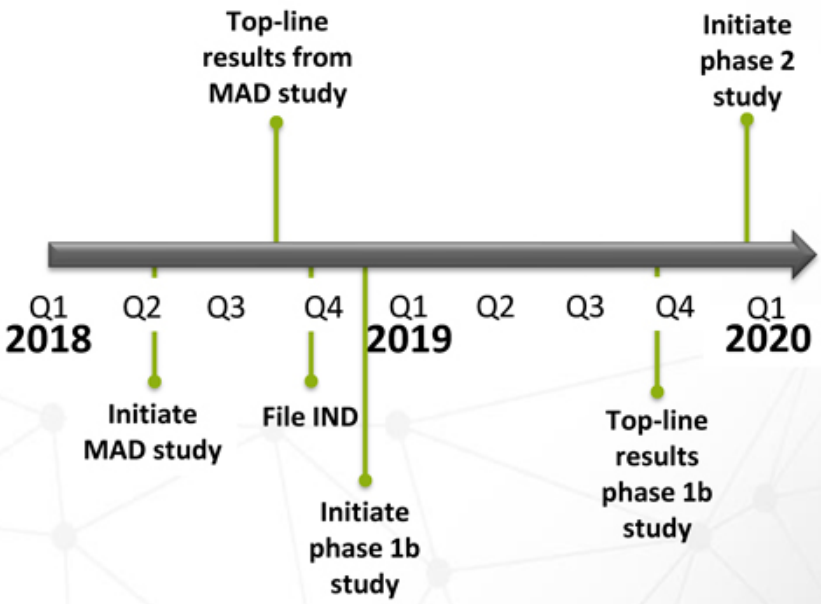
# AKB-4924 profile in IBD supports a significant market opportunity




IBD – Inflammatory bowel disease

# AKB-4924 in inflammatory bowel disease

| AKB-4924 Target Product Profile | |
|---|---|
| Primary Indication | - inducing and maintaining clinical response & remission<br>- improving endoscopic appearance of the mucosa<br>- achieving corticosteroid-free remission |
| Target Pt. Population | Moderate/Severe Ulcerative Colitis |
| Route of Administration | PO (enteric-coated tablet) |
| Dosing Schedule | Once daily |
| Efficacy | ≥ 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

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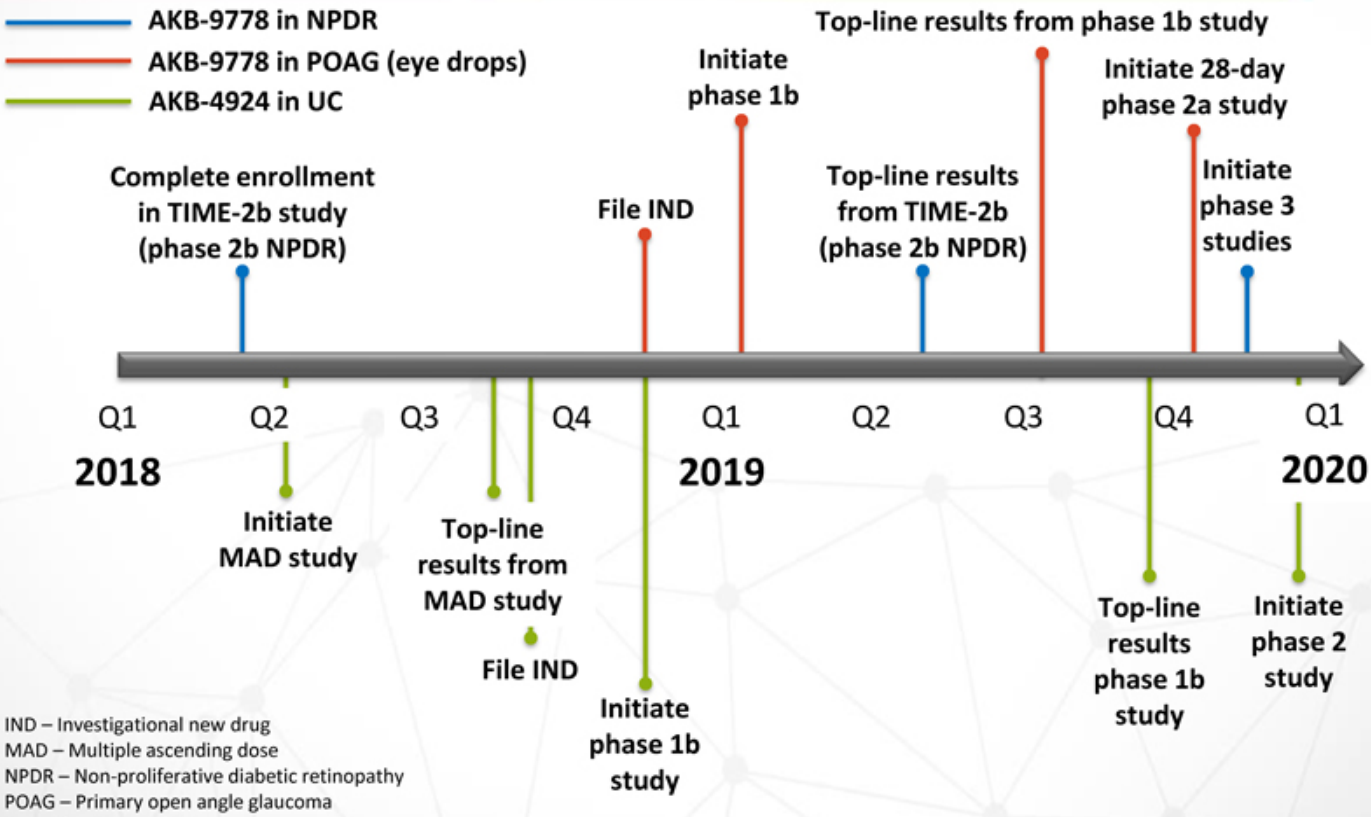
# Pipeline

# Aerpio pipeline based on novel mechanisms

| Product Candidate | Indication | Approach | Stage of Development | | | | Near-Term Milestones |
|---|---|---|---|---|---|---|---|
| | | | Preclinical | Phase 1 | Phase 2a | Phase 2b | |
| **AKB-9778** | **DR** | **Tie2 Activator (SC inj)** | | | | | **Top-line data available Q2 2019** |
| **AKB-9778** | **POAG/ OHT** | Tie2 Activator (eye drop) | | | | | Phase Ib data available in Q3 2019 |
| AKB-4924 | **IBD** | **HIF-1 Stabilizer** | | | | | Phase Ib data available in Q3 2019 |
| **ARP-1536** | **Chronic Indications** | **Tie2 Activator Antibody** | | | | | TBD |

DR – Diabetic retinopathy
IBD – Inflammatory bowel disease
POAG/OHT – Primary open angle glaucoma/ocular hypertension
SC – Subcutaneous

# Upcoming news events




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

# Corporate highlights

- Advancing first-in-class treatments for ophthalmic disease
  - Non-proliferative diabetic retinopathy (NPDR)
  - Primary open angle glaucoma (POAG)
- AKB-9778 is the most potent activator of the Tie2 pathway, proven essential for vascular stability
  - Phase 2b DR data expected Q2 2019
  - Proof-of-concept in DR demonstrated in Phase 2a DME study
  - Approximately 13 million DR patients in the US and 20 million in EU
    - Multi-billion dollar market potential
  - Strong rationale for efficacy in primary open angle glaucoma
    - hase 1b demonstration of intra-ocular pressure lowering Q3 2019
  - Potential for activity in systemic vascular complications of diabetes
- AKB-4924, a HIF-1$\alpha$ stabilizer in development for inflammatory bowel disease
  - Proof-of-concept target engagement data expected Q4 2018
- Aerpio holds global rights to all intellectual property

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