

**PROSPECTUS SUPPLEMENT NO. 9**  
**(To Prospectus Dated June 23, 2017)**



**Aerpio Pharmaceuticals, Inc.**  
**27,367,117 Shares**  
**Common Stock**

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This prospectus supplement no. 9 supplements the prospectus dated June 23, 2017, relating to the offering and resale of up to 27,367,117 shares of our common stock, par value \$0.0001 per share, that were privately issued to selling stockholders in connection with a merger transaction and a private placement.

This prospectus supplement incorporates into our prospectus the information contained in our attached current reports on Form 8-K, which were filed with the Securities and Exchange Commission on January 8, 2018 and April 2, 2018.

You should read this prospectus supplement in conjunction with the prospectus, including any supplements and amendments thereto. This prospectus supplement is qualified by reference to the prospectus except to the extent that the information in the prospectus supplement supersedes the information contained in the prospectus.

This prospectus supplement is not complete without, and may not be delivered or utilized except in connection with, the prospectus, including any supplements and amendments thereto.

Our common stock is presently quoted for trading on the OTC Markets – OTCQB tier, or OTCQB, under the symbol “ARPO.” On May 24, 2018, the closing price of our common stock, as quoted on the OTCQB, was \$4.00 per share.

**You should carefully consider matters discussed under the caption “Risk Factors” beginning on page 9 of the prospectus.**

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the prospectus is truthful or complete. Any representation to the contrary is a criminal offense.**

The date of this prospectus supplement is May 25, 2018.

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

**000-53057**  
(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)

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 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

<u>Exhibit No.</u>	<u>Description</u>
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



# 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





# 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<sup>1,3</sup>, Kevin J. Whitehead<sup>1,3</sup>, and Dean Y. Li<sup>1,2,3</sup>

<sup>1</sup>Department of Medicine, University of Utah, Salt Lake City, UT, 84112, USA

<sup>2</sup>Oncological Sciences, University of Utah, Salt Lake City, UT, 84112, USA

<sup>3</sup>Program in Molecular Medicine, University of Utah, Salt Lake City, UT, 84112, USA

### Angiotensin-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,<sup>†</sup> P. CHARLES LIN,<sup>‡</sup>  
ADRIANNE L. WONG,<sup>§</sup> PREMA RAO,<sup>¶</sup> LIWEN HUANG,<sup>\*\*</sup> MARK W. DEWEHST,<sup>\*\*</sup>  
AND SABITA SANKAR<sup>††</sup>

### Signaling and Functions of Angiotensin-1 in Vascular Protection

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

**Abstract**—Angiotensin-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**



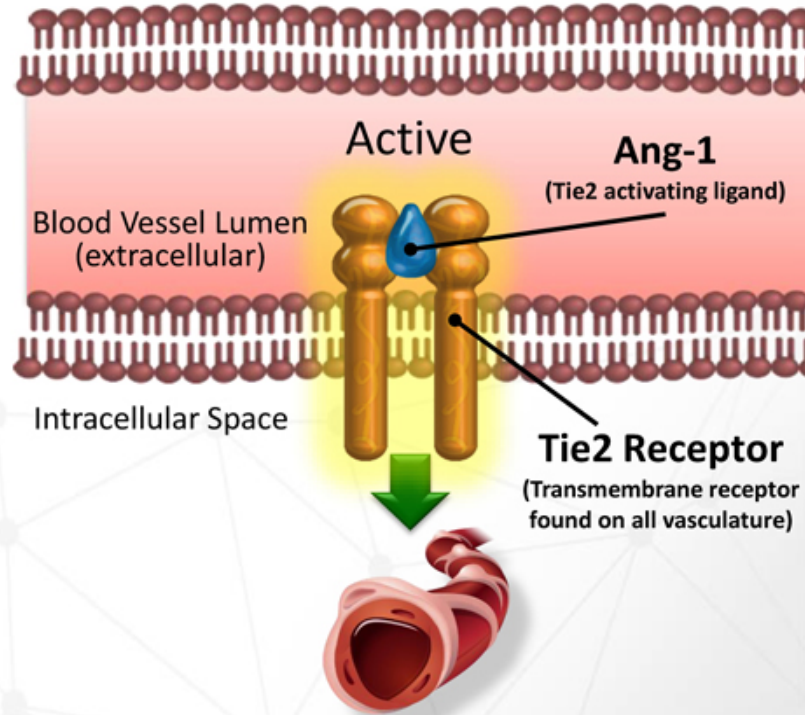
**Ang-2/VEGF Antibody**



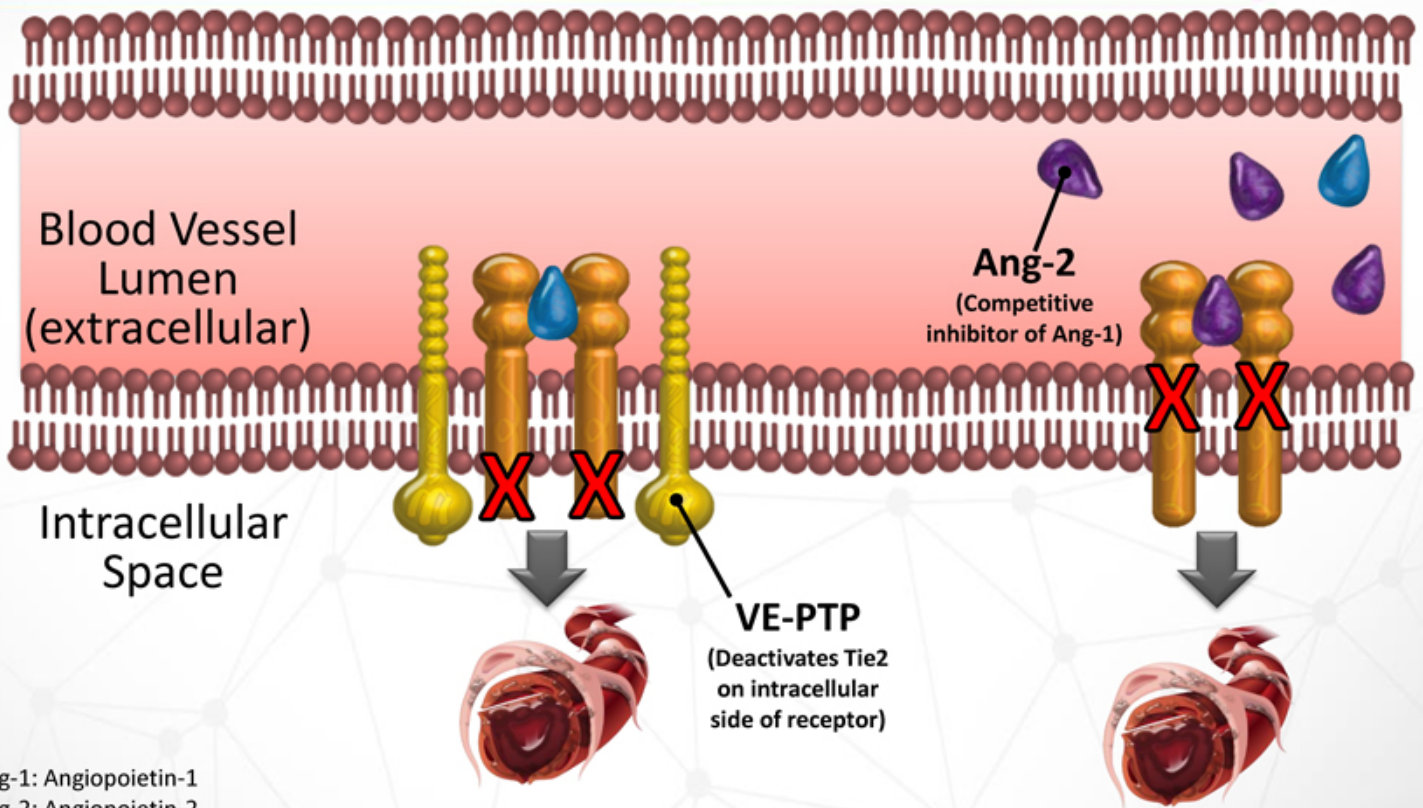
**VE-PTP Small Molecule**

AKB-9778 – Aerpio

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

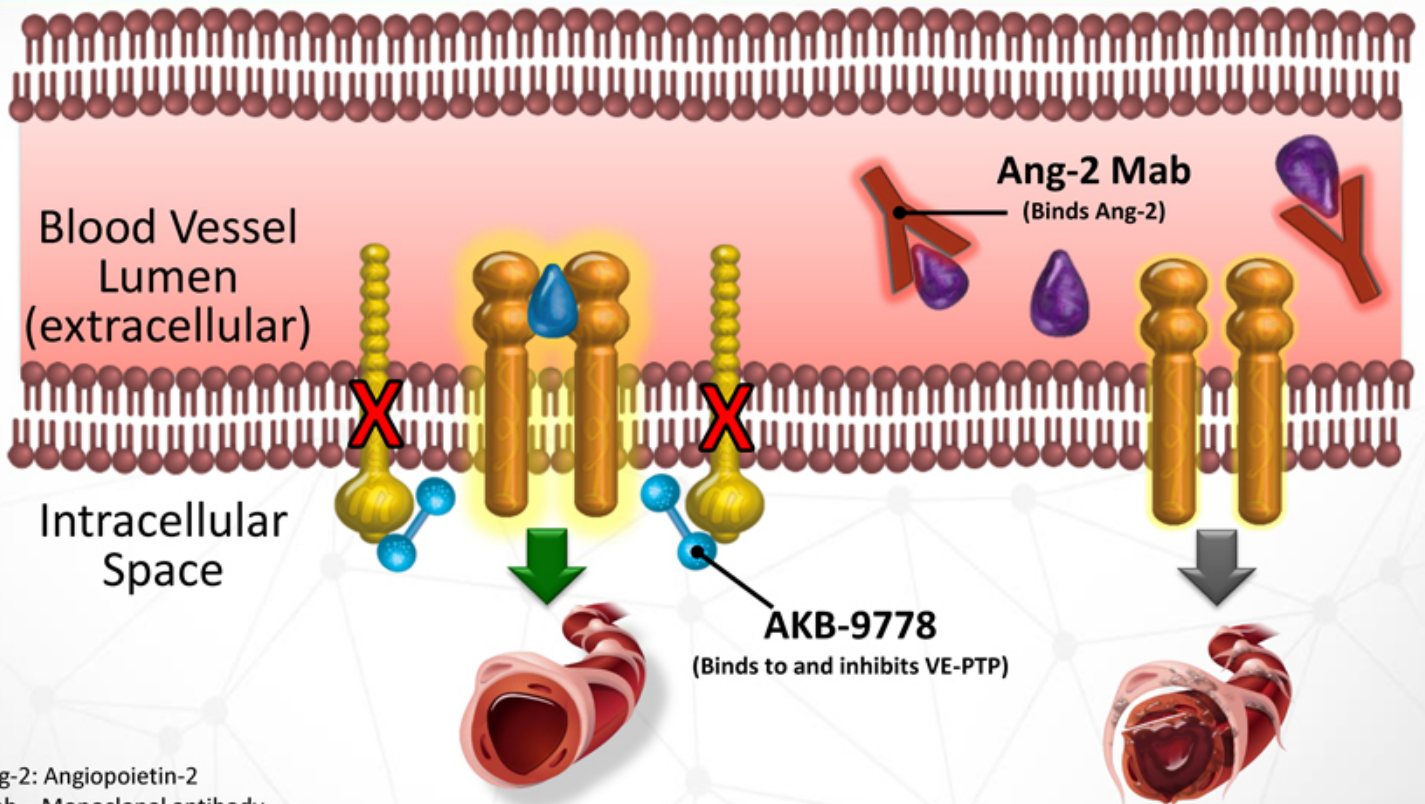


# In diabetic eye disease, VE-PTP and Ang-2 upregulation turns off Tie2



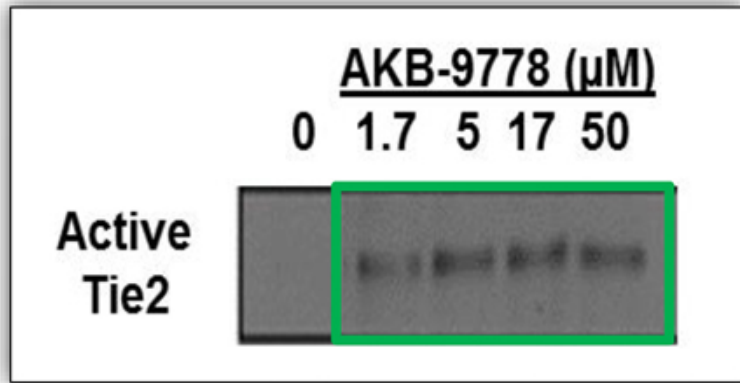
Ang-1: Angiotensin-1  
Ang-2: Angiotensin-2  
VE-PTP: Vascular endothelial protein tyrosine phosphatase

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

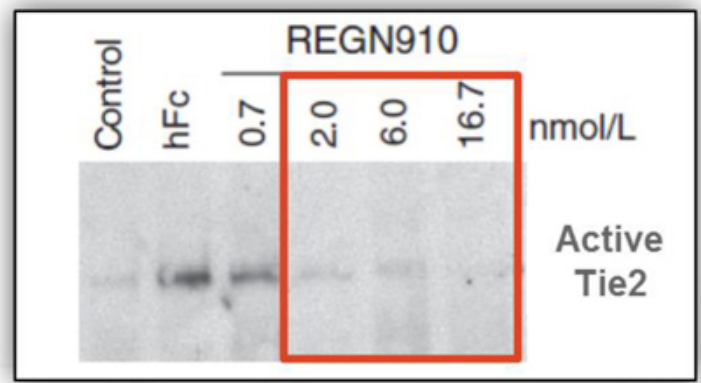


Ang-2: Angiotensin-2  
Mab – Monoclonal antibody  
VE-PTP – Vascular endothelial protein tyrosine phosphatase

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

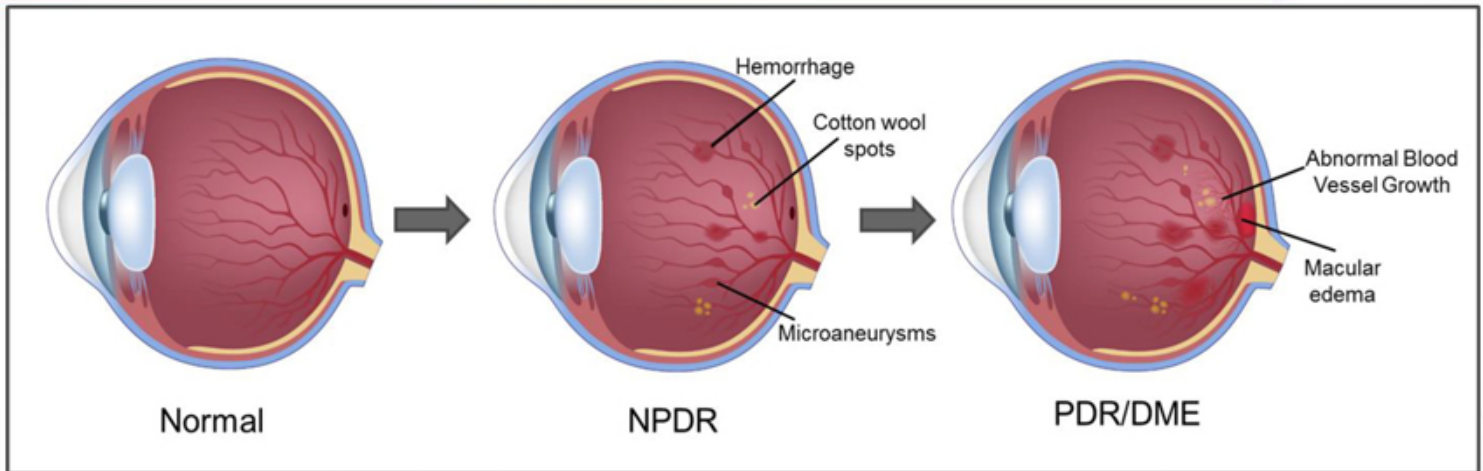


AKB-9778 robustly activates Tie2 in human endothelial cells



Nesvacumab (REGN910) minimally activates Tie2 in human endothelial cells

# 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

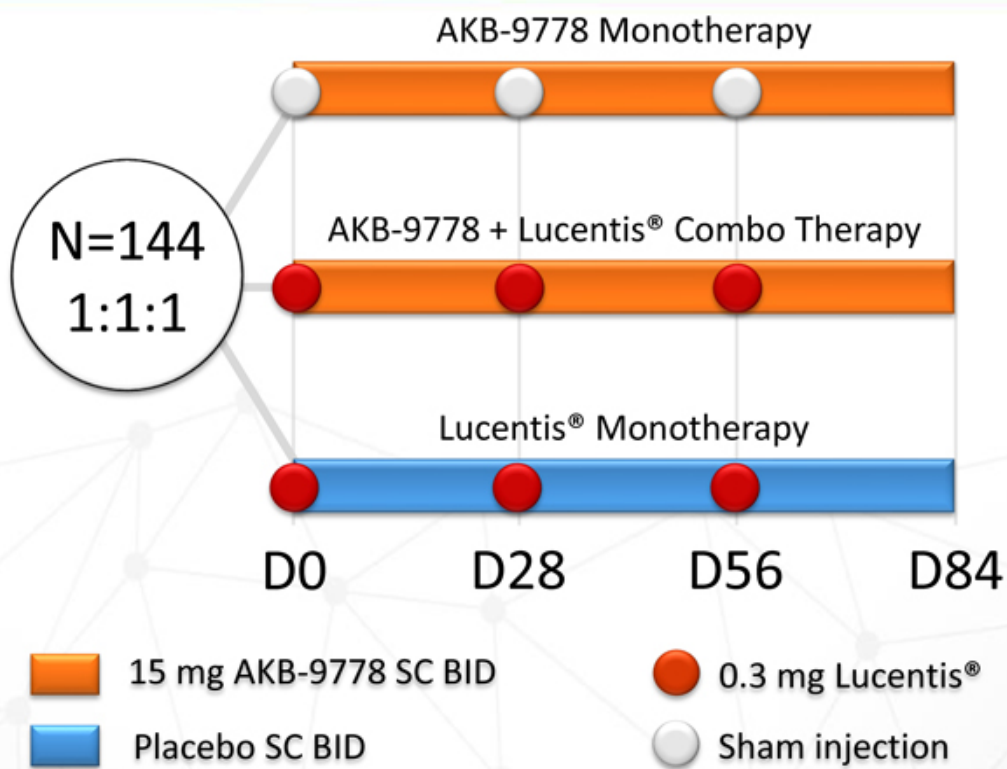
NPDR – Non-proliferative diabetic retinopathy  
PDR – Proliferative diabetic retinopathy  
DME – Diabetic macular edema



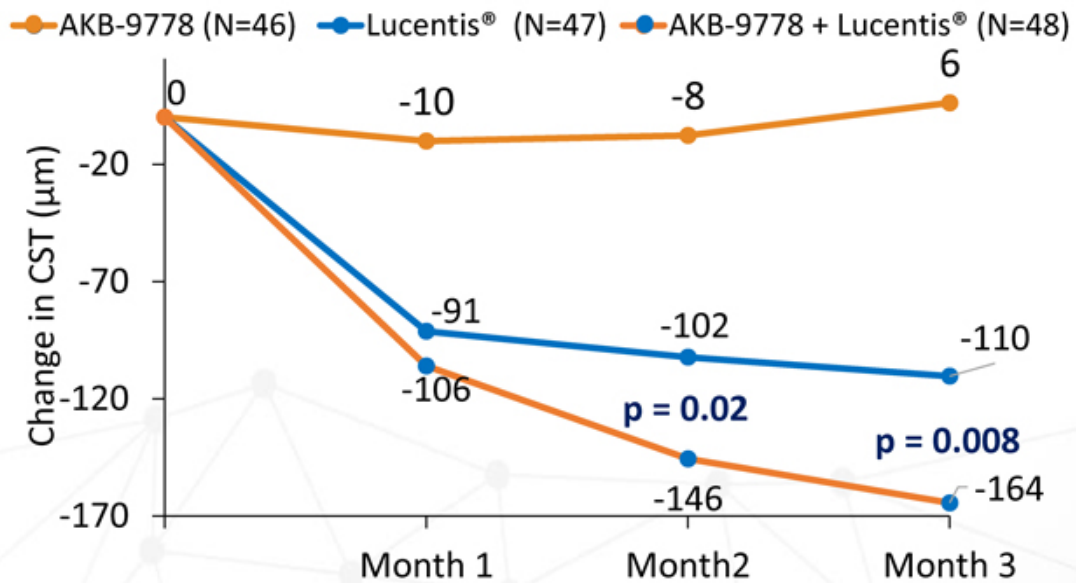
# AKB-9778 TIME-2 Clinical Data: Diabetic Macular Edema



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



# TIME-2: Change in retinal thickness over time

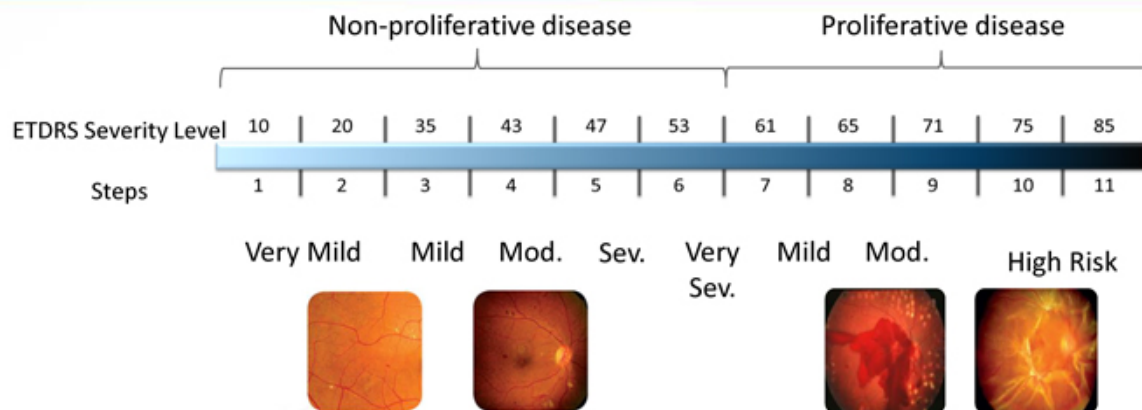


- P1 data showed efficacy as monotherapy in DME prompting testing of monotherapy in P2
- No efficacy seen as monotherapy in primarily VEGF-driven disease (DME)
- Vascular stabilizing effect of combination therapy significantly greater than either agent alone



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

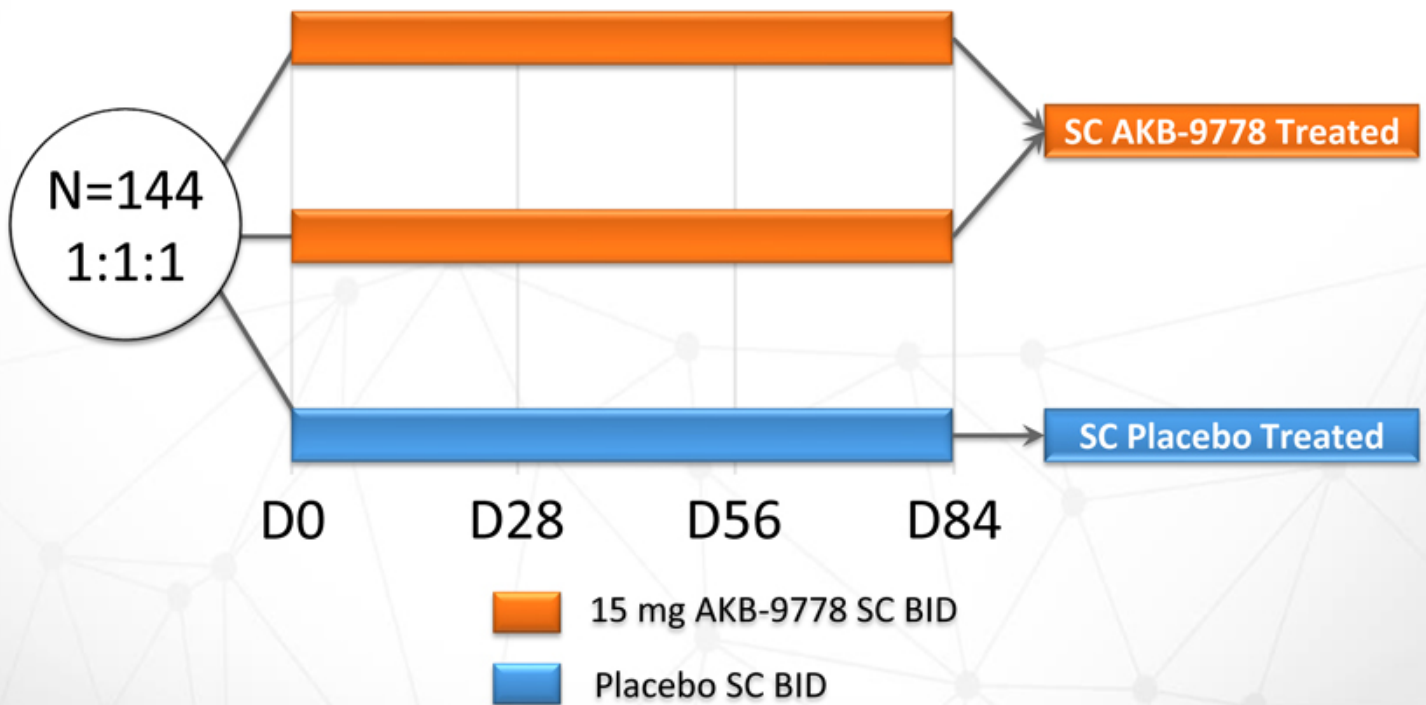
# Progression of diabetic eye disease is measured using a discreet 11-step scale (Diabetic Retinopathy Severity Score - DRSS)



- 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

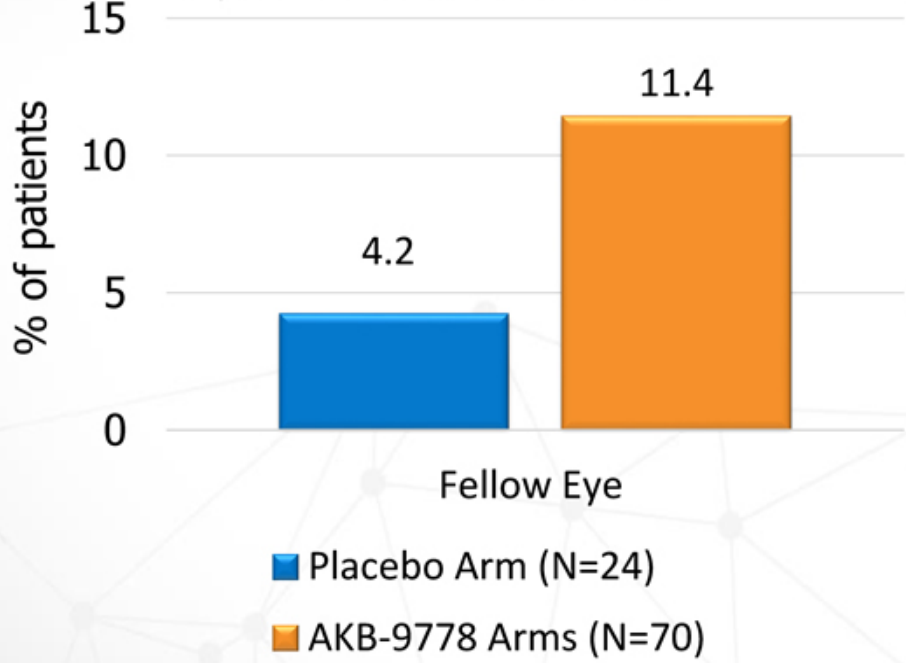
# Assessment of AKB-9778 on DRSS from the TIME-2 study

- 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

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



- 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

# 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

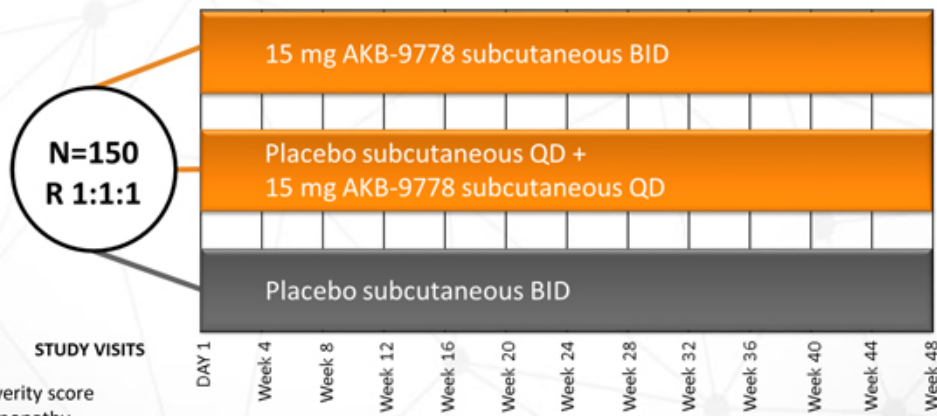




# TIME-2b Study

# 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
- 1<sup>o</sup> Endpoint:  $\geq 2$ -step improvement in DRSS at 48 weeks
- Key 2<sup>o</sup> 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



# Commercial Opportunity: AKB-9778 in Diabetic Retinopathy

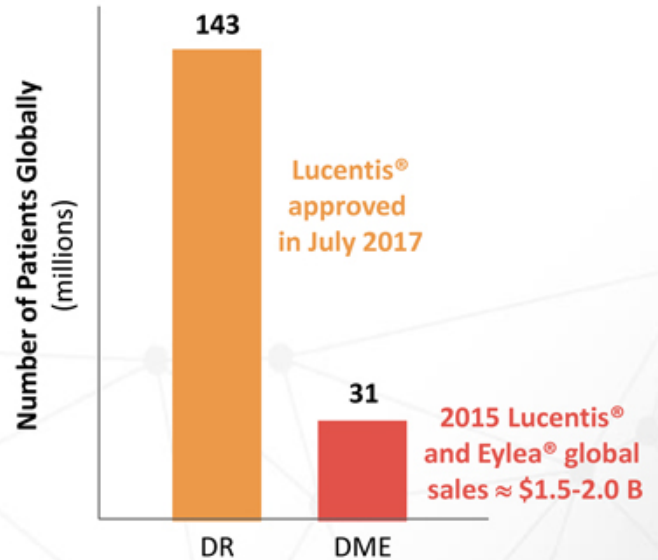
# DR represents a large unmet medical need with significant market potential

- 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.

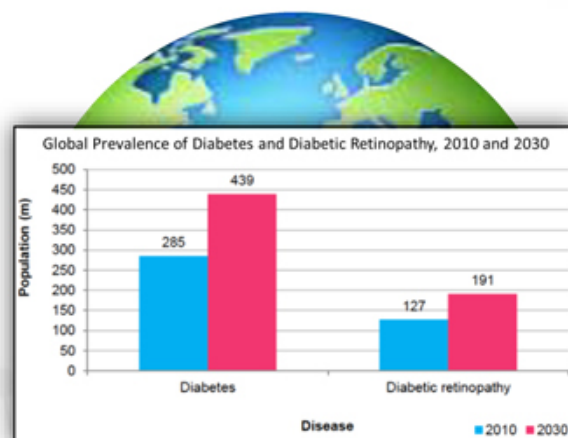
# Unmet need for the treatment of early diabetic eye disease is clear

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

## Need for Earlier Interventions

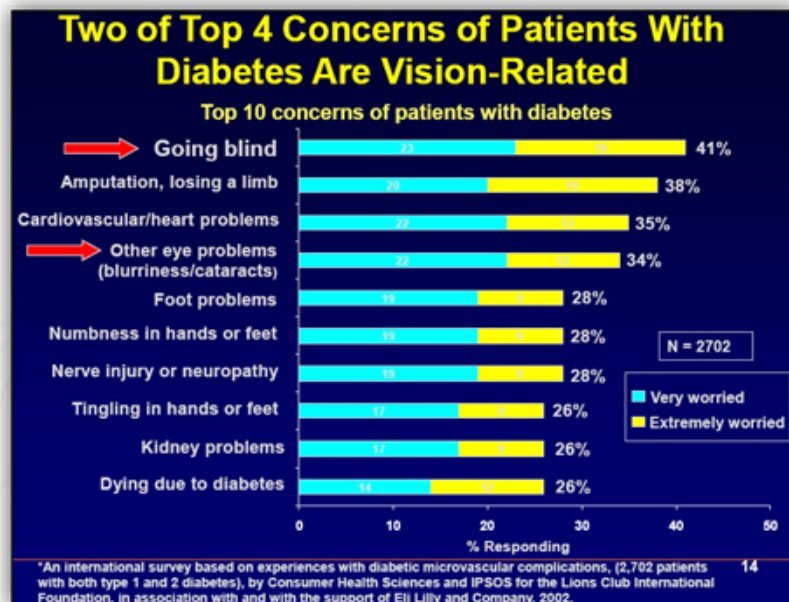
- Our current antiVEGF approaches to DME, and DR with DME, although more effective, are no more an ultimate worldwide therapeutic solution than was laser given the current barriers to access, treatment burden, required expertise, risks, etc.
- To be truly successful we will need low risk, low cost, effective 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

Approved dosing regimen for Lucentis® in DME and DR

12/year



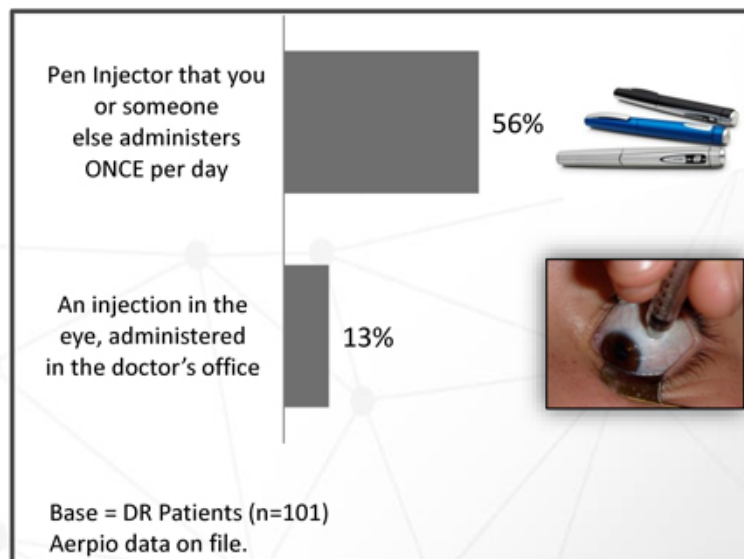
Study of real-world treatment of DME patients over a 12-month period

3.6/year

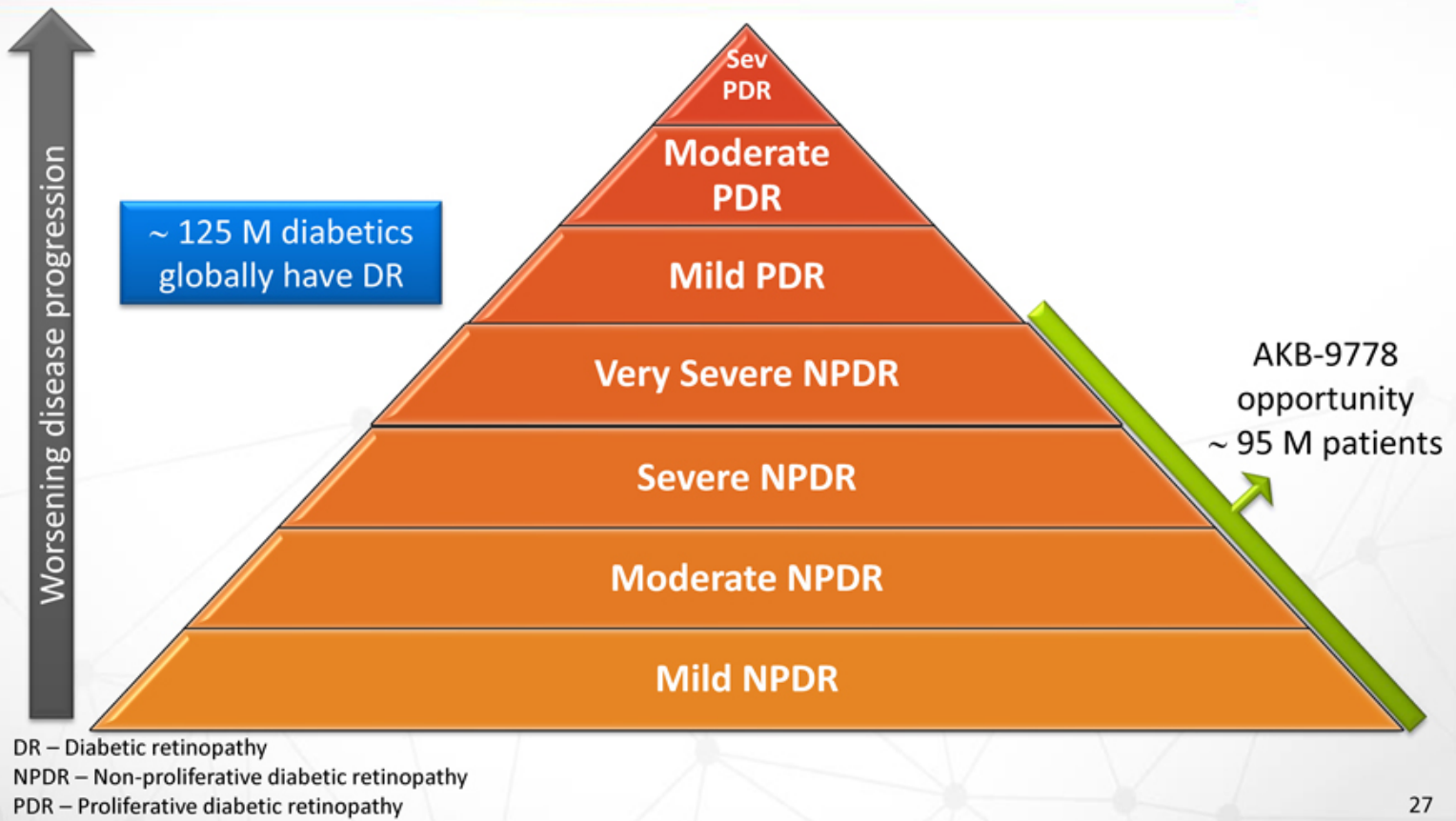


- In contrast, AKB-9778 is patient-administered via daily SC injection
  - Reduces treatment and visit burden
  - More acceptable treatment delivery, avoiding eye injections, for less symptomatic patients
  - Exposure to systemic vasculature may effectively treat both eyes and other vascular complications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

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

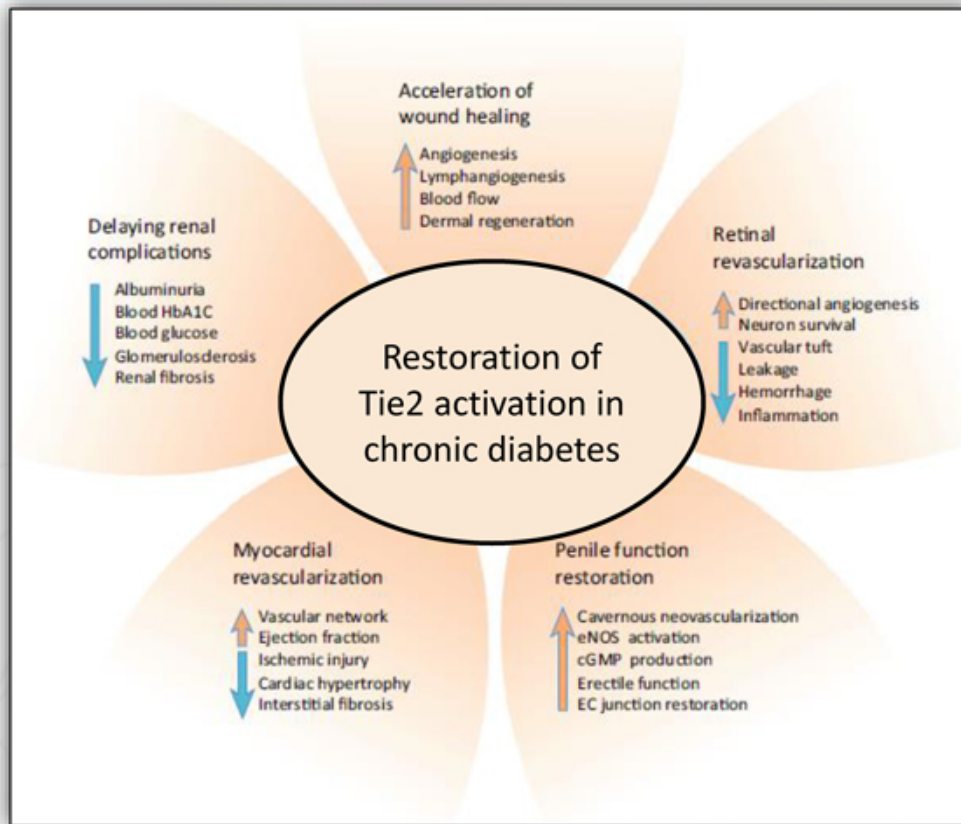


# AKB-9778 market opportunity includes the largest segment of diabetic eye disease





# Systemic Tie2 stabilization may have implications for other diabetic complications





# 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,<sup>1</sup> Stefan Heinen,<sup>7</sup> Marie Jeansson,<sup>1</sup> Asish 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>1</sup> Ann Flenniken,<sup>2</sup> Nicholas W. Gale,<sup>1</sup> Young-Kwon Hong,<sup>4</sup> Amani Fawzi,<sup>4</sup> Xiaorong Liu,<sup>4,2</sup> Tsutomu Kume,<sup>1</sup> and Susan E. Quaggin<sup>1,2</sup>

<sup>1</sup>Feiberg Cardiovascular Research Institute, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA, <sup>2</sup>Lorenzini-Sorenson 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>North 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

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

*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<sup>1</sup>, Petrova TV<sup>1,2</sup>.

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



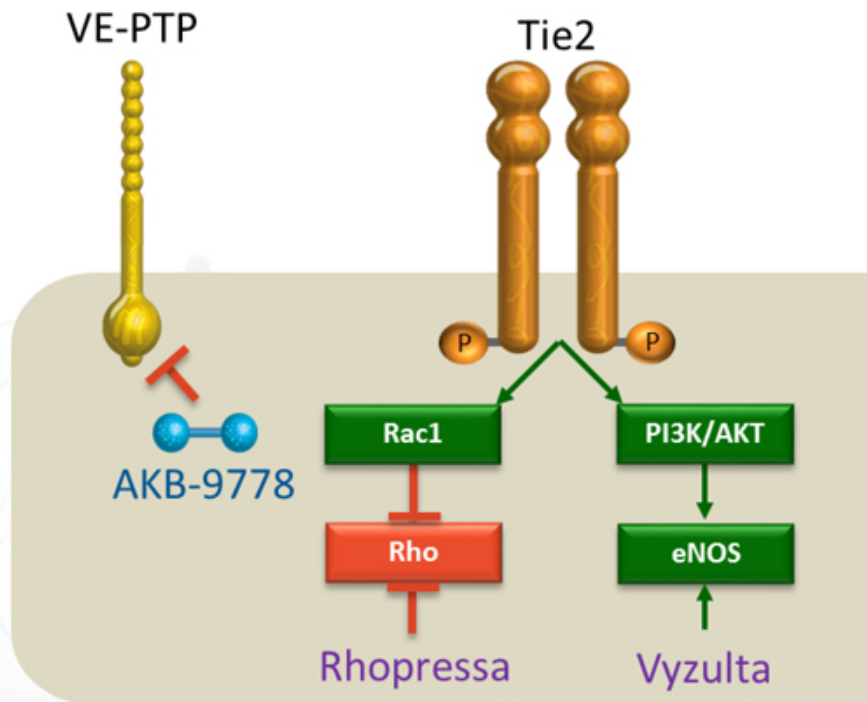
Weinreb, R. N. *et al.* (2016) Primary open-angle glaucoma. *Nat. Rev. Dis. Primers* doi:10.1038/nrdp.2016.67

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)	<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; SD = standard deviation

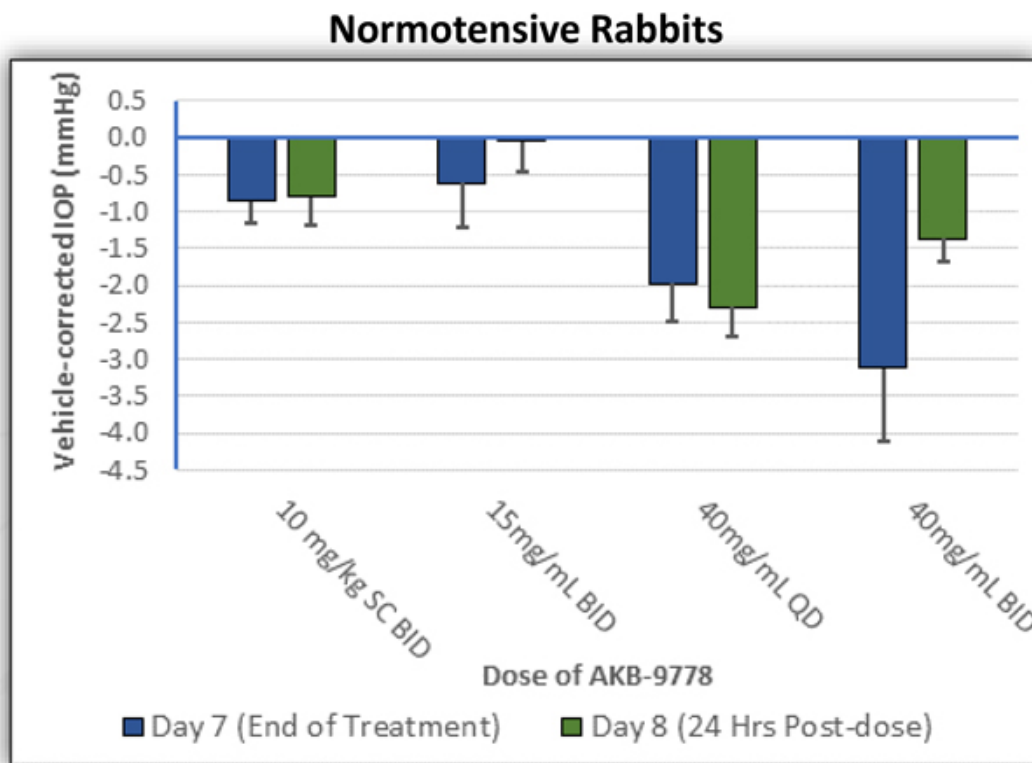
- Reduction of IOP increased to ~ 2-2.5 mm Hg in patients with baseline IOPs ≥ 16 mm Hg, similar to prostaglandin analogs in normotensive glaucoma
- Systemically administered β-blockers and nitrates, drugs used in glaucoma as topical drops, have shown a similar stat sig reductions in IOP when administered 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 Ophthalmol 218:96, 1982

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

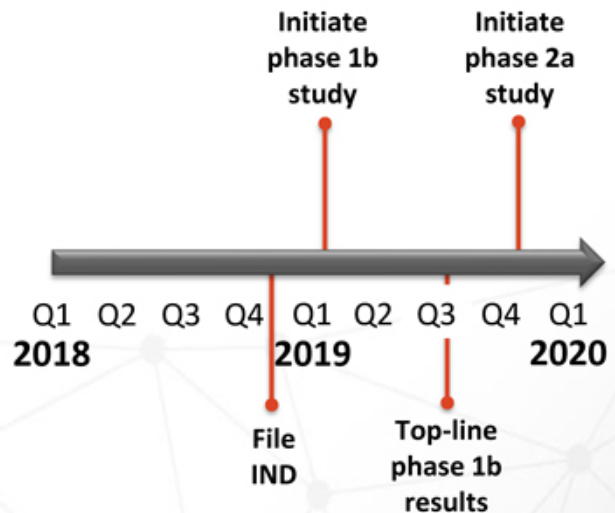


# AKB-9778 in primary open angle glaucoma

## 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 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 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







# AKB-4924: Inflammatory Bowel Disease

# AKB-4924 in inflammatory bowel disease

- First-in-class, HIF-1 $\alpha$  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

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

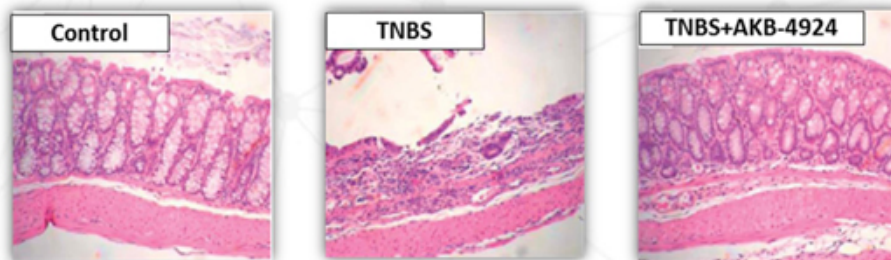
- AKB-4924 is a HIF-1 $\alpha$  stabilizer that represents a new therapeutic class of potentially transformative therapeutics in IBD
- MOA enhances both mucosal wound healing and the resolution of inflammation
  - HIF-1 $\alpha$  regulates innate immune responses by supporting broad-spectrum bactericidal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

HIF-1 $\alpha$  – 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 TNF $\alpha$  overexpression induced Crohn's Disease
  - Gut Graft Versus Host Disease



Normal Gut

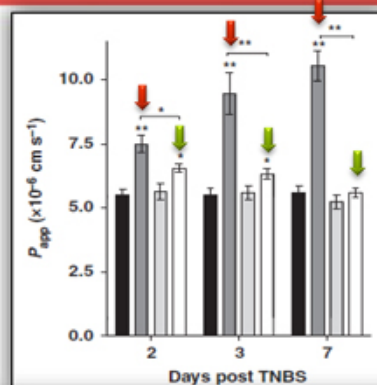
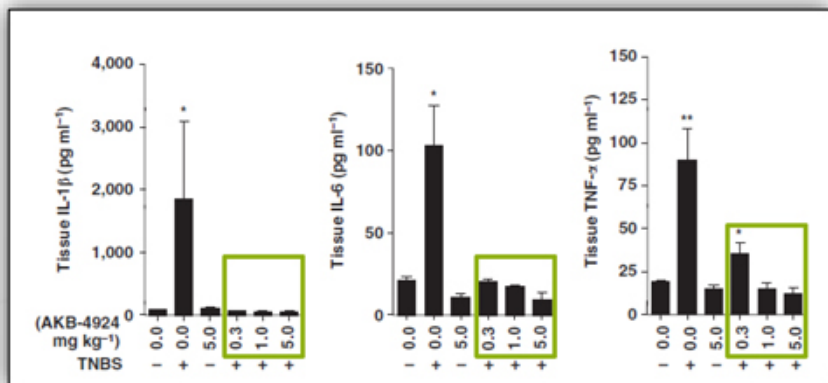
TNBS-Induced Colitis

AKB-4924 Prevention of TNBS Colitis

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

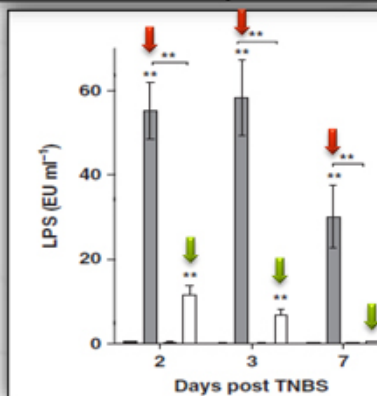
# AKB-4924 decreases colonic cytokine levels and enhances mucosal healing

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



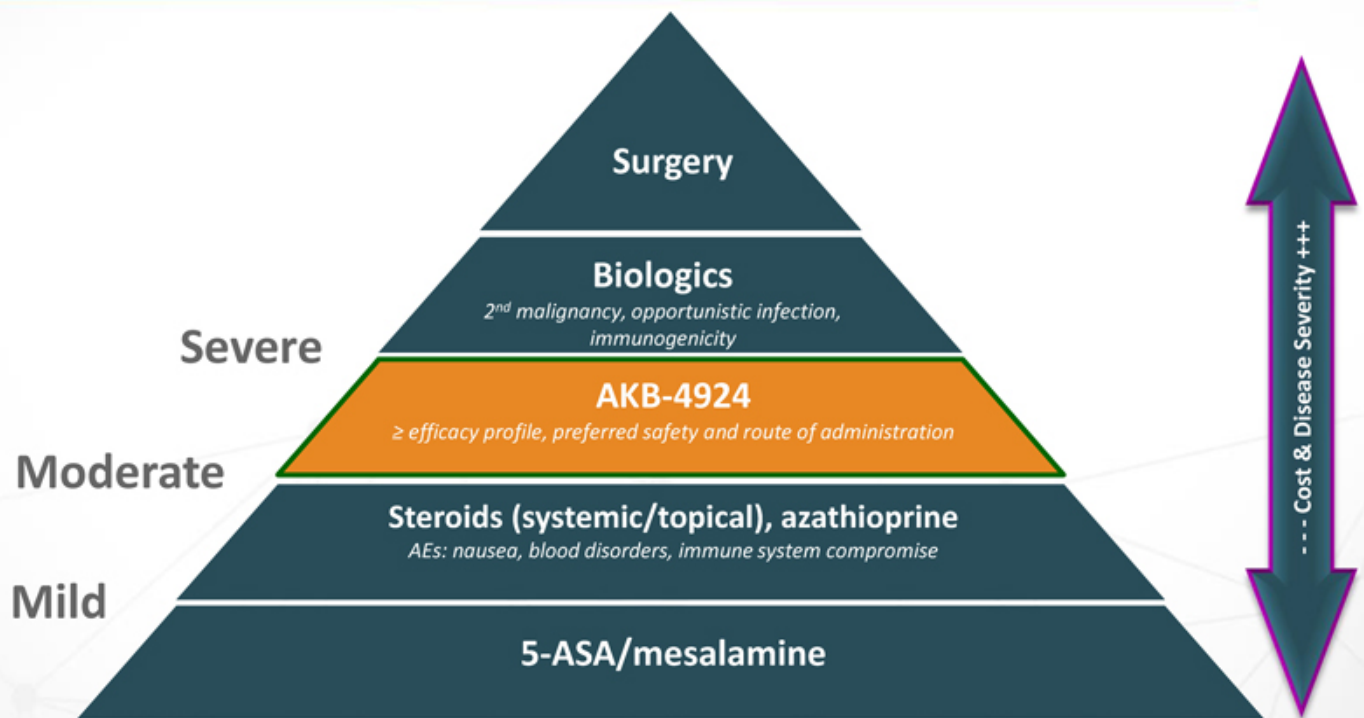
AKB-4924 significantly reduces TNBS-induced leak of fluorescent dextran from colon over 7 days

Legend: ■ EtOH + vehicle, □ EtOH AKB-4924 (5.0 mg kg<sup>-1</sup>), ■ TNBS vehicle, □ TNBS AKB-4924 (5.0 mg kg<sup>-1</sup>)



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

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



# AKB-4924 in inflammatory bowel disease

## AKB-4924 Target Product Profile

**Primary Indication**

- inducing and maintaining clinical response & remission
- improving endoscopic appearance of the mucosa
- achieving corticosteroid-free remission

**Target Pt. Population** Moderate/Severe Ulcerative Colitis

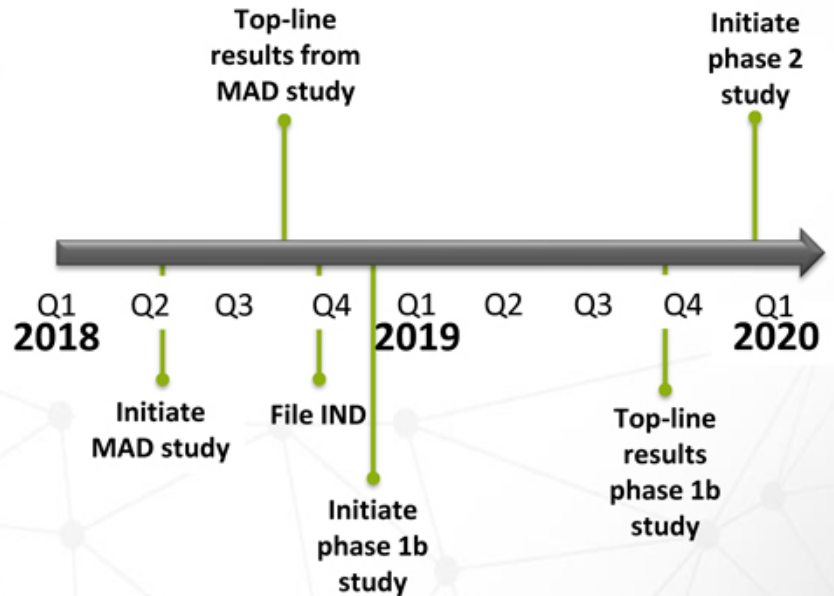
**Route of Administration** PO (enteric-coated tablet)

**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



# Pipeline

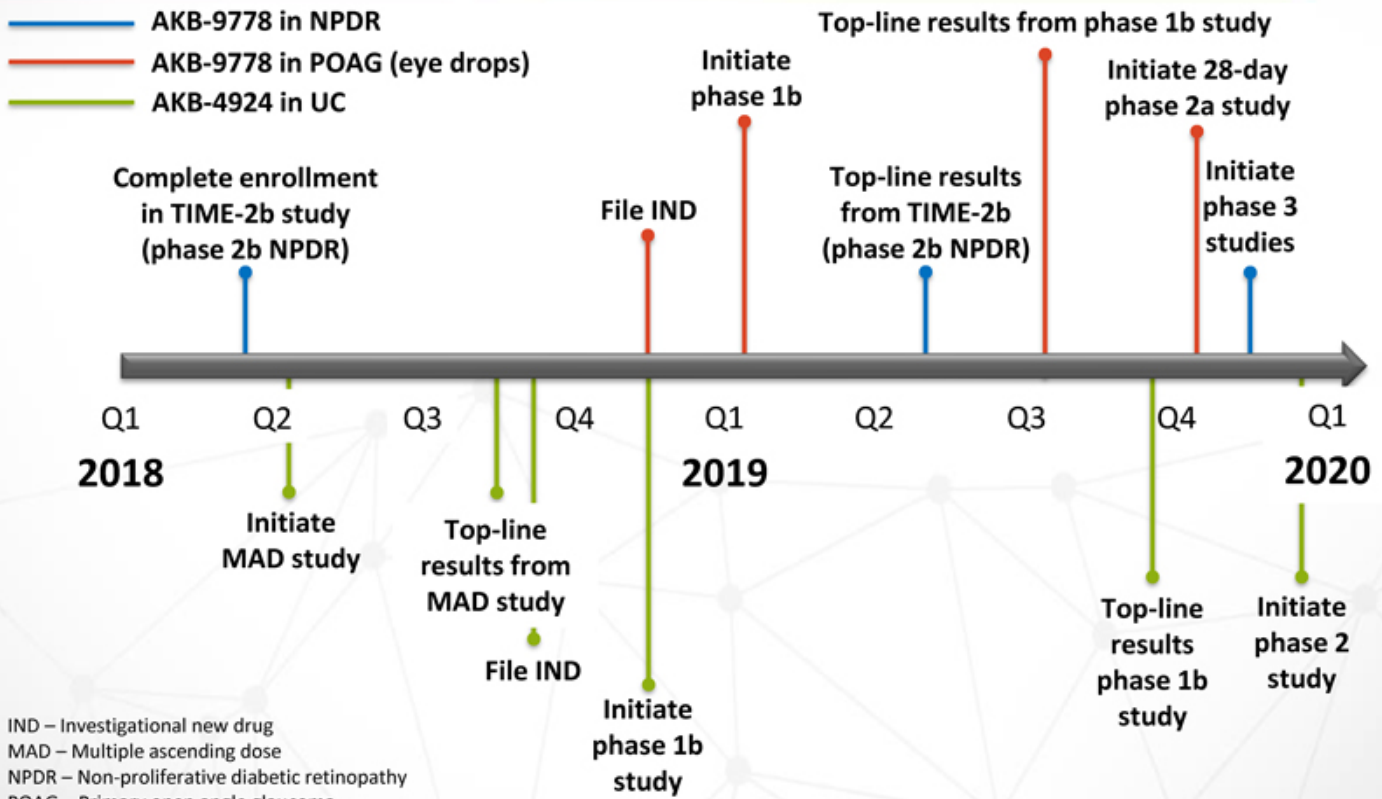


# Aerpio pipeline based on novel mechanisms

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 1b data available in Q3 2019
AKB-4924	IBD	HIF-1 Stabilizer					Phase 1b 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
    - 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
- Aerieo holds global rights to all intellectual property



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

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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): March 29, 2018**

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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)

**000-53057**  
(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 or Rule 12b-2 of the Securities Exchange Act of 1934.

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 1.01 Entry into a Material Definitive Agreement

On March 29, 2018, Aerpio Pharmaceuticals, Inc. (the “Company”) and Blue Ash Landings Acquisition, LLC (the “Landlord”) entered into a Fourth Amendment to Office Lease and Assignment and Assumption of Lease (the “Fourth Lease Amendment”), amending that certain Third Amendment to Office Lease dated February 27, 2015 by and between Aerpio Therapeutics, LLC (formerly known as Aerpio Therapeutics, Inc.), a Delaware limited liability company and wholly-owned subsidiary of the Company (“Aerpio Therapeutics”) and RT Landings Building II, LLC. The Fourth Lease Amendment provides for, among other things an assignment by Aerpio Therapeutics of all of its right, title and interest in and to the lease to the Company, and an assumption by the Company of all of the rights and obligations of Aerpio Therapeutics under the lease; an extension of the term of the lease until July 31, 2021; a change in the Minimum Annual Rent (as defined in the Fourth Lease Amendment) which amount shall initially begin at \$15.00 per square foot on August 1, 2018 and increase annually thereafter by \$0.38 per square foot; a change in the Monthly Rental Installments (as defined in the Fourth Lease Amendment) which amount shall initially begin at \$9,475 per month on August 1, 2018 and increase annually thereafter; and an option for the Company to renew the lease for one (1) successive period of five (5) years.

The Fourth Lease Amendment is filed as Exhibit 10.1 to this Current Report on Form 8-K, and the above description of the Fourth Lease Amendment is a summary and qualified in its entirety by reference to the complete text of the Fourth Lease Amendment.

### Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

<u>Exhibit No.</u>	<u>Description</u>
10.1	Fourth Amendment to Office Lease and Assignment and Assumption of Lease, dated March 29, 2018, by and between Blue Ash Landings Acquisition, LLC and Aerpio Pharmaceuticals, Inc.

**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 2, 2018

**AERPIO PHARMACEUTICALS, INC.**

By: /s/ Stephen J. Hoffman, M.D., Ph.D.  
Stephen J. Hoffman, M.D., Ph.D.  
Chief Executive Officer

**FOURTH AMENDMENT TO OFFICE LEASE  
AND ASSIGNMENT AND ASSUMPTION OF LEASE**

THIS FOURTH AMENDMENT TO OFFICE LEASE AND ASSIGNMENT AND ASSUMPTION OF LEASE (the "**Fourth Amendment**") is executed this 29<sup>th</sup> day of March, 2018 (the "**Effective Date**"), by and between BLUE ASH LANDINGS ACQUISITION, LLC, an Ohio limited liability company ("**Landlord**"), and AERPIO PHARMACEUTICALS, INC., a Delaware corporation ("**Tenant**").

**W I T N E S S E T H:**

WHEREAS, Duke Realty Ohio, an Indiana general partnership ("**Duke**"), and Akebia Therapeutics, Inc. a Delaware corporation, as tenant (the "**Original Tenant**") entered into a certain Office Lease dated September 29, 2009 (the "**Original Lease**"), whereby Tenant leased from Landlord that certain premises known as Suite 510 (the "**Original Leased Premises**") in an office building commonly known as Pfeiffer Place located at 10300 Alliance Road, Cincinnati, Ohio 45242; and

WHEREAS, the Original Lease was amended by that certain First Lease Amendment dated April 23, 2010 (the "**First Amendment**") whereby the Original Leased Premises was substituted for that certain space located at Suite 420 consisting of 7,580 rentable square feet (the "**Leased Premises**") in an office building commonly known as Landings II located at 9987 Carver Road, Blue Ash, Ohio 45242 (the "**Building**"); and

WHEREAS, on or about April 1, 2011, DP Landings Building II, LLC, a Delaware limited liability company ("**DP**") purchased the Building from Duke; and

WHEREAS, the Original Tenant, Aerpio Therapeutics, Inc., a Delaware corporation ("**Aerpio Therapeutics**") and DP executed a certain Second Amendment and Assignment and Assumption of Lease dated April 25, 2012 (the "**Second Amendment**") which included, among other things, the assumption of the obligations under the Original Lease, as amended, by Tenant; and

WHEREAS, on or about May 1, 2013, DP changed its name to RT Landings Building II, LLC, a Delaware limited liability company ("**RT**"); and

WHEREAS, Aerpio Therapeutics and RT executed a certain Third Amendment to Office Lease dated February 27, 2015 (the "**Third Amendment**"), which included, among other things, the extension of the Lease Term. The Original Lease, as amended by the First Amendment, the Second Amendment and the Third Amendment shall be collectively referred to herein as the "**Lease**"; and

WHEREAS, on or about February 8, 2016, Landlord purchased the building from RT; and is the successor-in-interest to the Original Landlord under the Lease; and

WHEREAS, Aerpio Therapeutics converted into a limited liability company and became a wholly-owned subsidiary of Tenant; and



WHEREAS, Aerpio Therapeutics desires to assign all of its right, title and interest in and to the Lease to Tenant, and Tenant desires to assume all of the obligations under the Lease; and

WHEREAS, Landlord and Tenant otherwise desire to amend certain provisions of the Lease, including extension of the Lease Term, as set forth herein.

NOW, THEREFORE, in consideration of the foregoing premises, the mutual covenants herein contained and each act performed hereunder by the parties, Landlord and Tenant hereby agree that the Lease is amended as follows:

1. Incorporation of Recitals. The above recitals are hereby incorporated into this Fourth Amendment as if fully set forth herein.

2. Assignment of Assumption of Lease. Aerpio hereby assigns all of its right, title and interest in and to the Lease to Tenant, and Tenant hereby accepts the assignment and assumption of the Lease and hereby assumes and agrees to be bound by all of the rights and obligations of Aerpio Therapeutics as tenant under the Lease and acknowledges that all provisions of the Lease remain in full force and effect. Tenant agrees to indemnify, defend and hold Aerpio Therapeutics harmless from and against any and all liabilities, claims, demands, damages and causes of action that may now or hereafter be made or asserted against Aerpio Therapeutics arising out of or related to the Lease, and arising or accruing prior to or on the date of this Fourth Amendment.

3. Amendment to Section 1.01 of Lease. Basic Lease Provisions and Definitions.

(a) Lease Term. The parties hereto acknowledge that the Lease Term is currently scheduled to expire June 30, 2018. Landlord and Tenant hereby agree that the Lease Term will hereby be extended by an additional thirty-seven (37) months. Accordingly, upon the Effective Date of this Fourth Amendment, the Lease Term will expire on **July 31, 2021**. Section 1.01(h) is hereby amended and modified to reflect such extended Lease Term.

(b) Minimum Annual Rent. During the extended Lease Term, the Minimum Annual Rent shall be as follows:

July 1, 2018 - July 31, 2018	\$0.00
August 1, 2018 - July 31, 2019	\$113,700.00 (\$15.00/psf)
August 1, 2019 - July 31, 2020	\$116,580.40 (\$15.38/psf)
August 1, 2020 - July 31, 2021	\$119,460.80 (\$15.76/psf)

Section 1.01(d) is hereby modified and amended to reflect such Minimum Annual Rent during the extended Lease Term

(c) Monthly Rental Installments. During the extended Lease Term, the Monthly Rental Installments shall be as follows:

July 1, 2018 - July 31, 2018	\$0.00
August 1, 2018 - July 31, 2019	\$9,475.00 per month
August 1, 2019 - July 31, 2020	\$9,715.03 per month
August 1, 2020 - July 31, 2021	\$9,955.07 per month

Section 1.01(e) is hereby modified and amended to reflect such Monthly Rental Installments during the extended Lease Term.

(d) Brokers: Colliers International representing Landlord and Cushman & Wakefield representing Tenant.

(e) Address for payments and notices are as follows:

**Current Property Manager / Rent Payment Address:**

Colliers International  
425 Walnut Street, Suite 1200  
Cincinnati, OH 45202  
Attn: Becky Ober

**Address of Landlord for Notices:**

Blue Ash Landings Acquisition, LLC  
c/o VanTrust Real Estate, LLC  
4900 Main Street, Suite 400  
Kansas City, MO 64112  
Attn: Jeff S. Smith

With a copy to:

Blue Ash Landings Acquisition, LLC  
c/o VanTrust Real Estate, LLC  
775 Yard Street, Suite 300  
Columbus, OH 43212  
Attn: Bill Baumgardner

With a copy to:

Dentons US LLP  
4520 Main Street, Suite 1100  
Kansas City, MO 64111  
Attn: John L. Snyder

**Address of Tenant for Notices:**

No change from Lease.

3. Condition of Leased Premises. Tenant acknowledges that neither Landlord nor any agent, contractor or employee of Landlord has made any representation or warranty of any kind with respect to the Leased Premises, specifically including, but not limited to, any representation or warranty of suitability or fitness of the Leased Premises for any particular purpose, except as expressly set forth in the Lease, as amended herein. Except as provided in Section 4 of this Fourth Amendment, Tenant accepts the Leased Premises in an “**AS IS - WHERE IS**” condition.”

4. Landlord Improvements. Landlord will perform or cause to be performed, at Landlord’s sole cost and expense, the improvements to the Leased Premises set forth on Exhibit A attached hereto (the “**Landlord Improvements**”). Landlord shall provide Tenant with a proposed schedule for the construction and installation of the Landlord Improvements and will

notify Tenant of any material changes to the schedule. Tenant will reasonably cooperate with Landlord in connection with the performance of the Landlord Improvements and will not materially interfere with Landlord's completion of the same; provided, however, Landlord hereby acknowledges Tenant will be occupying the Leased Premises during the completion of the Landlord Improvements and hereby agrees to make commercially reasonable efforts not to unreasonably interfere with Tenant's use and occupancy of the Leased Premises. Landlord will use commercially reasonable efforts to substantially complete the Landlord Improvements by July 1, 2018, subject to force majeure (as defined in Section 16.03 of the Lease) and delays caused by Tenant.

5. Controllable Expenses. The parties acknowledge and agree that the cap on Controllable Expenses, as provided in Section 3.06, shall remain in place and in full force and effect during the extended Lease Term.

6. Renewal Option. Provided that no Event of Default exists beyond any applicable notice and cure period, then Tenant is hereby granted the option to renew the Lease Term for all, but not part of, the Leased Premises for one (1) successive period of five (5) years (the "**Renewal Term**"), such Renewal Term to commence at the expiration of the extended Lease Term. Tenant shall exercise each option to renew by delivering written notice to Landlord at least nine (9) months prior to the expiration of the extended Lease Term. Any such renewal of this Lease shall be upon the same terms and conditions of the Lease, except the Minimum Annual Rent during the Renewal Term shall be the Fair Market Rent as of the commencement of the Renewal Term for the Leased Premises. Failure by Tenant to provide written notice to Landlord of its intent to renew by the period stated above shall nullify Tenant's renewal rights. Within thirty (30) days after receiving notice from Tenant of its intention to renew, Landlord will provide Tenant with the Fair Market Rent for the Renewal Term and Tenant shall then have thirty (30) days from receipt of Landlord's determination of Fair Market Rent to notify Landlord, in writing, that either (a) Tenant accepts Landlord's determination of Fair Market Rent, in which case Tenant shall be obligated to renew the Lease at the Fair Market Rent rate determined by Landlord, (b) Tenant does not accept Landlord's determination of the Fair Market Rent and withdraws the exercise of its renewal option, in which case Tenant's renewal rights and obligations hereunder shall be forever terminated, or (c) Tenant does not accept Landlord's determination of the Fair Market Rent, but that Tenant still desires to exercise its renewal option, in which case, Landlord and Tenant shall attempt to resolve their differences within thirty (30) days after Landlord's receipt of Tenant's notice. If the parties are unable to agree on the Fair Market Rent within the thirty (30) day period, then, within ten (10) days after the expiration of that period, each party, at its cost and by giving notice to the other party, shall appoint a qualified real estate appraiser or broker with at least ten years full time commercial appraisal experience in the Cincinnati, Ohio area to appraise and set the Fair Market Rent for the Leased Premises. The two appraisers or brokers appointed by the parties as stated in this paragraph shall meet promptly and attempt to establish the Fair Market Rent for the Leased Premises. If they are unable to agree within thirty (30) days after the second appraiser or broker has been appointed, they shall attempt to select a third appraiser or broker meeting the qualifications stated in this paragraph within ten (10) days after the last day the two appraiser or brokers are given to set the Fair Market Rent. Each of the parties shall bear one-half (1/2) of the cost of appointing the third appraiser or broker and of paying the third appraiser or broker's fee. The third appraiser or broker, however selected, shall be a person who has not previously acted in any capacity for either party. Within thirty (30) days

after the selection of the third appraiser or broker, a majority of the appraisers or brokers shall set the Fair Market Rent for the Leased Premises. If a majority of the appraisers or brokers are unable to set the Fair Market Rent within the stipulated period of time, the three appraisals shall be added together and their total divided by three; the resulting quotient shall be the Fair Market Rent for the Leased Premises.

For purposes of determining Fair Market Rent, the parties agree that **“Fair Market Rent”** shall be reasonably determined by Landlord, or the brokers or appraisers, if applicable, in accordance with this Section, based on comparable renewing tenants, including leasing concessions, then being offered for comparable office buildings, both in size and in quality, in the submarket for the Building. The Leased Premises will be provided in its then-existing condition (on an “as-is” basis) at the time the Renewal Term commences and Tenant shall not be entitled to any construction, build out or other allowances with respect to the Leased Premises during the Renewal Term except as may be included as part of the determination of Fair Market Rent. All other terms, covenants, and provisions of the Lease shall continue in full force and effect and be applicable to the Renewal Term.

7. Addition of Section 3.05. Landlord’s Options for Payment of Rent. As to the entire Leased Premises for the Lease Term from and after the date hereof, the following Section 3.05 is hereby added to the Lease:

- “(a) Landlord, from time to time, may designate a lock box collection agent or other person to collect rent hereunder. In such event, Tenant’s payment of rent to the lock box collection agent or other person is deemed to have been made (a) as of the date the lock box collection agent or other person receives Tenant’s payment (if the payment is not dishonored for any reason); or (b) if Tenant’s payment is dishonored for any reason, the date Landlord or Landlord’s agent collects the payment. Neither Tenant’s payment of any amount of rent to the lock box collection agent or other person nor Landlord’s or Landlord’s agent’s collection of such amount if the payment is dishonored constitutes Landlord’s waiver of any default by Tenant in the performance of Tenant’s obligations under this Lease or Landlord’s waiver of any of Landlord’s rights or remedies under this Lease. If Tenant pays any amount to the lock box collection agent or other person other than the actual amount due Landlord, then Landlord’s or Landlord’s agent’s receipt or collection of such amount does not constitute an accord and satisfaction, Landlord is not prejudiced in collecting the proper amount due Landlord (or in pursuing any rights or remedies available under this Lease, at law or in equity as a result of Tenant’s failure to pay the full amount when due) and Landlord may retain the proceeds of any such payment, whether restrictively endorsed or otherwise, and apply the same toward amounts due and payable by Tenant under this Lease.
- (b) Landlord, from time to time at Landlord’s option, may require Tenant to pay all rent by ACH wire transfer to an account designated by Landlord.”

8. Amendment of Section 6.01. Services to be Provided. As to the entire Leased Premises for the Lease Term from and after the date hereof, Section 6.01 of the Lease is hereby amended by deleting subsections (a), (d), and (e), and substituting the following in lieu thereof:

- “(a) During business hours, heating, ventilation and air conditioning to the Leased Premises sufficient to maintain, in Landlord’s reasonable judgment, comfortable temperatures in the Leased Premises. During other times, Landlord will provide heat and air conditioning upon Tenant’s reasonable advance notice. Tenant will pay Landlord, as Additional Rent, for such extended service on an hourly basis at the prevailing rates Landlord reasonably establishes.
- (d) Elevator service to be used by Tenant in common with other tenants. Landlord may restrict Tenant’s use of elevators for freight purposes to the freight elevator and to hours Landlord reasonably determines. Landlord may limit the number of elevators in operation at times other than during business hours.
- (e) Cleaning and janitorial service in the Leased Premises and Common Areas five (5) times per week; provided, however, Tenant shall be responsible for carpet cleaning other than routine vacuuming.”

9. Intentionally deleted.

10. Amendment of Section 7.03. Alterations. As to the entire Leased Premises for the Lease Term from and after the date hereof, Section 7.03 of the Lease is hereby amended by deleting the entirety of Section 7.03 and substituting the following in lieu thereof:

- “(a) Landlord Approval. Tenant will not make any Structural Alterations to the Leased Premises or any Alterations to the Common Areas, without Landlord’s prior written consent, which consent may be withheld in Landlord’s sole discretion. Tenant will not make any other Alterations without Landlord’s prior written consent, which consent Landlord will not unreasonably withhold, condition or delay; provided, however, that Landlord may require, as a condition of its consent, that Tenant remove the Alterations at the end of the Lease Term and repair all damage caused by such removal. Notwithstanding anything to the contrary contained herein, Tenant shall have the right, without Landlord’s consent and in compliance with all other provisions of this Section, to make any non-structural alterations to the Leased Premises which do not materially impact the Buildings mechanical or electrical systems, do not adversely affect the Building’s appearance or value, and the cost of which does not exceed Fifteen Thousand Dollars (\$15,000.00) per project, provided that Tenant gives Landlord fifteen (15) business days prior written notice of any such alterations, along with copies of plans and specifications related thereto. Along with any request for Landlord’s consent, Tenant will deliver to Landlord plans and specifications for the Alterations and names,

addresses of all prospective contractors for the Alterations. If Landlord approves the proposed Alterations, Tenant, before commencing the Alterations or delivering (or accepting delivery of) any materials to be used in connection with the Alterations, will deliver to Landlord for Landlord's reasonable approval copies of all contracts, proof of insurance required by Section 7.03(b), copies of any contractor safety programs, copies of all necessary permits and licenses and such other information relating to the Alterations as Landlord reasonably requests. Tenant will not commence the Alterations before Landlord, in Landlord's reasonable discretion, approves the foregoing deliveries. Tenant will construct all approved Alterations or cause all approved Alterations to be constructed (i) promptly by a contractor Landlord approves in writing in Landlord's reasonable discretion, (ii) in a good and workmanlike manner, (iii) in compliance with all applicable laws, regulations and building codes, (iv) in accordance with all orders, rules and regulations of the Board of Fire Underwriters having jurisdiction over the Leased Premises and any other body exercising similar functions, (v) during times that Landlord reasonably determines in order to minimize interference with other tenants' use and enjoyment of the Building, and (vi) in full compliance with all of Landlord's rules and regulations applicable to third party contractors, subcontractors and suppliers performing work at the Property. For purposes hereof, "**Alterations**" means any changes, alterations, additions or improvements to any portion of the Leased Premises or the Building, and "**Structural Alterations**" means any Alterations involving the structural, mechanical, electrical, plumbing, fire/life safety or heating, ventilating and air conditioning systems of the Building.

- (b) Tenant's Responsibility for Cost and Insurance. Tenant will pay the cost and expense of all Alterations, including, without limitation, any reasonable third-party out of pocket costs related to review of Tenant's proposed plans. Prior to commencing the Alterations, Tenant will deliver the following to Landlord in form and amount reasonably satisfactory to Landlord: (i) builder's "all risk" insurance in an amount at least equal to the value of the Alteration; (ii) evidence that Tenant has in force commercial general liability insurance insuring against construction related risks, in at least the form, amounts and coverages required of Tenant under this Lease, and (iii) copies of all applicable contracts and of all necessary permits and licenses. The insurance policies described in clauses (i) and (ii) of this section must name Landlord, Landlord's lender (if any) and Property Manager as additional insureds. At Landlord's option, Landlord may procure the insurance policy described in clause (i) of this Section (which may include loss of rents coverage), and Tenant shall reimburse Landlord, at Landlord's option as either Additional Rent or a deduction from any applicable improvement allowance, all costs and expenses incurred by Landlord in connection therewith.

- (c) Construction Obligations and Ownership. Landlord may inspect construction of the Alterations. Immediately after completing the Alterations, Tenant will furnish Landlord with full and final lien waivers and receipted bills covering all labor and materials expended and used in connection with the Alterations. Tenant will remove any Alterations Tenant constructs in violation of this Section 7.03 within ten (10) days after Landlord's written request and in any event prior to the expiration or earlier termination of this Lease. All Alterations Tenant makes or installs (including all telephone, computer and other wiring and cabling located within the walls of and outside the Leased Premises, but excluding Tenant's movable trade fixtures, furniture and equipment) shall become the property of Landlord and a part of the Building immediately upon installation and, unless Landlord requires Tenant to remove the Alterations and repair any damage caused by such removal by notifying Tenant at the time Landlord consents to the Alterations, Tenant will surrender the Alterations to Landlord upon the expiration or earlier termination of this Lease at no cost to Landlord.
- (d) Liens. Tenant will keep the Leased Premises and Building free from any mechanics', materialmen's, designers' or other liens arising out of any work performed, materials furnished or obligations incurred by or for Tenant or any person or entity claiming by, through or under Tenant. Tenant will notify Landlord in writing fifteen (15) days prior to commencing any Alterations in order to provide Landlord the opportunity to record and post notices of non-responsibility or such other protective notices available to Landlord under applicable law. If any such liens are filed and Tenant, within fifteen (15) days after such filing, does not release the same of record or provide Landlord with a bond or other security satisfactory to Landlord protecting Landlord and the Property against such liens, Landlord, without waiving its rights and remedies based upon such breach by Tenant and without releasing Tenant from any obligation under this Lease, may cause such liens to be released by any means Landlord deems proper, including, but not limited to, paying the claim giving rise to the lien or posting security to cause the discharge of the lien. In such event, Tenant will reimburse Landlord, as Additional Rent, for all amounts Landlord pays (including, without limitation, reasonable attorneys' fees customarily charged and costs).
- (e) Indemnification. To the fullest extent allowable under the applicable law, Tenant releases and will indemnify, protect, defend (with counsel reasonably acceptable to Landlord) and hold harmless Landlord and the Property from and against any claims in any manner relating to or arising out of any Alterations or any other work performed, materials furnished or obligations incurred by or for Tenant or any person or entity claiming by, through or under Tenant.

(f) Contractor Rules. All contractors, subcontractors, suppliers, and materialmen performing work at the Leased Premises, the Building, or the Park, regardless of whether such work constitutes an Alteration, a Structural Alteration, or otherwise, are bound to comply with the rules and regulations adopted from time to time by Landlord, the current version of which are attached hereto as **Exhibit B-2**.”

11. Amendment of Section 8.05. Landlord’s Insurance. As to the entire Leased Premises for the Lease Term from and after the date hereof, Section 8.05(a) of the Lease is hereby amended by deleting the entirety of Section 8.05(a) and substituting the following in lieu thereof:

“(a) Liability Insurance. Commercial general liability insurance against claims for bodily injury, personal injury, and property damage occurring at the Building in such amounts would other commercially reasonable landlords in the market area in which the Building is located (which may be issued under blanket policies.”

12. Reaffirmation of Section 16.16. Patriot Act. Landlord and Tenant hereby reaffirm Section 16.16 of the Lease.

13. Waiver of Option to Terminate. The parties hereto acknowledge and agree that the option to terminate as set forth in Section 16.17 of the Lease is hereby waived by Tenant and is null and void and of no force and effect.

14. Waiver of Right of First Refusal. The Right of First Refusal set forth in Paragraph 7 of the First Amendment is hereby waived by the Tenant and is hereby null and void and of no force and effect.

15. Exhibits.

(a) The Contractor’s and Vendors’ “Rules of Conduct” attached as Exhibit B-2 to the Lease are hereby deleted and replaced with the Contractor Rules attached as **Exhibit B-2** to this Fourth Amendment.

(b) The Building Rules and Regulations attached as Exhibit E to the Lease are hereby deleted and replaced with the Building Rules attached as **Exhibit E** to this Fourth Amendment.

16. Broker. The parties represent and warrant that, the only real estate brokers involved in the negotiation and execution of this Lease are the Brokers and that no other party is entitled, as a result of the actions of the respective party, to a commission or other fee resulting from the execution of this Lease. Each party shall indemnify the other from any and all liability for the breach of this representation and warranty on its part and shall pay any compensation to any other broker or person who may be entitled thereto. Landlord shall pay any commissions due Brokers based on this Lease pursuant to separate agreements between Landlord and Brokers.



17. Representations and Warranties.

(a) Tenant hereby represents and warrants that (i) Tenant is duly organized, validly existing and in good standing (if applicable) in accordance with the laws of the State under which it was organized; (ii) Tenant is authorized to do business in the State where the Building is located; and (iii) the individual(s) executing and delivering this Fourth Amendment on behalf of Tenant has been properly authorized to do so, and such execution and delivery shall bind Tenant to its terms.

(b) Landlord hereby represents and warrants that (i) Landlord is duly organized, validly existing and in good standing (if applicable) in accordance with the laws of the State under which it was organized; (ii) Landlord is authorized to do business in the State where the Building is located; and (iii) the individual(s) executing and delivering this Fourth Amendment on behalf of Landlord has been properly authorized to do so, and such execution and delivery shall bind Landlord to its terms.

18. Examination of Fourth Amendment. Submission of this instrument for examination or signature to Tenant does not constitute a reservation or option, and it is not effective until execution by and delivery to both Landlord and Tenant.

19. Definitions. Except as otherwise provided herein, the capitalized terms used in this Fourth Amendment shall have the definitions set forth in the Lease.

20. Incorporation. This Fourth Amendment shall be incorporated into and made a part of the Lease, and all provisions of the Lease not expressly modified or amended hereby shall remain in full force and effect.

[SIGNATURES CONTAINED ON THE FOLLOWING PAGES]

IN WITNESS WHEREOF, the parties have caused this Fourth Amendment to be executed on the day and year first written above.

**LANDLORD:**

BLUE ASH LANDINGS ACQUISITION, LLC, an Ohio limited liability company

By: VanTrust Real Estate, LLC, a Delaware limited liability company, as Agent for Landlord

By: /s/ David Harrison

Name: David Harrison

Title: President

STATE OF Missouri )  
                                  ) SS:  
COUNTY OF Jackson )

Before me, a Notary Public in and for said County and State, personally appeared David Harrison, by me known and by me known to be the President, VanTrust Real Estate, LLC, a Delaware limited liability company, as Agent of BLUE ASH LANDINGS ACQUISITION, LLC, an Ohio limited liability company, who acknowledged the execution of the foregoing "Fourth Amendment to Amended and Restated Office Lease" on behalf of said limited liability company.

WITNESS my hand and Notarial Seal this 29 day of March, 2018.



/s/ Cynthia Aitken

Notary Public

/s/ Cynthia Aitken

Printed Signature

My commission Expires: 4-26-2019

**TENANT:**

AERPIO PHARMACEUTICALS, INC., a Delaware corporation

By: /s/ Joseph H. Gardner

Printed: Joseph H. Gardner, PhD

Title: President

STATE OF Ohio )  
 ) SS:  
COUNTY OF Hamilton )

Before me, a Notary Public in and for said County and State, personally appeared Joseph Gardner, by me known and by me known to be the President of AERPIO PHARMACEUTICALS, INC., a Delaware corporation, who acknowledged the execution of the foregoing "Fourth Amendment to Office Lease" on behalf of said limited liability company.

WITNESS my hand and Notarial Seal this 23<sup>rd</sup> day of March, 2018.

/s/ Jennifer Alicia Tarvin

Notary Public

Printed Signature



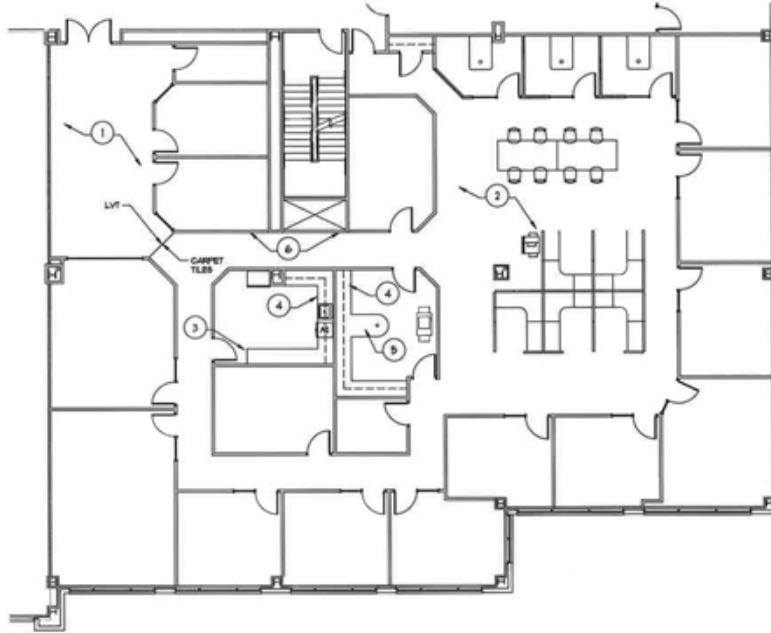
My commission Expires: My Commission Expires August 2, 2020

**EXHIBIT A**

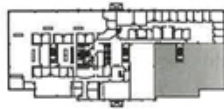
**LANDLORD IMPROVEMENTS**

*[TO BE ATTACHED]*

Exhibit A  
Page 1 of 1



FLOOR PLAN  
1/8"=1'-0"



KEY PLAN  
NTS

PRELIMINARY DRAWING - NOT FOR CONSTRUCTION  
SPACE HAS NOT BEEN FIELD VERIFIED BY CASLER DESIGN GROUP

KEY NOTES

1. NEW GOOD PLANK LVT IN LOBBY. PRICE AS AN ALTERNATE GOOD LAMINATE FLOORING SUCH AS PERISOP.
2. NEW CARPET TILES THROUGHOUT OPEN AREAS AND CORRIDORS. MATERIAL COST \$4.00 PER SQ. YARD. OFFICES AND CONFERENCE ROOMS TO REMAIN AS IS.
3. PATCH AND REPAIR FLOORING IN BREAK ROOM.
4. REPAIR ALL CABINETS IN BREAK AND COPY ROOM.
5. NEW 3/4" X 8" CPY. WORKSURFACE. ATTACH TO AND MATCH EXISTING LAMINATE COUNTERTOP.
6. TOUCH UP PAINT IN CORRIDOR.
7. PRICE AS AN ALTERNATE NEW COUNTERTOPS IN BREAK ROOM.

November 16, 2017

Becky Ober  
 Colliers International  
 Senior Property Manager  
 Cincinnati, Ohio

Proposal # 17.195.587-5  
 Becky.Ober@colliers.com  
 513-587-6691

**Re: Aerpio, 9987 Carver Rd. Suite 420**

The Scope of Work below includes the complete installation of all required items defined below.

**Scope of Work Inclusions:**

**General Conditions:**

- Trash haul and dumpsters
- Thorough final cleaning
- Site Management

**Cabinetry:**

- Installation of new round end countertop with support leg in copy room. Plastic laminate to match existing countertop
- See below for alternate pricing for new breakroom countertop

**Flooring:**

- Furnish and install new carpet tile and vinyl base in corridors and open office areas; work includes moving workstations and large work table
- Work has been priced as after-hours or weekend work
- Furnish and install new LVT and vinyl base in lobby
- Minor repair to existing VCT in breakroom (exact color match not guaranteed)
- Remove and dispose of existing flooring materials

**Paint and Coatings:**

- Paint (1) wall as designated on plan from corner-to-corner, approximately 34' long, and from base to ceiling
- Paint open cube area outside of the copy room
- Painting of doors and frames are not included in this proposal

<b>Total Consideration for Above Scope of Work</b>	<b>\$20,924.00</b>
<b>ADD Alternate #1:</b> Furnish and install new LVT flooring in breakroom in lieu of VCT repairs	<b>\$ 1,148.00</b>
<b>ADD Alternate #2:</b> Furnish and install new plastic laminate countertop in breakroom	<b>\$ 1,940.00</b>
<b>ADD ALTERNATE #3:</b> Furnish and install two (2) new plastic laminate wall cabinets 5 lineal feet to match the existing cabinetry	<b>\$ 812.00</b>
<b>ADD Alternate #4:</b> Furnish and install new LVT flooring in workroom in lieu of VCT repairs	<b>\$ 1,044.00</b>

**Qualifications:**

- All flooring work to be performed after business hours or on weekends
- All other work to be performed during normal business hours
- Furniture moving is included for carpet tile work areas, however worksurfaces must be completely clear of all equipment and accessories, and all electronic equipment (including all computer equipment) must be un-plugged and removed from the worksurface and the work area in general
- No security

**Payment Terms:**

- 50% deposit prior to start up for material order
- 50% upon completion of project

**This proposal was based on a site visit with all responsible trades. All conditions are approximate and subject to field and drawing verification. Any changes resulting from new construction documents may result in additional construction costs or deductions dependent on scope modifications.**

We appreciate the opportunity to provide you with this proposal and trust the contents contain the information you require to select a2i as your Design | Build partner.

Thank you,

Betsy Moore  
Project Manager

**Signature acceptance by:** \_\_\_\_\_

**Print name and title:** \_\_\_\_\_

**Date:** \_\_\_\_\_



**Schedule of Values**

AERPIO

9987 CARVER RD. SUITE 420

16-Nov-17

A ITEM NO.	B DESCRIPTION OF WORK	C SCHEDULED VALUE
01-000	General conditions (dumpster and hauling, cleaning, misc.)	\$ 2,350.00
06-400	Architectural woodwork (new round-end countertop w support leg in copy room)	\$ 1,575.00
09-600	Flooring (carpet tile + vinyl base + LVT in lobby + vct repair in breakroom)	\$ 12,248.00
09-900	Paint & coatings	\$ 1,865.00
	Overhead & management fees	\$ 2,886.00
	<b>Grand Total</b>	<b>\$ 20,924.00</b>
	<b>ADD Alternate #1: furnish and install LVT in breakroom</b>	<b>\$ 1,148.00</b>
	<b>ADD Alternate #2: furnish and install new plastic laminate countertop in breakroom</b>	<b>\$ 1,940.00</b>
	<b>ADD Alternate #3: furnish and Install two (2) new plastic laminate wall cabinets 5 lln. ft. to match existing cabinetry</b>	<b>\$ 812.00</b>
	<b>ADD Alternate #4: furnish and install LVT in workroom</b>	<b>\$ 1,044.00</b>



**EXHIBIT B-2**

**CONTRACTOR RULES**

Contractors, subcontractors, suppliers, materialmen (hereinafter, each a “**Contractor**”), shall be advised of the following rules and regulations (the “**Contractor Rules**”) concerning their proper conduct within the building commonly known as Landings II, located at 9987 Carver Road, Blue Ash, Ohio 45242 (the “**Building**”), and that certain Leased Premises (as defined in the Lease, as amended by the Fourth Amendment). All referenced material, labor, services, taxes, after hour’s costs, shipping, permits, fees or construction and/or other reference processes performed by Contractor, shall be hereinafter referred to as the “**Work.**” Any defined terms not otherwise defined herein shall have the same meaning as set forth in the Lease (as defined above).

It is the Contractor’s responsibility to ensure its personnel, subcontractors, suppliers, and materialmen read and understand these Contractor Rules. Ignorance of these Contractor Rules is not a waiver of liability or responsibility. Failure to comply with these Contractor Rules may result in Contractor being asked to leave the job site. Contractor is ultimately responsible for the conduct of its personnel, subcontractors, suppliers, and materialmen. The signature on the last page of these Contractor Rules shall act as the written approval by the Contractor of these Contractor Rules.

1. Prior to starting any Work in the Building, Contractor, at its sole expense, shall procure and maintain during the term of its contract to perform the Work, insurance covering Contractor, its subcontractors and anyone directly or indirectly employed by any of them, issued by an insurance company which has an A.M. Best rating of A-VII or better and is authorized to transact business in the state which the Leased Premises is located. All policies are to protect the Landlord against liabilities arising out of the operations of Contractor and its subcontractors in the performance of the Work, including at least and in amount not less than the following and such other types and amounts of insurance as Landlord deems necessary:

a. Commercial General Liability Insurance. Commercial general liability insurance to protect against claims for bodily injury and property damage arising out of premises operations, products, and completed operations, and advertising and personal injury liability, written on an occurrence basis using ISO Form CG0001 (or its equivalent) with no amendments to the definition of an insured contract, in limits of not less than \$1,000,000 inclusive, per occurrence, and \$2,000,000 annual aggregate per project with a \$2,000,000 Products/Completed Operations Aggregate, or such higher limits as Landlord may require. Completed Operations to remain in force for maintained for the duration of the applicable statute of repose following project completion. To the extent permitted by applicable law, such policy(ies) shall include a waiver of any right of subrogation of the insurers thereunder against Landlord, VanTrust Real Estate, LLC (“**VTRE**”), Property Manager, and all mortgagees of Landlord;

b. Commercial Automobile Liability Insurance. Commercial automobile liability insurance to include contractual liability insurance for the indemnities set forth in this Contract covering all owned, non-owned and hired automobiles, in limits of not less than \$1,000,000 combined single limit (each accident), or such higher limits as Landlord may require. To the extent permitted by applicable law, such policy(ies) shall include a waiver of any right of subrogation of the insurers thereunder against Landlord, VTRE, Property Manager, and all mortgagees of Landlord;

c. Employer's Liability Insurance and Workers Compensation. Employer's Liability insurance, with minimum limits of not less than \$1,000,000 bodily injury each accident, \$1,000,000 bodily injury by disease policy limit and \$1,000,000 bodily injury by disease each employee, and Worker's Compensation, in form and amount as required by applicable state law. To the extent permitted by applicable law, such policy shall include a waiver of any right of subrogation of the insurers thereunder against the Landlord, VTRE, Property Manager, and all mortgagees of Landlord;

d. Umbrella Liability Insurance. Umbrella liability insurance over the primary general liability, automobile liability and employer's liability insurance policies in limits of not less than \$5,000,000 inclusive per occurrence, and \$5,000,000 annual aggregate, per project, or such higher limits as Landlord may require. To the extent permitted by applicable law, such policy(ies) shall include a waiver of any right of subrogation of the insurers thereunder against Landlord, VTRE, Property Manager, and all mortgagees of Landlord; and

e. Builder's Risk Insurance. Builder's Risk insurance on a "Special Form" basis (including collapse) using a completed value (non-reporting) form for full replacement cost covering all work which Contractor is performing and all materials and equipment used or installed in or about the project, off site and in transit. This insurance shall include: (i) interests of Landlord, VTRE, Property Manager, all tenants, all mortgagees of Landlord, Contractor, subcontractors and sub-subcontractors; and (ii) a mutual release and waiver of subrogation for all parties. At Landlord's option, Landlord may procure the insurance policy described in this subsection (e) (which may include loss of rents coverage), and Tenant shall reimburse Landlord, at Landlord's option as either Additional Rent or a deduction from any applicable improvement allowance, all costs and expenses incurred by Landlord in connection therewith.

f. Certificates of insurance must be provided to Landlord prior to the start of the Work on the project site. Landlord, VTRE, Property Manager, all mortgagees, (and others who may be required, as evidenced by inclusion in an Acord Certificate as additional insureds), will be named as primary non-contributing additional insureds on the insurance coverages described in subsections (a) and (d) above, including completed operations with respect to all matters arising out of the performance of services under this Contract. It is Contractor's sole responsibility to procure and maintain insurance covering its personal property located at the project site. All policies required above shall contain no exclusions for work expressly within the Contractor's scope of work. It is Landlord's sole responsibility to procure and maintain property insurance covering Landlord's real property where the project is located (other than the Work) and Landlord's personal property and the personal property of others located at the project site that are under Landlord's care, custody or control.

2. If required pursuant to the Lease, Contractors working in or about the Building must have prior written approval from the Landlord before any type of Work may commence. A list of subcontractors must be provided by the Contractor to the Landlord and Property Manager along with suitable scheduling and delivery / stocking information before construction begins. Any persons not on the approved contractor list will be denied access to the Building—no exceptions. This list will include phone numbers and contacts for Contractor and its subcontractors, including home and emergency telephone numbers.

3. An initial walk through of the job site among Contractor's superintendent, representatives of Contractor's key subcontractors, the Property Manager, the Property Manager's engineer, and any other Landlord representatives will be conducted prior to construction. The foregoing shall review these Contractor Rules, as well as check for existing conditions of the Leased Premises.

4. Contractors and all its subcontractors must be licensed in the state in which the Work is performed, and have work experience in commercial properties similar to the Building.

5. Where applicable, permits must be obtained, by Contractor, from the applicable municipal building department or other governing agency prior to the commencement of Work. Permits must be posted at the job site in accordance with local governmental requirements. All applicable construction Work will require a permit. Approval of drawings, details, schedules, etc., by Landlord or Property Manager shall not relieve the Contractor from the responsibility for compliance with local, county, state or federal laws, rules, ordinances, or rules and regulations of commissions, boards, or other authorities having jurisdiction.

6. Contractor shall keep the Leased Premises and improvements free and clear of all liens arising out of or claimed by reason of any Work performed, materials furnished or obligations incurred. Contractor is responsible for the payment of all bills for labor and materials furnished by or to it and its subcontractors performing Work at the Building.

7. No one shall be allowed to endanger the Building or its occupants in any manner whatsoever. If such a situation occurs, the Contractor shall immediately take steps to correct and eliminate the hazardous condition. In the event that the Contractor to eliminate the hazardous condition in a satisfactory manner, Landlord and Property Manager reserve the right to immediately take steps to remedy the hazardous condition at the Contractor's sole expense.

8. Contractor is not permitted to post any sign on the job site advertising the name of the Contractor or its subcontractors.

9. It is imperative that good business/professional conduct be maintained by all Contractor's personnel while they are at the Park and that they are properly dressed for the environment they are working in and the Work being performed. Contractor shall not employ any unfit person or anyone not skilled in the task assigned to Contractor. Respect must be shown to the Building tenants at all times. Rude and obscene behavior (harassment, sexual or otherwise), including foul and abusive language, will not be tolerated. Offenders will be asked to remove themselves from the Park and shall not be permitted to return.

10. All Contractors' personnel will enter and exit through the South Building entrance (which will be the designated construction entrance), and will only use the designated elevator or designated stairwell except in the event of an emergency evacuation. Use of Building main floor, lobbies, or elevator lobbies is prohibited for storing material even on a temporary basis. Specific Building moving and freight policies are established and must be reviewed with Landlord and/or Property Manager. Where applicable such freight policies may include fines for breaking such policies.

11. Landlord and/or Property Manager, prior to the commencement of the project, must approve hours in which the Work will commence and end each day. No variation to the agreed upon hours will be permitted unless authorization is obtained from Landlord and/or Property Manager. These Contractor Rules as stated herein will further limit hours. Landlord and/or Property Manager must be notified of "after hours" Work in advance. "After hours" work is defined to be before 7 am and after 6 pm or as governed by the City where the project resides and their guidelines. All Contractors working over the weekend and after the normal hours shall provide Landlord and Property Manager a list of workers prior to the worker being on site or they will be denied access. The list should also include an estimated time the Contractors will be working, the location of the work to be done and a 24-hour emergency contact for the supervisor of the Work.

12. Contractor shall designate a superintendent to oversee all workmen at all times. Such superintendent may be given access cards and keys, these cards/keys will grant access to the Building for all workmen associated with the project. The superintendent issued the cards/keys not permitted to give such cards/keys to any workmen for access to the Building. In no event shall any workmen be unsupervised at any time.

13. All deliveries are to be accepted, moved and delivered to the contracted suite before 7 am and after 6 pm unless prior Landlord approval has been granted in writing; stocking will not be allowed during business hours once any tenant occupancy has taken place within the building. When accepting deliveries, masonite must be laid to protect walls and floor finishes and elevator pads must be installed prior to delivery. It is the Contractor's responsibility to keep public areas clean at all times.

14. No windows shall be removed without prior approved permission provided by Property Manager or Landlord.

15. All construction waste and debris shall be removed between the hours of 6 pm to 7 am once any tenant occupancy within the Building has taken place. No construction waste or debris may be placed in the building dumpster /compactor. The Contractor will provide for removal of waste and debris from the building at his own expense. If a dumpster is required (space allowing), the location shall be authorized by the Landlord and Property Manager, must be in a safe location, and will meet the Building's standard relating to aesthetics. It will be the responsibility of the Contractor to keep the area around the container neat and orderly daily. It will also be the Contractor's responsibility to place plywood under the dumpster and to take other protective measures to protect the asphalt and concrete where the dumpster is to be placed. It will be important to assure that a trail of debris is not left between the Work areas and refuse container.

Exhibit B-2

Page 4 of 8

16. Construction personnel shall at all times maintain the highest level of project cleanliness. All construction debris shall be removed through the service elevator or stairs on a daily basis and shall never be allowed to produce a fire hazard. In the event that the Contractor fails or refuses to keep the Leased Premises free of accumulated waste, Landlord and/or Property Manager reserve the right, but not the obligation, to enter the Leased Premises and remove the debris, on behalf of the Contractor, at the Contractor's expense. In addition, all public areas, i.e., corridors, restrooms, janitor's closets, etc. shall be maintained and kept free of construction debris, dust, etc.

17. No one is permitted to use the janitorial closets without permission. Contractor shall be responsible for stocking and re-stocking of restroom supplies as well as clean-up of the subject restrooms being utilized, provided such authorization of use has been granted by Landlord, throughout the duration of construction. Upon completion of each tenant improvement, the Contractor will be responsible for restoring the facility to its original state. All carpeted corridors will be properly protected by masonite or carpet mask (Polytech brand only) flush with the base, from the point of entry to the job site to the restroom. Contractor will provide walk-off mats to be placed at all locations where Contractors enter public areas of the building. These walk-off mats will be maintained and cleaned daily or more frequently if required, so that construction material is not transferred unto any other areas of the building. Any flammable or hazardous materials (i.e., paint) may only be stored on premises with permission of Landlord and Property Manager who shall designate an area for such storage.

18. Pre-filters shall be installed over all return air openings on floors under construction. If Building filters or equipment requires replacement or cleaning due to construction dust, the Contractor will be charged.

19. Contractor should cover air transfers when working next to tenanted space to control the transmission of dust and dirt. Covering must be removed at the completion of daily construction. All tenant entrance and exit doors must be kept closed to restrict the movement of dust or dirt. Temporary openings with polyurethane must be closed off. Due to local fire codes, no openings may be made on a tenanted floor to the corridor unless the door to be made on the tenanted floor to the corridor remains closed unless materials are being delivered. All HVAC filters in fan rooms shall also be delivered in operable condition at time of completion (thus a temporary filter should be added to the existing filter).

20. Electrical Panels must be closed up at the end of each working day. Interior panels can be covered or barricaded. Doors to all electrical rooms must remain locked when not occupied or protected by barrier. No storage is allowed in the electrical room. **DO NOT TAPE OVER LOCKS TO LEAVE DOOR OPEN OR USE ANY MECHANICAL DEVICE TO PROP OPEN. REPEATED VIOLATIONS WILL BE FINED \$500 PER EVENT.**

21. Any and all safety equipment, such as traffic control, flagmen, barricades, rigging, fire extinguishers, first aid supplies, etc., as may be necessary or required by any agency having jurisdiction, shall be the sole responsibility of, and at the expense of, Contractor. It is the responsibility of the Contractor to protect all individuals surrounding the Work area. All liability shall be the responsibility of the Contractor. Contractor (and its subcontractors) shall inaugurate and maintain an accident prevention program and an employee safety-training program. Proof of compliance for the state and city where the project resides of your safety plan shall be maintained and followed. All employees on the job, regardless of whose direct payroll they are on, shall be required to respond to safety instructions from the Contractor's supervision. Persons who do not respond shall be removed from the job. Contractor, its subcontractors, labor, agents and invitees shall be responsible for complying with all OSHA rules and regulations, including, without limitation, having all safety, first aid and Material Safety Data Sheet (MSDS) documentation on the jobsite at the Building.

22. All Contractors are to take precautions to prevent the accidental tripping of the fire alarm system. The smoke detectors must be covered during working hours and uncovered at the end of the working day.

False alarms shall be fined at:

First offense: \$200

Second offense: \$500

Third offense: \$1000 and, at the Landlord's discretion, may terminate Contractor.

23. No gasoline operated devices, i.e., concrete saws, coring machines, welding machines, etc., shall be permitted within the Building. All work requiring such devices shall be by means of electrically operated substitutes.

24. All approved gas and oxygen canisters shall be properly chained and supported to eliminate all potential hazards. At the completion of use, said containers shall be removed from the Building.

25. Please contact the Property Manager to schedule work on the following building systems 24- hours in advance (Any disruption of services will be scheduled at the Property Manager's discretion):

a. Domestic water;

b. Fire alarm or speaker;

c. Electrical tie-ins to base building or the addition of equipment to any area other than the tenant suite except sub panels located within the Leased Premises;

d. Sprinkler system;

e. Any work that will take place outside the demised tenant space;

f. Work in occupied tenant spaces. This includes any core drilling, plumbing, and electrical, etc., where you will enter an adjacent tenant space;

g. Roof access. Any corrective work required in conjunction with or as a result of this Contractor's scope of work shall be performed by a firm authorized as such by roofing manufacturer (Landlord and/or Property Manager will coordinate with Contractor in determining) for purposes of ensuring that the roofing warranty is not jeopardized in any way.

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Note: If a utility or building alarm is turned off for Contractor's work, Contractor must notify the Property Manager upon completion so the system can be turned back on as soon as possible.

26. Construction personnel are not permitted to block open stairway doors. These doors provide the fire protection required by code. A repeated violation of this provision shall be subject to a \$500 fine. Doors to janitorial spaces shall be kept closed at all times.

27. No graffiti or vandalism will be tolerated. Any individual caught in the act shall be immediately removed from the Leased Premises and will not be allowed to return. In addition, all repairs will be at the Contractor's expense.

28. No tobacco smoking or chewing will be permitted in the Building or on the roof. No radios or other sound producing equipment will be permitted in the Building or on the roof. No eating or drinking will be allowed in the Common Areas. Building management will either provide a designated smoking area or designate the property to be non-smoking.

29. Since Work may occur while other businesses in the Building are operating, noise is a major consideration. Therefore, excessive noise, which may disturb tenants, will force us to halt Work temporarily. No hammer drilling, core drilling or any tenant disturbances will be allowed between the hours of 7 am and 6 pm, Monday through Friday. It is the responsibility of the Contractor to instruct all construction personnel that noise will be minimized at all times. Landlord and Property Manager shall determine acceptable noise level.

30. Wet paint sign must be posted in all public areas when appropriate.

31. The odors, which arise when various construction procedures are done, can cause discomfort to the tenants of the Building. Examples of these odor concerns are carpet adhesive, wallpaper sizing, wood stains and finishes and painting. These activities which sometimes produce odor problems for tenants in the Building will be done during evening non-business hours, as approved by Landlord and/or Property Manager. Also, Landlord and/or Property Manager should be alerted to arrange for added ventilation. Cost associated with additional ventilation shall be at Contractor's sole expense. In addition, all TI Contractors will cooperate with shell building contractor's air quality reading measurements as is required by LEED, when applicable. This may include temporary shutdown of activity that jeopardizes air quality readings before and during actual testing of same.

32. Contractor shall provide temporary electrical devices within the Leased Premises for its subcontractor's use. Contractor will not be permitted to run extension cords through public space on occupied floors or through occupied tenant spaces.

33. Contractor shall use reasonable measures to minimize energy consumption in the construction area when possible. The Building shall pay for normal electrical consumption during the construction process. All lights and equipment must be extinguished at the end of the Contractor's business day. In the event that the Contractor continues to leave lights and equipment on during off-hours, Landlord reserves the right to receive just compensation for excessive electrical consumption.

34. Contractor/Sub-contractor may park in designated spaces only. This on-site parking is limited to that which is available on-site. Contractor shall be prepared to make additional arrangements should supplemental parking be required for any and all workforces working under their contracted scope. Any vehicles found in unauthorized spaces will be subject to posted parking rates, tickets, towing or other steps as may be needed to avoid conflicts with adjacent tenant and neighbor parking. Specific instructions should be obtained from Property Manager.

35. No work is to be performed, nor materials stored in any area other than the suite under construction without prior authorization. No staging of trucks or materials will be allowed in areas that may affect traffic flow.

36. Rubber wheels are required on all vehicles transporting materials in the Building.

37. All equipment and material will be designed and attached for seismic loading in accordance with governmental agencies having jurisdiction over the Work.

38. Commencement of any work shall constitute acceptance or contractor will take full responsibility for communicating these Contractor Rules to all Contractor's personnel and subcontractors, and enforcing these Contractor Rules in regards to employees of Contractor and subcontractors.

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**EXHIBIT E**

**BUILDING RULES**

Notwithstanding anything to the contrary contained herein, in the event of a conflict between the terms and conditions of the Building rules and regulations, now or hereafter promulgated by Landlord, and the terms and conditions of the Lease, the Lease shall control.

1. The sidewalks, entrances, passages, courts, elevators, vestibules, stairways, corridors or halls shall not be obstructed or used for any purpose other than ingress and egress. Landlord shall control the Common Areas.

2. No awnings or other projections shall be attached to the outside walls of the Building. No curtains, blinds, or screens shall be attached to or hung in, or used in connection with, any window or door of the Leased Premises other than Landlord standard window coverings without Landlord's prior written approval. Neither the interior nor the exterior of any windows shall be coated or otherwise sunscreensed without written consent of Landlord.

3. No sign, advertisement, notice or handbill shall be exhibited, distributed, painted or affixed by any tenant on, about or from any part of the Leased Premises, the Building or in the Common Areas including the parking area without the prior written consent of Landlord. In the event of the violation of the foregoing by any tenant, Landlord may remove or stop same without any liability, and may charge the expense incurred in such removal or stopping to tenant. The lobby directory will be provided exclusively for the display of the name and location of tenants only, and Landlord reserves the right to exclude any other names therefrom. Nothing may be placed on the exterior of corridor walls or corridor doors other than Landlord's standard lettering.

4. The sashes, sash doors, windows, and doors that reflect or admit light and air into halls, passageways or other public places in the Building shall not be covered or obstructed by tenant.

5. The sinks and toilets and other plumbing fixtures shall not be used for any purpose other than those for which they were constructed, and no sweepings, rubbish, rags, or other substances shall be thrown therein. All damages resulting from any misuse of the fixtures shall be borne by the tenant who, or whose subtenants, assignees or any of their servants, employees, agents, visitors or licensees shall have caused the same.

6. No tenant shall mark, paint, drill into, or in any way deface any part of the Leased Premises or the Building (except for nails for the display of artwork). No boring, cutting or stringing of wires or laying of any floor coverings shall be permitted, except with the prior written consent of the Landlord and as the Landlord may direct. Landlord shall direct electricians as to where and how telephone or data cabling are to be introduced. No boring or cutting for wires or stringing of wires will be allowed without written consent of Landlord.

7. No bicycles, vehicles, birds or animals of any kind (except seeing eye dogs) shall be brought into or kept in or about the Leased Premises, and no cooking shall be done or permitted by any tenant on the Leased Premises, except microwave cooking, and the preparation of coffee, tea, hot chocolate and similar items for tenants and their employees. No tenant shall cause or permit any unusual or objectionable odors to be produced in or permeate from the Leased Premises.

8. The Leased Premises shall not be used for manufacturing or for the storage of merchandise except as such storage may be incidental to the Permitted Use of the Leased Premises. No tenant shall occupy or permit any portion of the Leased Premises to be occupied as an office for the manufacture or sale of liquor, narcotics, or tobacco in any form, or as a medical office, or as a barber or photographic or print shop or an employment bureau without the express written consent of Landlord. The Leased Premises shall not be used for lodging or sleeping or for any immoral or illegal purpose.

9. No tenant shall make, or permit to be made any unseemly, excessive or disturbing noises or disturb or interfere with occupants of this or neighboring buildings or premises or those having business with them, where by the use of any musical instrument, radio, phonograph, unusual noise, or in any other way. No tenant shall throw anything out of doors, windows or down the passageways.

10. No tenant, subtenant or assignee nor any of its servants, employees, agents, visitors, or licensees, shall at any time bring or keep upon the Leased Premises any flammable, combustible or explosive fluid, chemical or substance or firearm.

11. No additional locks or bolts of any kind shall be placed upon any of the doors or windows by any tenant, nor shall any changes be made to existing locks or the mechanism thereof.

12. No tenant shall overload the floors of the Leased Premises. All damage to the floor, structure or foundation of the Building due to improper positioning or storage items or materials shall be repaired by Landlord at the sole cost and expense of tenant, who shall reimburse Landlord immediately therefor upon demand. All removals or the carrying in or out of any safes, freight, furniture, or bulky matter of any description must take place during the hours that Landlord shall reasonably determine from time to time. The moving of safes or other fixtures or bulky matter of any kind must be done upon previous notice to Landlord and under Landlord's supervision, and the persons employed by any tenant for such work must be acceptable to Landlord. Landlord reserves the right to inspect all safes, freight or other bulky articles to be brought into the Building and to exclude from the Building all safes, freight or other bulky articles which violate any of these Rules and Regulations or the Lease of which these Rules and Regulations are a part. The Landlord reserves the right to prescribe the weight and position of all safes, which must be placed upon supports approved by Landlord to distribute the weight.

13. Landlord shall have the right to prohibit any advertising by any tenant that, in Landlord's reasonable opinion tends to impair the reputation of the Building or its desirability as an office location, and upon written notice from Landlord, any tenant shall refrain from or discontinue such advertising.

14. The business hours for the Building shall be 7:00 a.m. to 6:00 p.m. Monday through Friday and 8:00 a.m. to 1:00 p.m. on Saturday, excluding legal holidays. Landlord reserves the right to require all persons entering the Building between the hours of 6:00 p.m. to 7:00 a.m. and at all hours on Saturday, Sunday, and legal holidays to register with Landlord's security personnel. Each tenant shall be responsible for all persons entering the Building at tenant's invitation, express or implied. Landlord shall in no case be liable for damages for any error with regard to admission to or exclusion from the Building of any person. In case of an invasion, mob riot, public excitement or other circumstances rendering such action advisable in Landlord's opinion, Landlord reserves the right without any abatement or rent to require all persons to vacate the Building and to prevent access to the Building during the continuance of the same for the safety of the tenants and the protection of the Building and the property in the Building.

15. No tenant shall purchase janitorial or maintenance of other like services, from any person or persons not approved by Landlord. Any persons employed by any tenant to do janitorial work or other work in the Leased Premises shall, while in the Building and outside of the Leased Premises, be subject to and under the control and direction of Landlord (but not as an agent or servant of Landlord), and tenant shall be responsible for all acts of such persons.

16. Canvassing, soliciting and peddling in the building are prohibited, and each tenant shall report and otherwise cooperate to prevent the same.

17. All office equipment of any electrical or mechanical nature shall be placed by tenant in the Leased Premises in setting that will, to the maximum extent possible, absorb or prevent any vibration, noise and annoyance.

18. No future air-conditioning unit or other similar apparatus shall be installed or used by any tenant without the written consent of Landlord.

19. There shall not be used in any space, or in the public halls of the Building, either by any tenant or others, any hand trucks except those equipped with rubber tires and rubber side guards.

20. The scheduling of tenant move-ins shall be before or after normal business hours and on weekends, subject to the reasonable discretion of Landlord.

21. The Building is a smoke-free Building. Smoking is strictly prohibited within the Building. Smoking shall only be allowed in areas designated as a smoking area by Landlord. Tenant and its employees, representatives, contractors or invitees shall not smoke within the Building or throw cigar or cigarette butts or other substances or litter of any kind in or about the Building, except in receptacles for that purpose. Landlord may, at its sole discretion, impose a charge against monthly rent of \$50.00 per violation by tenant or any of its employees, representatives, contractors or invitees, of this smoking policy.

22. Tenants will insure that all doors are securely locked, and water faucets, electric lights and electric machinery are turned off before leaving the Building.

23. Parking spaces associated with the Building are intended for the exclusive use of passenger automobiles. Except for intermittent deliveries, no vehicles other than passenger automobiles may be parked in a parking space without the express written permission of Landlord. Tenant, its employees, customers, invitees and guests shall, when using the parking facilities in and around the Building, observe and obey all signs regarding fire lanes and no-parking and driving speed zones and designated handicapped and visitor spaces, and when parking always park between the designated lines. Landlord reserves the right to tow away, at the expense of the owner, any vehicle which is improperly parked or parked in a no-parking zone or in a designated handicapped area, and any vehicle which is left in any parking lot in violation of the foregoing regulation. All vehicles shall be parked at the sole risk of the owner, and Landlord assumes no responsibility for any damage to or loss of vehicles except to the extent arising out of the negligence or willful misconduct of Landlord, the managing agent or any of their respective partners, directors, officers, agents or employees.

24. Tenant shall be responsible for and cause the proper disposal of medical waste, including hypodermic needles, created by its employees.

25. It is Landlord's desire to maintain in the Building and Common Areas the highest standard of dignity and good taste consistent with comfort and convenience for tenants. Any action or condition not meeting this high standard should be reported directly to Landlord. The Landlord reserved the right to make such other and further rules and regulations as in its judgment may from time to time be necessary for the safety, care and cleanliness of the Building and Common Areas, and for the preservation of good order therein.