Neuroprotection in Glaucoma with the Novel Amyloid β Aggregation Modulator GAL-101

Glaucoma 360
San Francisco
February 1, 2019

Hermann Russ, M.D., Ph.D.
Chief Scientific Officer

© GALIMEDIX

Introducing Galimedix

- US/Israel Biopharma in Phase 2
- Novel first-in-class drug with unique potential to slow progression in glaucoma and dry AMD
- Experienced management team, mostly ex-Pharma
- Raising funding to prepare and conduct two Phase 2 studies in glaucoma, dry AMD, aiming to start in 2H 2019

© GALIMEDIX

Galimedix Thanks its Top Clinical Advisors

GLAUCOMA

Prof. Jeffrey Liebmann – Vice-Chair of Ophthalmology and Director Glaucoma Service, Columbia University,

Prof. Leonard Levin – Chair of Ophthalmology and Visual Sciences, McGill University, Montreal

Prof. David S. Greenfield, Douglas R. Anderson Distinguished Professor and Vice-Chair of Ophthalmology, Co-Director Glaucoma Service, Bascom Palmer Eye Institute, Miami, FL

Prof. Jeffrey Goldberg – Chair of Ophthalmology, Byers Eye Institute, Stanford University

Prof. Robert N. Weinreb – Chair of Ophthalmology, University of California – San Diego

Dry AMD

Prof. Jeffrey Heier – Co-President & Medical Director Director of Retina Service, Retinal Research Ophthalmic Consultants of Boston

Prof. Baruch Kuppermann – Chair of Ophthalmology, University of California – Irvine

Prof. David Boyer – Sr. Partner, Retina-Vitreous Associates Medical Group, Clin. Prof. Ophthalmology, USC/Keck School of Medicine, Los Angeles, CA

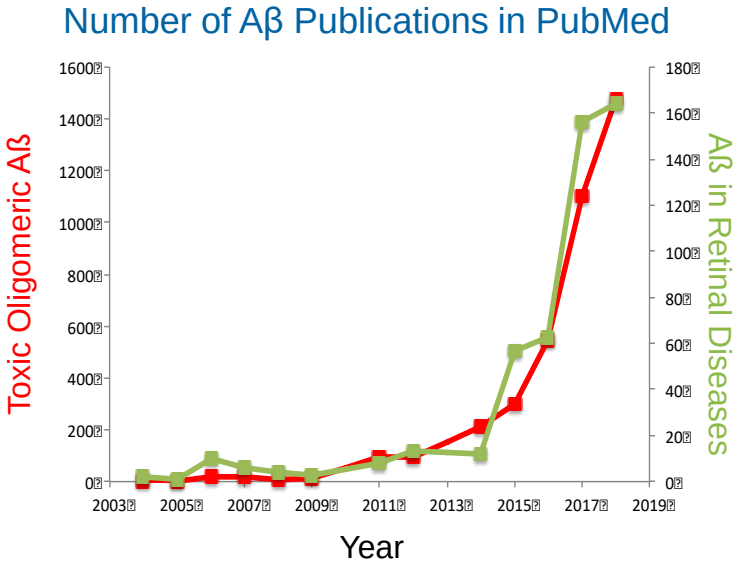
Prof. Frank Holz – Chairman, Department of Ophthalmology, University of Bonn, Germany

Prof Steffen Schmitz-Valckenberg - Department of Ophthalmology), University of Bonn, Germany

Assoc. Prof. Eleonora Lad – Assoc. Prof. Ophthalmology, Director of Grading, Duke Reading Center, Duke University

Amyloid β is an Emerging Hot Topic in Glaucoma

- In PubMed few publications until 2014 about Aβ in glaucoma and dry AMD
- Same for oligomeric Aβ as the toxic form
- Interest in both topics is increasing markedly since 2015



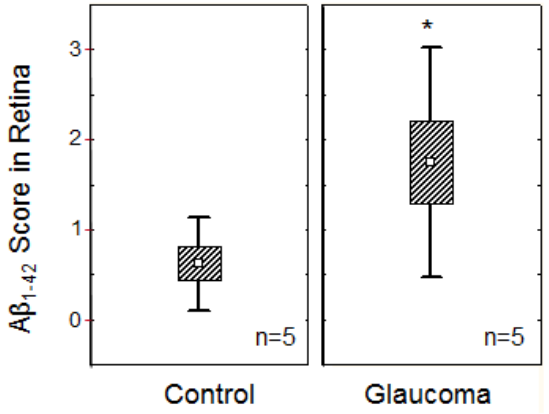
Search term (abeta OR ß-amyloid OR beta-amyloid OR aß) AND (oligomer OR oligomers OR aggregated OR protofibrils) AND 2018[Date]
Values for 2018 were extrapolated to predict those for the whole year - analysis made on 30/07/2018. Values for 2010 and 2013 were omitted from this graph due to an apparent anomaly

© GALIMEDIX

Amyloid β is Involved in the Pathology of Glaucoma

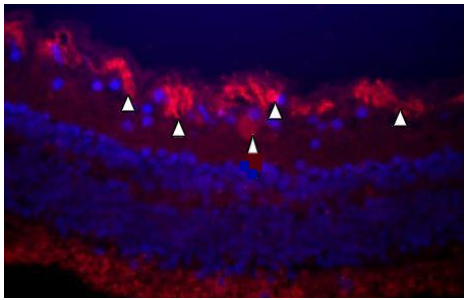
Growing body of evidence that Aβ plays a major role in the neuro-degeneration of the RGCs

- Fig. A: In glaucomatous eyes of patients Aβ is significantly increased#
- Fig. B: Aβ is localized in RGC layer
- Recent human genetic studies further suggest Aβ as a root cause of glaucoma pathology ##



A

$A\beta_{1-42}$ staining in glaucomatous retina



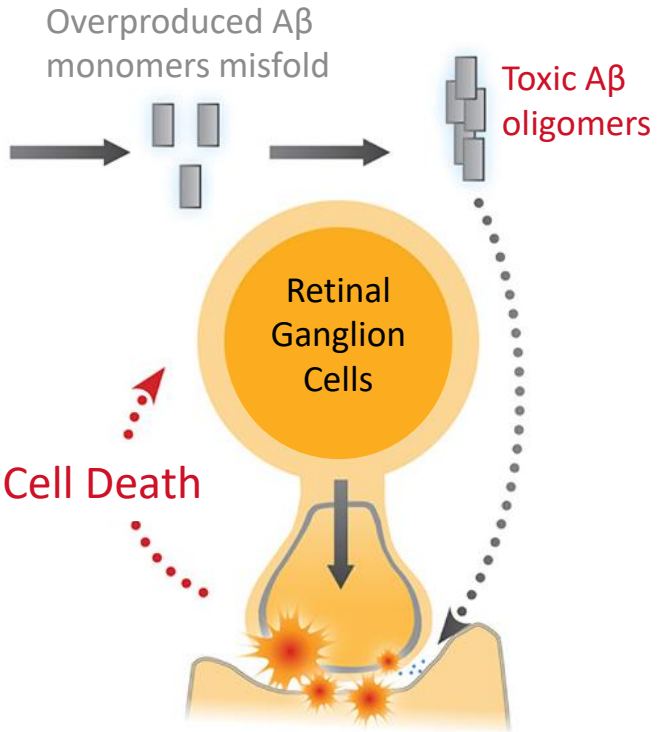
B

Böhm et al. (2012) Aβ is significantly increased in RGCs of glaucoma patients (poster presentation)
van der Heide et al. (2018) Abstract, Int. Soc. for Eye Research Meeting, Belfast, UK.
Hauser, ARVO abstract 1183, 2018: "Association of APBB2 links mechanisms of neuro-degeneration in glaucoma and Alzheimer's disease

© GALIMEDIX

Amyloid β in the CNS and Retina

- Amyloid β (Aβ) monomers are required for normal synaptic function in the eye and brain
- Overproduction of Aβ monomers leads to misfolded monomers
- These aggregate spontaneously to form Aβ oligomers, which are highly toxic to neuronal cells

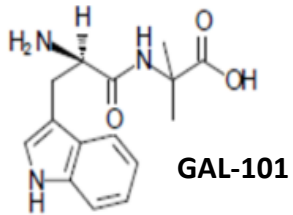


Parsons et al. (2018) Neuropharmacology 92: 158-169

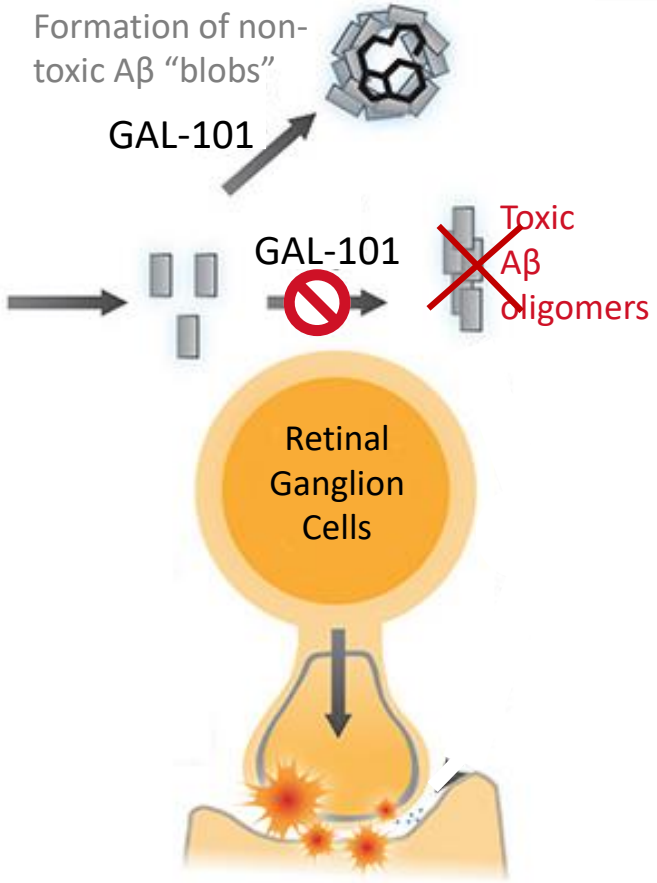
© GALIMEDIX

GAL-101 Eliminates all Toxic Forms of Aβ

- GAL-101 causes the misfolded Aβ monomers to rapidly form amorphous Aβ assemblies (“blobs”), rather than toxic Aβ oligomers
- In the eye, GAL-101 eliminates toxic Aβ oligomers in the retina



GAL-101



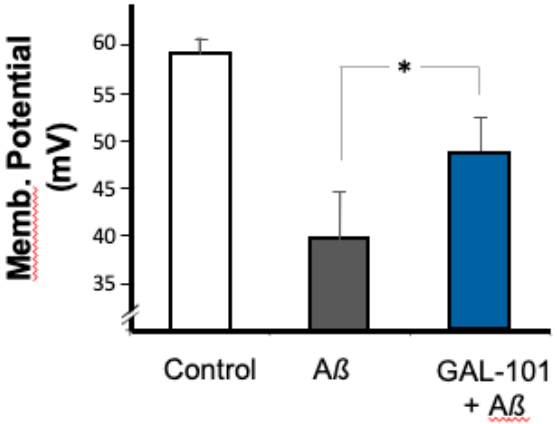
Parsons et al. (2018) Neuropharmacology 92: 158-169

© GALIMEDIX

Aβ toxicity to RGCs *in vitro* is blocked by GAL-101

- Adding toxic Aβ oligomers to cultured RGCs reduces their cell membrane potential (toxic effect)
- However, in the presence of GAL-101, Aβ toxicity is attenuated

Cultured Retinal Ganglion Cells (RGCs)
(Patch Clamp)



(n=5 per group)

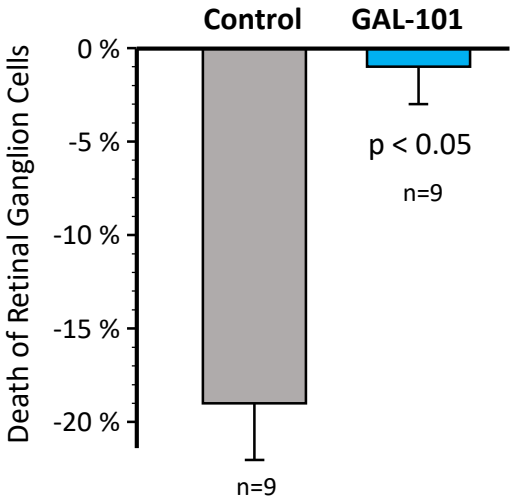
Parsons et al. (2018) Neuropharmacology 92: 158-169

© GALIMEDIX

In Glaucoma Animal Models GAL-101 protects RGCs

- Morrison Model: increased IOP in rats over 6 weeks leads to 19% loss of RGCs (control)
- Overexpression of Aβ in RGC layer induced by elevated IOP
- 1% loss of RGCs with GAL-101 drops 3x daily
- Confirmed several times in independent labs

Retinal Ganglion Cells in Rats

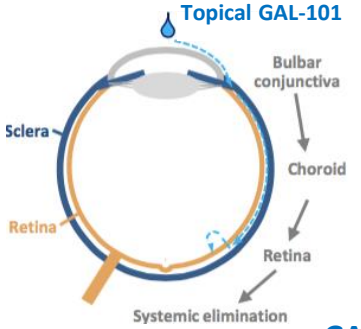


Salt et al. (2014) Neurotox Res 26(4): 440-446, Gravius et al (2013) Invest Ophthalmol Vis Sci. 54: 2625

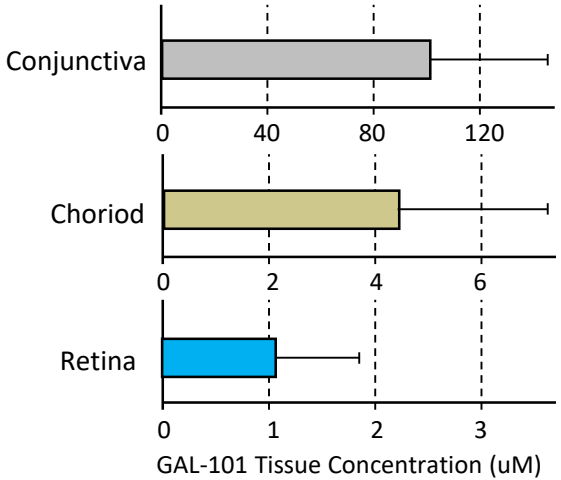
© GALIMEDIX

Eye Drops Deliver GAL-101 to the Retina

- PK study with GAL-101 drops in multiple cynomolgus monkeys
- GAL-101 retinal concentration >30x therapeutic threshold in 5 min, lasts hours
- Route of delivery: transscleral via the choroid*
- Eye drops with small molecule drugs are used clinically e.g. dorzolamide in RP**
- Other recent small molecule drops show retinal delivery via choroid as well ***



GAL-101 levels 5 min after application

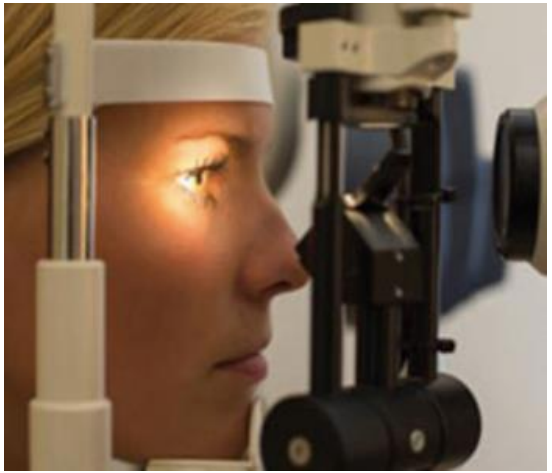


* Lindsey JD, Crowston JG, Tran A, Morris C, Weinreb RN. Invest Ophthalmol Vis Sci. 2007 Feb;48(2):752-5.
** Genead MA et al. (2010) Arch Ophthalmol 128(9):1146-50
*** SciFluor's SF0166 and Panoptica's PAN-90806

© GALIMEDIX

In Phase 1 with GAL-101 Eye Drops Completed Successfully

- Phase 1 FDA study protocol: 40 healthy subjects and 30 glaucoma patients, up to 3x 3 drops daily
- 16 days exposure (double-blind, placebo-controlled)
- No effect on IOP
- No treatment related AEs



➡ GAL-101 eye drops ready to start Phase 2

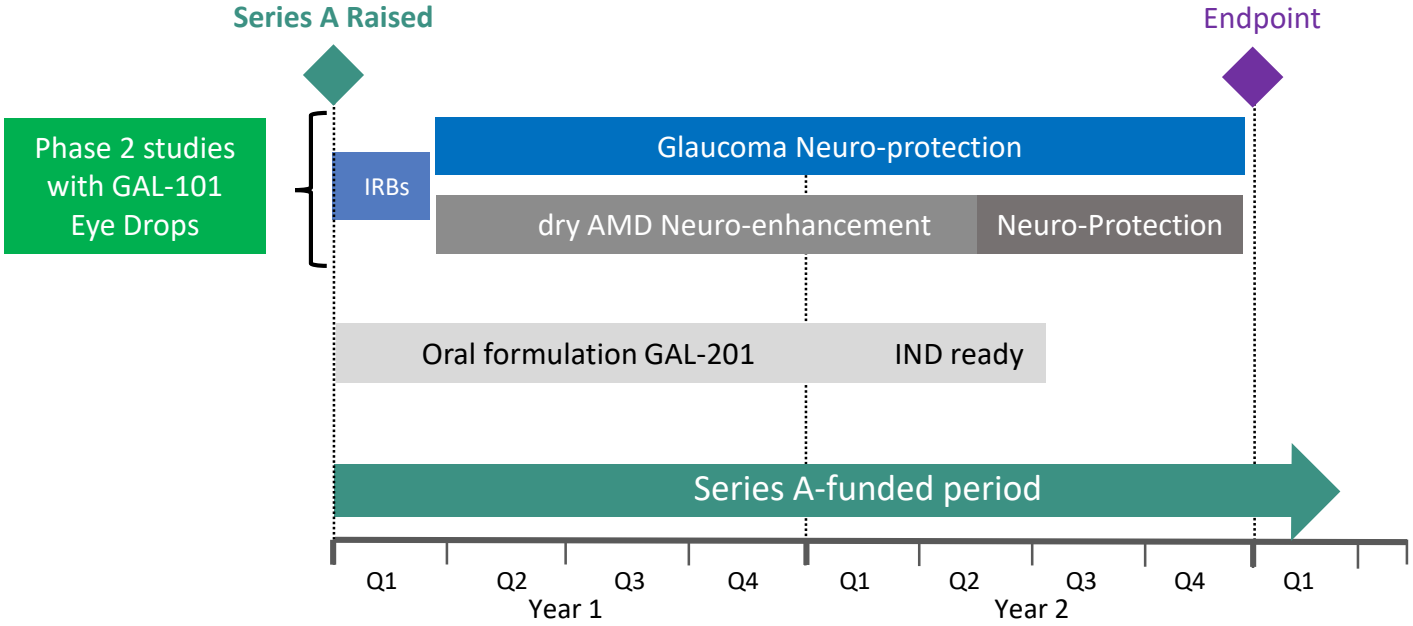
© GALIMEDIX

Phase 2 Study with GAL-101 Eye Drops to Launch H2/2019

- Glaucoma neuroprotection study with GAL-101 eye drops twice daily
- Placebo-controlled “add on” treatment to standard IOP drugs
- Rate of Visual Field Progression as primary endpoint

© GALIMEDIX

Development Plan – to be Funded by Series A

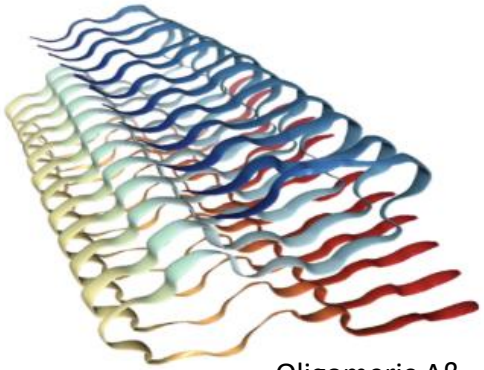


Goal: Proof of Concept in one or both indications

© GALIMEDIX

Galimedix: Wrap Up

- Novel eye drops to slow progression in glaucoma and dry AMD
- >90% neuroprotection in key animal studies
- Excellent retinal delivery in monkey models
- Phase 1 clinical studies completed - safe, no toxicity
- Backed by many leading experts in glaucoma and dry AMD
- >$30m invested, full pharma data package
- Raising funding to prepare and conduct two Phase 2 studies H2/2019: Glaucoma and dry AMD



Oligomeric Aβ

© GALIMEDIX

Thank you !

© GALIMEDIX