

## OTI-2024 Strategic Update: A Journey of Billion \$ Drug Discovery from Big Data.

Monday January 6th 2025.

Dear Esteemed Colleagues and Advisors, Ladies and Gentlemen,

Happy New Year!

As we open the new chapter of 2025, I thought to summarize the journey of this **Breakthrough discovery of MMP (matrix metalloproteinase)** platform therapy for treating glaucoma neural degeneration (please see the chart below); This is a billion-dollar drug discovery process from big data (not AI) with no additional study costs-**Unprecedented!** We discover the pressure sensor/sensing cell as chief regulator of IOP. We are setting new standards for glaucoma disease management in decades to come. To protect the pressure sensing cells (front) is to protect the retinal ganglion cells (back) for glaucoma. We have the answer re: "chicken & eggs, which comes first" in glaucoma.

**A Derisked Platform Therapy:** OTI-2024 is a Derisked glaucoma neural protection asset with 800 patients' experience. Like anti-VEGF therapy for wAMD, MMP therapy is a Platform Therapy, which can be delivered by Durysta, iDose and SLT laser but with side effects and clinical limitation. And OTI-2024 is the best in class and first in class Adenosine derived MMP-14 therapeutic drug with no clinical side effect (and can be repeated). The Drug Discovery journey started in May 2015 of the first discovery of Trabodenoson/MMP on trabecular meshwork rejuvenation (TM), resumed on 2021 with the first provisional patent filed, to 2022 discovery of MMP on drug holiday (evidenced by Druysta), and 2023 first PCT filing followed by the 2nd PCT filing in Jan 2024, which completed the holy grail discovery in glaucoma (RGC neural protection via a new MoA), 2-3 years on the patenting process.

**Business Due Diligence** on Inotek Pharma/Rocket: We have done deep scientific due diligence on old IOP patents (expired) and remaining asset of Trabodenoson. Following FDA meeting on October 2024, we made **the Final Decision of not developing the abandoned old eye drop program (commercial risks related to the old eye drops formula IP expiration)**, also determined that the old IND holds no commercial values to partners. With this in-depth due diligence, we helped our potential partners pave a clear business and clinical regulatory path forward, and saved hundreds of million costs on inquiring/due diligence, acquiring or developing Inotek's old IOP lowering drop product. OTI has freedom to operate.

**Emerging Evidence (Durysta)** further confirms that MMP on IOP normalization is so far the most effective treatment for stabilizing the visual field in patients with glaucoma. Durysta with single implant has led to 85% patients on IOP drug holiday for 11-13 months! OTI-2024 will outperform pro inflammatory PG drugs and Durysta in clinics: OTI-2024 treats *non responders and refractory glaucoma and solves poor compliance* via IOP normalization.

- OTI continues to leverage its strength in data know-how, with our SAB members, Dr Louis Cantor and Prof Clive Wilson onboarded, we have mapped out the next steps of New Eye drop formulation & IND enabling study plans with potential collaborators & CROs.

**OTI-2024 Product Positioning** evolves with the patent territory changing from IOP lowering to RGC protection. Many of you have reviewed Trabo-/OTI-2024, as an IOP lowering drug (2021), or IOP drug holiday inducer/stabilizer (2023), glaucoma neural protection drug (2024), sustained released implant etc.

Herein I like to take the opportunity to thank Dr. Michael Robinson, Dr Wiley Chamber and Dr William Boyd for your valuable discussions and advice on a Ph3 IOP clinical trial & Endpoint in 2022-2023. Also, special thanks to Mr. Laurent Attias, Jane Rady, SVP, Andrew Pillon, OD, Mr. Michael Lowes, Joeseeph Simeone, PhD, Kendra Rose, PhD, Mayssa Attar, PhD and Keith Lurther, PhD for your tireless efforts on reviewing of our pipeline changes, back and forth. With a clear map and priority, we would love to welcome back for each of you here to revisit this high impact blockbuster opportunity in 2025! Thank You.