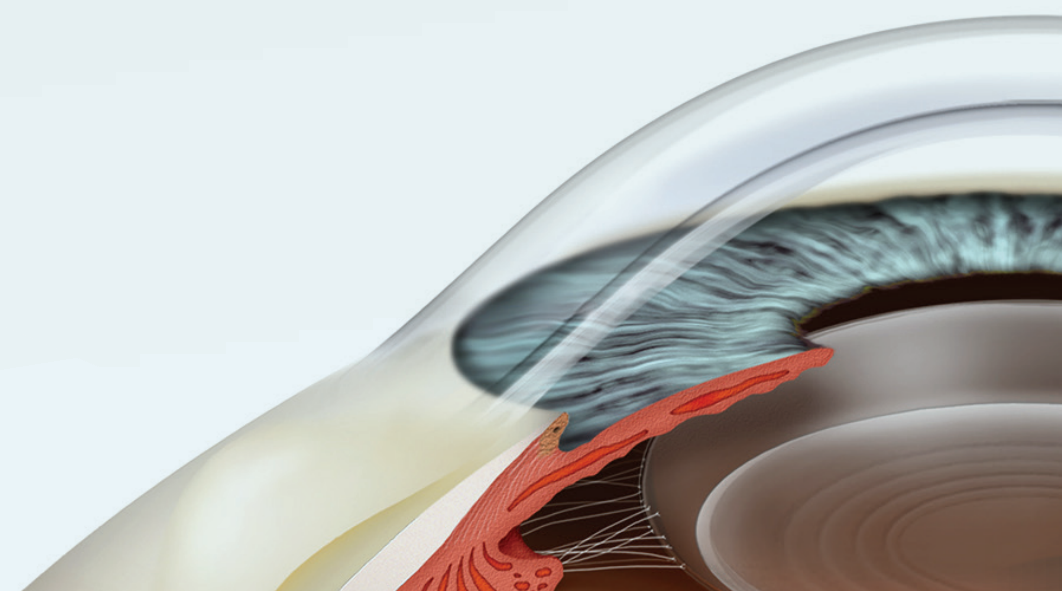


GLAUCOMA PIPELINE

A VIEW INTO ONGOING INNOVATION

2021 SURGICAL INNOVATION

Filtering Bleb Procedures



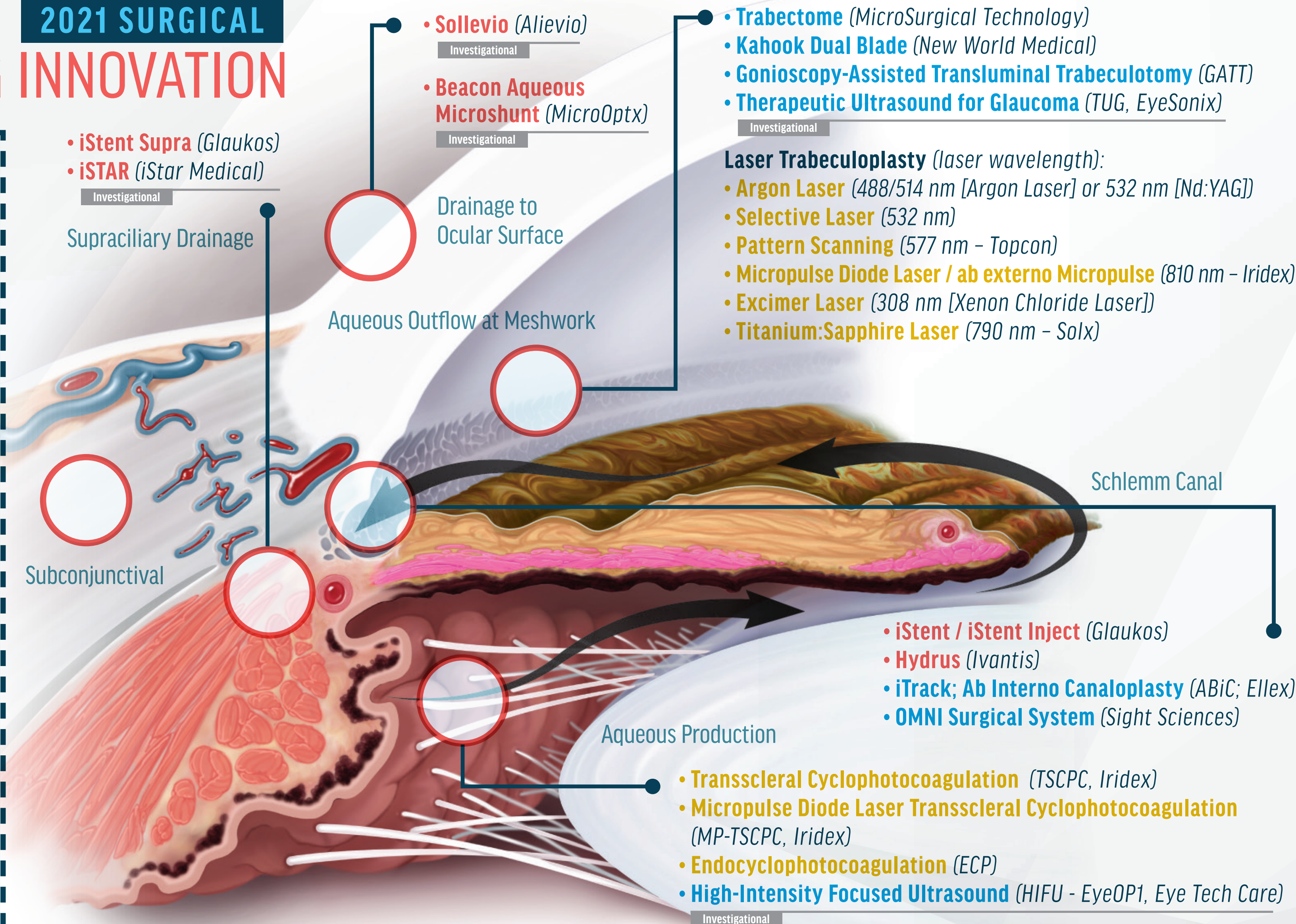
TRADITIONAL INCISIONAL SURGERIES

- Trabeculectomy
- Aqueous Drainage Devices
 - Baerveldt Glaucoma Implant (Johnson & Johnson Vision)
 - Ahmed Glaucoma Valve (New World Medical)
 - Ahmed ClearPath (New World Medical)
 - Molteno3 (Molteno Ophthalmic)
 - PAUL Implant (Advanced Ophthalmic Innovations)
US Investigational
 - eyeWatch (Rheon Medical)
US Investigational
- Ex-PRESS (Alcon) – external

MINIMALLY INVASIVE BLEB SURGERIES

- XEN45 / XEN63 Gel Stent (Allergan) – internal/external
- PreserFlo MicroShunt (Santen) – external
US Investigational
- Minimally Invasive Micro Sclerostomy (MIMS, Sanoculis)
US Investigational

COLOR LEGEND
Implant
Surgical Device/Instrument
Laser



IQBAL IKE K. AHMED, MD, FRCS

With the potential to reduce or eliminate adherence issues, topical side effects, and the requirement for daily instillation associated with medications, procedural management is quickly becoming a popular option for patients with glaucoma. Lasers, devices, and surgeries also offer the promise of avoiding fluctuation. Lastly, they can be targeted to specific areas along the aqueous pathway where resistance is thought to occur. For all these reasons, development in this area is certainly robust. In this poster, we present the currently available options and a selection of some of the promising procedural options in development.

CRST **GT**
 Cataract & Refractive Surgery Today Glaucoma Today
MODERNOPTOMETRY



Protecting the World's Vision

Our Commitment to Eye Care
Will Always Endure

Santen

Imagine Your Happiness

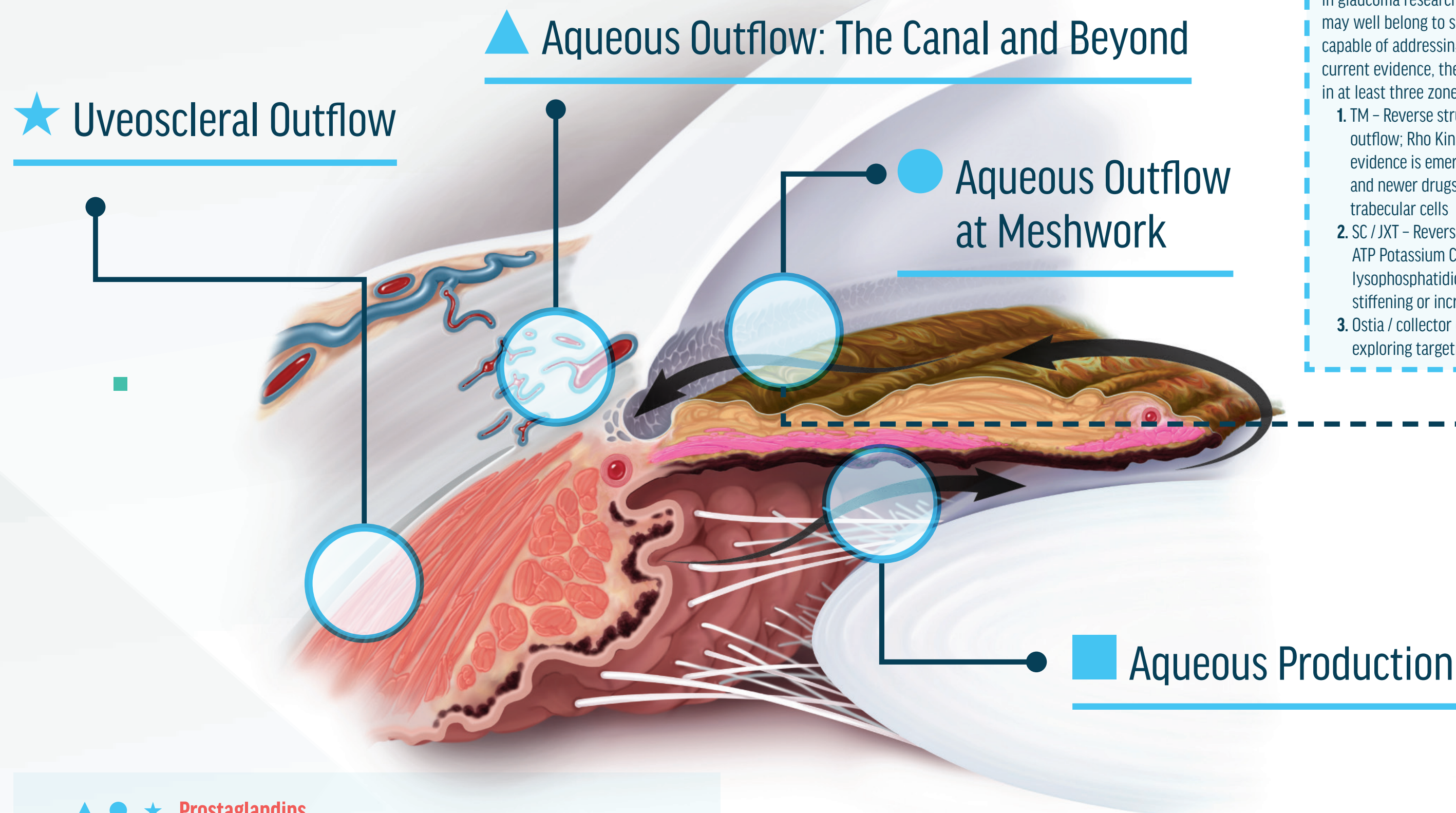
GLAUCOMA PIPELINE

2021 PHARMACEUTICAL

A VIEW INTO ONGOING INNOVATION

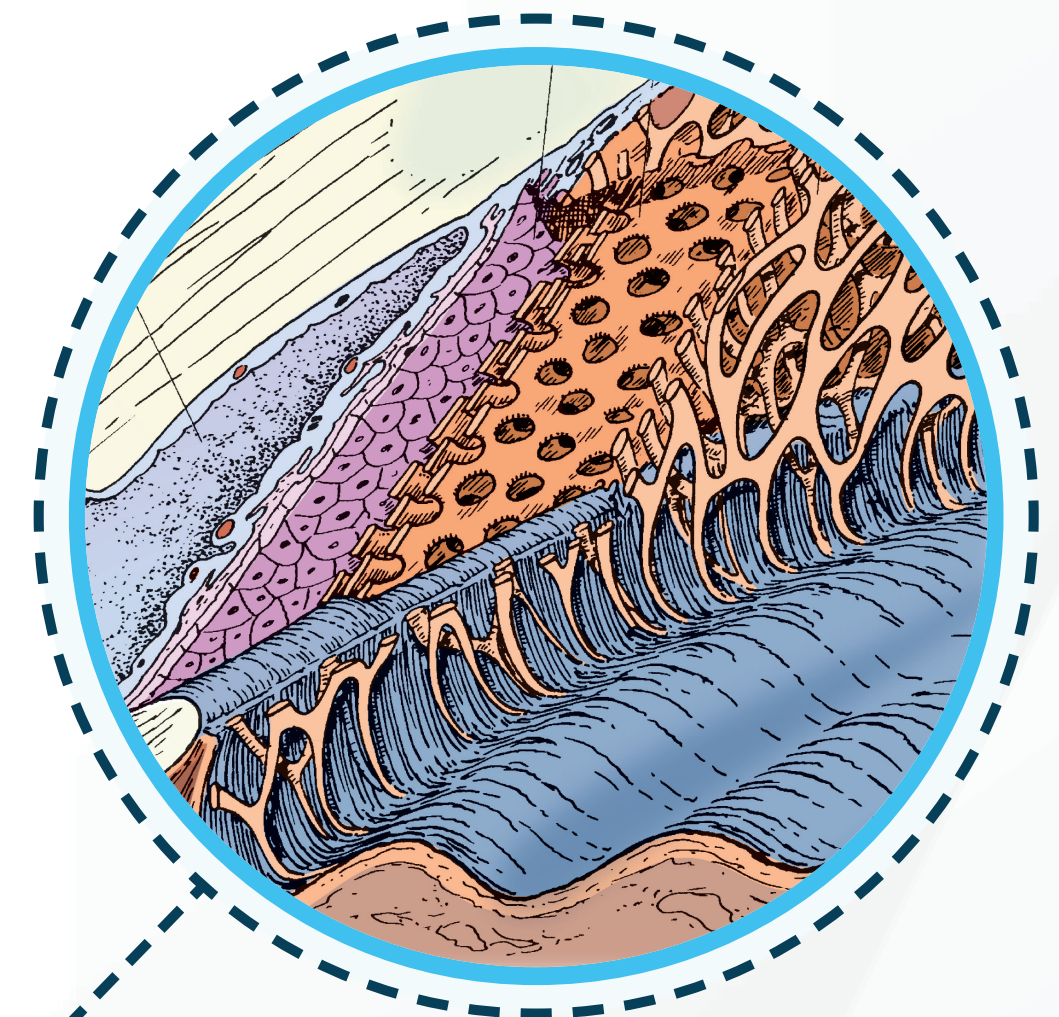
Content guidance and source: John R. Samples, MD, and Iqbal Ike K. Ahmed, MD, FRCS; *Editorially independent content supported by advertising from Santen

Outflow at Meshwork/Schlemm Canal



The concept of disease modification has garnered a lot of attention in glaucoma research. The future of pharmaceutical management may well belong to small and large molecules and antibodies capable of addressing the cause(s) of elevated pressure. Based on current evidence, there is potential for such therapeutic targeting in at least three zones:

1. TM – Reverse structural/functional damage to facilitate outflow; Rho Kinase Inhibitors likely exhibit this effect, evidence is emerging that prostaglandins have a similar effect, and newer drugs may stimulate macrophage-like activity by trabecular cells
2. SC / JXT – Reversing SC stiffening in high-pressure glaucoma; ATP Potassium Channel Modulators and Autotaxin-lysophosphatidic acid may work here, either reversing stiffening or increasing function of the extracellular matrix
3. Ostia / collector channels / veins – Several lines of research are exploring targeting potential beyond the canal



R. Rand Allingham MD, Sayoko E. Moroi MD, PhD, M. Bruce Shields MD, Karim F. Damji MD, MBA. *Shields' Textbook of Glaucoma*. Wolters Kluwer Health, Inc. 2020.

- ▲ ● ★ Prostaglandins
- ▲ ● ★ Nitric Oxide-Donating Compounds
- ▲ ● ★ Rho Kinase Inhibitors
- ★ Omidenepag Isopropyl (DE-117, Santen)
- ▲ ● ★ NCX 470 (Nicox)
- ★ Muscarinic Agonists (Miotics)
- Beta-Blockers
- ★ Alpha-Agonists
- Carbonic Anhydrase Inhibitors
- ▲ ATP Potassium Channel Modulators
- ★ Autotaxin-Lysophosphatidic Acid
- AKB-9778 (Aerpio) (Presumed mode of action)

COMBINATION MEDICATIONS

(Advantages ↑ compliance, adherence ↓ preservative, copay)

- ▲ ● ★ Rocklatan (Netarsudil and Latanoprost; Aerie)
- Cosopt / Cosopt PF (Dorzolamide HCl & Timolol Maleate; Akorn)
- ★ Combigan (Brimonidine Tartrate & Timolol Maleate; Allergan)
- ★ Simbrinza (Brimonidine & Brimonidine tartrate; Novartis)

COLOR LEGEND

Commercially Available in US; Predominant Mode(s) of Action
Pipeline Candidate

Extended Duration Options

INTRACAMERAL DEVICES

- DURYSTA (Allergan)
- iDose (Glaukos)

PUNCTAL PLUGS

- OTX-TP (Ocular Therapeutix)
- Evolute (Mati Therapeutics)
- Latanoprost Punctal Plug Delivery System (L-PPDS, Mati Therapeutics)

INJECTABLE SYSTEMS

- GB-401 (Graybug Vision)

OCULAR INSERTS AND INTRAOCULAR IMPLANTS

- Eye-D (ViSci)
- Latanoprost FA SR Ocular Implant (PA5108, PolyActiva)
- Subconjunctival / Sub-Tenon / Scleral Drug-Eluting Implants and Delivery Mechanisms

OCULAR SURFACE

- Helios (Allergan)
- MicroProst (Eyenovia)
- Drug-Eluting Contact Lenses
- Long-Acting Drops

Potential Candidates in Neuroprotection*

PRESSURE-LOWERING MEDICATIONS WITH SUGGESTED NEUROPROTECTIVE BENEFIT†

- Alpha-Agonists (Brimonidine)
- Rho Kinase Inhibitors (Netarsudil and Ripasudil)
- Adenosine A1 Agonist (Trabadenoson)
- Carbonic Anhydrase Inhibitors

NEUTROPHILS AND GROWTH FACTORS

- Ciliary Neurotrophic Factor (Delivered by live cells)
- Recombinant Human Nerve Growth Factor
- Brain-Derived Growth Factor

BLOOD FLOW REGULATION†

- Ginkgo
- Calcium Channel Blockers
- Citicoline

ANTIOXIDANTS‡

- Nicotinamide
- Ascorbic Acid

OTHER TARGETS AND TREATMENTS

- TIE2 Inhibitors (AKB 9778, Aerpio)
- Caspases
- Resveratrol
- Melatonin
- Goji Berries

* The quality of the literature supporting neuroprotective benefits of the following is widely variable; these agents and molecules may or may not have neuroregenerative properties, which would be associated with beneficial effect on retinal ganglion cells

† Pressure-lowering drug classes with alleged neuroprotection effect; no human studies have been conducted to date

‡ Nutrient-overlap

†† Indirect neuroprotective mechanism



JOHN R. SAMPLES, MD

Pharmaceutical management of glaucoma is a tried-and-true strategy for lowering IOP. As evidenced by the over 100 molecules currently in various stages of development from pre-clinical to late stage, there is abundant interest in bringing novel agents with novel mechanisms to market. This is certainly good news for patients, as newer agents offer the prospect of filling current unmet needs, achieving greater efficacy and/or safety, and, ultimately, helping patients avoid loss of vision.