SUSTAINED RELEASE OCULAR THERAPEUTICS

In this article, Michael O'Rourke, President and Founder of Scotia Vision Consultants, gives an overview of the current state of the ophthalmics market, going into greater detail on the opportunities offered in the area of sustained-release technologies and therapies.

INTRODUCTION

The ophthalmic pharmaceutical market is projected to grow from an estimated US$24.5 billion (£18.3 billion) to $28.9 billion by 2022, with retina being the most significant sector, growing to $13.9 billion (Figure 1).

In the majority of cases, retinal diseases, including wet age-related macular degeneration (w-AMD), continue to be treated by intravitreal injections (IVT), with an estimated 22.3 million procedures performed in 2017 (Figure 2). Despite the reliably successful treatment provided by this delivery route, the necessity of monthly to bi-monthly injections remains a challenge for patients. Additionally, complications potentially may occur, the most serious (but rarely occurring) of which include endophthalmitis,[1] cataract, retinal detachment and vitreous or choroidal haemorrhage.[2]

At present, within the glaucoma segment, an estimated $5.3 billion market by 2022, approved therapeutics are delivered almost exclusively by the topical route. Topical therapy also has delivery challenges, however, with patient compliance being the most common issue. In interviews with patients and their doctors, 95% of patients claim to take every drop; doctors think 80% of patients are compliant; but in reality, patients are only taking drops 70% of the time.[3]

Therefore, given the current state of affairs within these multi-billion dollar segments, there are clear opportunities for new delivery approaches through sustained release drug delivery technologies.

SUSTATINED RELEASE TECHNOLOGIES

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IVT agents have to date demonstrated that sustained release implantable technology is not, in and of itself, a prerequisite for commercial success, but that the sustained clinical efficacy of the drug is critical.

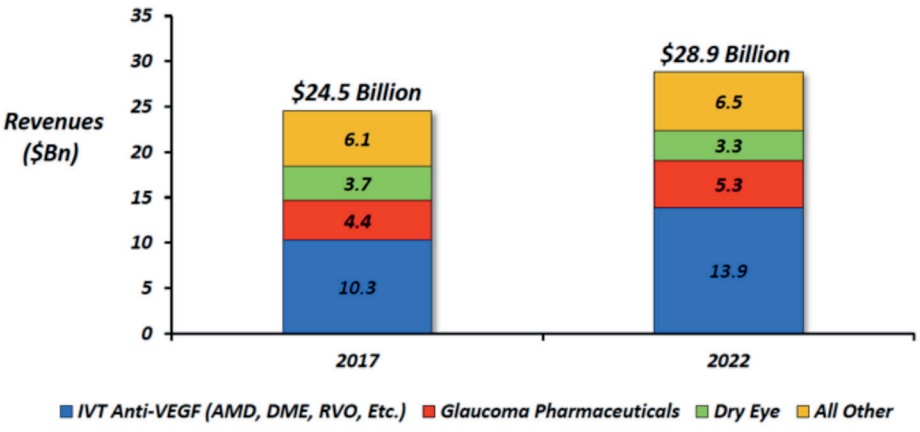

Figure 1: Global ophthalmic pharmaceutical market revenues by speciality. Courtesy of Dave Harmon, Market Scope estimates 2017.

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However, the market potential for sustained release versions of current anti vascular endothelial growth factor (anti-VEGF) products is significant, and this situation is changing with a significant effort being made to deliver large molecules – i.e. biologics (including proteins, peptides and aptamers).

Developing and achieving global regulatory approval for new sustained-release intraocular technologies is still relatively rare in ophthalmology. Only four have been approved to date:

- Vitrasert (ganciclovir), 1995, for CMV Retinitis, non-biodegradable, 4-6 months delivery.
- Retisert (fluocinolone acetonide), 2005, for posterior non-infectious uveitis (PNIU), non-bio degradable, 30 months delivery.
- Ozurdex (dexamethasone), 2007, for macular oedema after branch retinal vein occlusion or central retinal vein occlusion, PNIU, with several months estimated delivery.
- Iluvien (fluocinolone acetonide), 2012, for diabetic macular oedema in patients who have previously been treated with a course of corticosteroids and did not have a clinically significant rise in intraocular pressure.

However, despite the challenges, there is an intense development effort underway across the industry to bring new technologies to the market. In a recent analysis (Table 1) there were at least 15 novel technologies in preclinical or later-stage development for w-AMD and diabetic eye disease, 19 for glaucoma and, if we consider anterior sustained release systems, at least nine technologies covering a range of target indications including the emerging segment of sustained delivery targeting dry eye. Of note, however, is the corresponding approximate number of therapeutics (preclinical to Phase III) in development in the absence of any drug release technology: 69 therapeutic development programmes

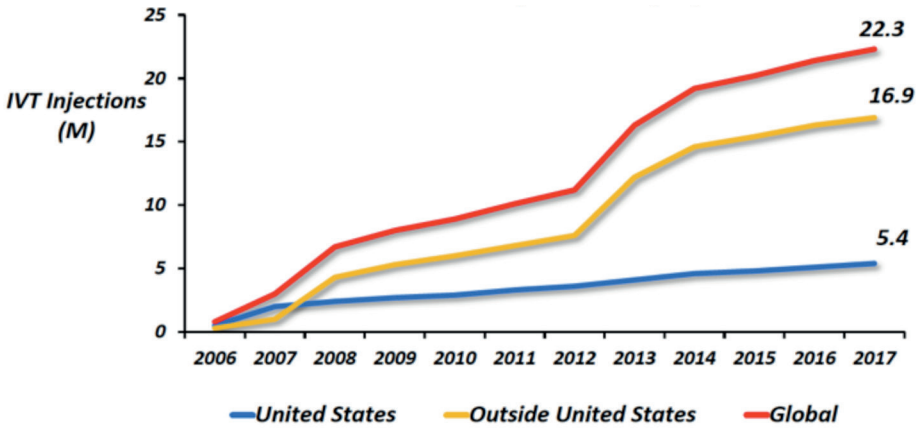

Figure 2: Global anti-VEGF injections. Courtesy of Dave Harmon, Market Scope estimates 2017.

Segment	Sustained Release Technology	New Product Development
Glaucoma	19	6
Retina	15	69
• wet AMD		• 30
• dry AMD		• 12
• DME		• 23
• ME		• 4
Posterior Uveitis	1	13
Anterior	9	50
• Dry Eye		• 17
• Anterior Uveitis		• 4
• Post Cataract Inflammation		• 4
• Infection		• 4
• Presbyopia		• 2
• Allergy		• 2
• Blepharitis		• 2
Orphan	–	15
Gene Therapy	–	12
Stem Cell	1	4

Table 1: Drug delivery and new product development in the ophthalmic sector.[4]

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just within the field of retina alone, at least six in glaucoma and at least 50 in the anterior segment.

From a development perspective these numbers appear reasonable. The four systems that have approved to date have incorporated generic drugs (i.e. steroids and an anti-viral). There has been no sustained release, ocular delivery system approved to date that incorporates a new chemical entity, in part due to the elevated risk and expense of achieving success with the combination of both a new technology, with its physical characteristics, and a novel drug product, with its own chemical and pharmacokinetic properties. The approach so far has been to increase the chances of success by working with a well-documented and approved drug. However, that is expected to change in the future and we are already witnessing this in some early-stage glaucoma programmes.

Of particular note is the wide range of technologies and methods being considered for drug release systems – to name but a few:

- Refillable drug reservoirs
- Photocrosslinking technology with UV light for both small and large molecules
- Microparticle and nanoparticle systems for w-AMD, glaucoma (including neuroprotection) and potentially the anterior segment for dry eye and corneal disease
- Prostaglandin analogue delivery systems for ocular hypertension and open-angle glaucoma
- Topical semifluorinated alkane delivery, enhancing drug solubility and ocular surface retention for anterior and posterior segment applications
- Proprietary hydrogel technology
- Suprachoroidal delivery or implants, including injectable suspensions
- Injectable polymer-based protein delivery systems
- Topical peptides for neovascular AMD and corneal injuries
- Contact lens delivery systems
- Iontophoresis.

CONCLUSION

In summary, the opportunity for future development in sustained release technology remains a multi-billion dollar prospect. Some of the greatest (and most challenging) possibilities include sustained release delivery (three months minimum, four to six months optimal) of large molecules (proteins, peptides, aptamers) for retinal diseases, thus avoiding frequent injections, and prolonged release of therapeutics for glaucoma. The future for sustained release ocular drug delivery lies in reducing the treatment burden, with innovations in delivery technology, biologics delivery, targeting gene therapy to the appropriate cell types and combining effective small-molecule therapeutics with the appropriate drug delivery system. Reimbursement, patient compliance and convenience will be the key driver for drug delivery. However, in addition to just compliance, a demonstration of enhanced efficacy and compelling pharma economics for a new product may be essential if the delivery technology is to achieve a competitive advantage and commercial success.

ABOUT THE AUTHOR

Michael O'Rourke is the President and Founder of Scotia Vision, a specialised ophthalmic consulting company with extensive expertise in global ocular drug delivery commercial and product development strategies. Mr O'Rourke has over 30 years drug delivery experience across ophthalmology, periodontal and pulmonary markets in sales, marketing, product launch, strategy development and global commercialisation. In addition to multiple Scotia Vision clients, his career experience includes several leading global organisations and start-ups, including 3M, Alza, Chiron Vision, Bausch + Lomb, GrayBug Vision, and Re-Vana Therapeutics.

REFERENCES

1. *Ta CN, "Minimizing the risk of endophthalmitis following intravitreous injections". Retina, 2004, Vol 24, pp 699-705.*
2. *Jager RD et al, "Risks of intravitreous injection: a comprehensive review". Retina, 2004, Vol 24, pp 676-98.*
3. *"Harry Quigley, MD, shares glaucoma pearls at SECO" Optometry Times, March 2014.*
4. *Product Development Analysis - Scotia Vision Consultants: Data on file, September 2017.*