Eye on Innovation

The Official Publication of OIS

Next Generation Ocular Drug Delivery Platforms

Is the wait for a Holy Grail product in ophthalmology medical technology soon to be over for researchers, patients and stakeholders?

The human eye measures approximately one inch in diameter, but traversing that blink-of-an-eye distance to achieve safe, effective and stable delivery of ophthalmology drugs via minimally or non-invasive medical devices to treat major eye diseases has taken more than 40 years to accomplish.

Is the wait for a Holy Grail product in ophthalmology medical technology soon to be over for researchers, patients and stakeholders?

There are multiple questions to be answered and issues to be resolved in the ophthalmology sector, including:

- Is the drug delivery issue ultimately solvable, particularly related to back of-the-eye diseases?
- Do innovators have a grasp on the science to scale the clinical hurdles and convince investors of the eventuality of commercialization?
- Which prospective drug delivery technologies are currently showing the most clinical potential?

Despite these decades of research, there are only four approved intraocular sustained release drug delivery products approved for use and approved globally or specific to Europe. Vitrasert® 1995 ganciclovir 4.5mg. Retisert® 2005, fluocinolone acetonide 0.59mg. Ozurdex® dexamethasone 0.7mg. Iluvien® fluocinolone acetonide 190µg.

In parallel, the growth of intravitreal injections with drugs without sustained release benefits has been impressive. There are approx eleven million to twelve million ocular injections administered to patients annually for anti VEG F treatments, and, by many market forecast accounts, the patient base for serious ophthalmology diseases is expected to grow at least 50 percent through 2020 and double by 2050, in what must be currently be considered an area of unmet need that is growing bigger.

The predominant factors that are influencing the ophthalmology drug and device market dynamics are well known by players and stakeholders.

Foremost is the melding patient base of the aging baby boomers, elderly Greatest Generation and the growing demographic class of young people being diagnosed with diabetes. The incidence of diabetes continues to increase, particularly among adolescents and young adults. The Centers for Disease Control in the USA projects the number of diabetic retinopathy cases will double by 2050.

Increasing global diabetes incidence portends misfortune for millions of patients, as well as for patients-in-waiting, considering the proliferation of diabetes cases among adolescents and young adults. That inauspicious development indicates diabetes is no longer a disease reserved for the golden years, but a scourge that now threatens to chronically impair or rob the vision of many in a younger generation before they even reach the prime of their lives.

Data compiled by Scotia Vision Consultants LLC, a specialized ophthalmic consulting company with expertise in global ocular drug delivery strategies, enumerates the trends, challenges and opportunities that define an ophthalmology disease market that will likely be in an epidemic category if novel drug delivery technologies do not keep pace with blinding and impairing ocular diseases.

Primary ophthalmic disease trends in the U.S. underscore the need for innovative technologies to treat major eye diseases, which are expected to more than triple by mid-century.

- 4.2 million Americans aged 40 or older were blind or had a visual impairment in 2010, up from 3.3 million in 2000.

- Of the 4.2 million, 1.3 million were blind, up from 1 million in year 2000.

- 13 million Americans aged 40 or older will have a visual impairment or be blind by the year 2050.

- At least 10 million Americans currently suffer retinal degenerative diseases, with an annual cost estimated at $70 billion by 2020.

The global cost of vision loss is approximately $3 trillion dollars ($2,954 billion USD) for the 733 million people living with low vision and blindness in 2010. The four major blinding diseases (age-related macular degeneration, diabetic retinopathy, diabetic macular edema and glaucoma) that affect the posterior segment of the eye offer the most substantial opportunity for augmenting existing ocular drug therapy administration and creating commercialization prospects for drug delivery technologies in the future.

The posterior segment diseases continue to proliferate and rank up front not only in prevalence, but also in the opportunity to address that pervasiveness with innovation. The global ophthalmology drug and device market to is forecasted to reach $36 billion by 2014, at a compound annual growth rate (CAGR) of 5.4% from 2009-2014, and to increase to $52.4 billion by 2017. The pharmaceutical segment of this market is

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expected to increase to $19.8 billion by 2014, growing at a CAGR of 4% from 2009-2014, with AMD and diabetic retinopathy drugs worth $5.84 billion by 2014. Retinal diseases such as AMD and diabetic retinopathy are projected to soon surpass glaucoma as the most valuable sector.

Comparatively few sustained-release ophthalmic drug delivery products are approved to treat the expanding disease incidence and the roster of injectable drugs that are effectively conveyed by medical device systems is also sparse.

Injection (non-implant) drug delivery products that allow for a measure of efficacy do have a history of significant market impact. Numerous breakthrough products in this sector, beginning with Novartis' Visudyne® intravenous injection, approved in 2000 and peaking around $500m in revenue in 2005, and currently led by Genentech's Lucentis® and Regeneron's Eylea®, together accounting for projected sales exceeding $4 billion in 2013, have been responsible for a profound revenue trend shift that has seen a surge in profitability that has particularly transformed the posterior eye disease segment into a vital and lucrative market.

While the incidence of disease affords opportunity for those who endeavor to treat or cure it, the prospect also comes with significant challenges. The key problem relative to treating diabetes-related ocular diseases and other eye diseases is mainly not a

pharmacologic or biotechnology drug issue, as there are several approved ophthalmic drugs that have effective therapeutic compositions. In the ophthalmology market, it's all about Delivery, Delivery, Delivery. Getting the medicine, in an uncompromised state, to the ocular treatment site, while maintaining its presence long enough to dispense an effective dose , with minimal side effects, is what is keeping the sector's clinical minds up at night.

The foremost clinical challenge involves the delivery of effective doses of drugs to the posterior segment of the eye. Approximately 2 million people over the age of 65 in the U.S. are afflicted with Age related Macular Degeneration (AMD), with the number estimated to increase by 200,000 new cases per year through 2020. Additionally, severe vision loss from AMD and other diseases affecting the back of the eye, including glaucoma, diabetic retinopathy and retinitis pigmentosa, accounts for the majority of global cases of irreversible blindness.

Although patients afflicted with ophthalmic diseases such as glaucoma and AMD are benefitting from the accessibility of patently effective therapeutics, the technologies for delivering those drugs to the eye still largely subject patients to unappealing procedures or they allot unpredictable outcomes that can leave much to be desired relative to critical issues involving safety, stability and efficacy.

For example, it is estimated that topical eye drop therapies result in 5 percent or less corneal penetration with resulting minimal benefit to posterior eye conditions.

This treatment model results in an excessive waste of costly drugs, efficacy and compliance limitations and potentially exposes patients to unsafe levels of drugs as they overcompensate to offset the percentage of their dosages that never make it to the targeted treatment location.

The current standard of care to deliver ophthalmologic drugs, particularly to the posterior involves the variability of eye drop applications for anterior segment diseases that must be administered multiple times a day to achieve effective dosage. The third major option involves pills taken orally that do reach the eye, but also unnecessarily expose the full body to the drug.

The intravitreal injection does represent an advancement in ocular medical technology; however, it has drawbacks that leave opportunity for more efficient device technologies or enhanced intravitreal delivery to emerge offering extended duration and less potential side effects or inflammation. Patients have never had an affinity for the hypodermic needle, even in local skin applications such as vaccinations, local anesthesia and fluid samples that are administered as few times as annually to once every five to 10 years. So it is practical to assume there is no bated anticipation on their part to embrace the intravitreal injection to the eye every month, even to treat the proliferating incidence of ophthalmic diseases that are compromising or threatening to pilfer the eyesight of a burgeoning patient base. In addition, current AMD and diabetic eye disease treatments offer no regression of the disease, so the need for more effective therapeutics combined with drug delivery technology is a major market opportunity.

Consideration and management of some key areas can facilitate best practices strategies that stand to optimize the overall drug delivery technology development process.

Regarding the archetype drug delivery technology system, Scotia Vision market research has established a top ten list of characteristics designated by industry executives as desirable for developing the optimal drug delivery technology system. The attributes comprise a range of issues, but at the top is the requirement to achieve a less frequent delivery schedule – a primary concern and objective shared by patients, practitioners, researchers, investors and regulators.

Desirable Drug Delivery Technology Attributes

Item	Rationale
*4-12 month delivery	Obviates frequent office visits
No adverse or minimal side effects	Avoids giving patient glaucoma and/or cataract
Ability to vary dosage - change of posology	Customized dosing for patients - perhaps complete withdrawal of a drug if needed
Minimal intraocular debris	Debris from drug delivery can lead to inflammation and 'floaters'
Clearly developed and executed dose-ranging studies	Appropriate dose is identified in phase ll or phase ll/lll studies to reduce risk of extended regulatory delays
High patient compliance	Better patient outcomes will trump less compliant regimens
Demonstrated safety and efficacy	This is the minimum requirement, the gatekeepers minimum threshold
Cost-effective manufacturing	Manufacturers require acceptable gross margins to participate in this space
Continuous, controlled long-term delivery of small or large molecule therapies	Zero order kinetics/steady state delivery over 1+ years will meet patient/physician need for an improved treatment paradigm
Good understanding of the strategic marketing landscape, regulatory and clinical challenges	Plan for long term development with a competitive product, think outside the box

*Four months may not be required for many acute and sub acute conditions. You may start with two months with perhaps less potential for side effects. It's important to keep in mind that some diseases are potentially curable (e.g. macular edema) while others are manageable, but not curable (glaucoma) - this might affect the target treatment period. Also, some diseases may require variable amount of medication to maintain a desired effect and some drugs may have more side-effects than others, or if given at a constitutively high level rather than, for example, a pulsed pattern (e.g. steroids). There is always an issue of developing tolerance to a drug over time (e.g. a drug becomes ineffective if used constantly for a long time, or an increasing dose may be needed to maintain the desired effect).

There are other best practices strategies that can facilitate advancement of drug delivery agendas.

Focus on initial concepts

Building the drug delivery platform with established drug products is expedient. Patent expiration in ophthalmology is picking up over the next five years, so there are a number of compounds with excellent profiles to consider for drug delivery platforms, for example, in glaucoma.

Be aggressive in preclinical phase activity

Talk to regulatory agencies early through a scientific advice or pre-Investigational New Drug /Investigational Device Exemption meeting to initiate dialogue. Also look at other therapeutic areas to support your claims for safety, inasmuch as the ocular field is behind many other areas in drug delivery development.

Reach out to engage regulatory

From a regulatory perspective, those proposing a new drug/drug delivery system must understand many critical aspects. They include different requirements of the EU and U.S. regulators for drug delivery systems; how the product's MOA affects the regulatory pathway; and the status of the proposed active ingredient in the targeted regulatory jurisdiction.

In the U.S., there are no fees to obtain guidance from the FDA. Always make sure you take advantage of the opportunity to have a face-to-face meeting with the agency. Provide a comprehensive meeting briefing document in advance of the meeting to educate the agency on your product and ask questions that will help you finalize study designs and projects plans.

Lastly, consider a stepwise development approach with new delivery systems. Developing a new chemical entity together with a new delivery system may create both regulatory and development challenges with many unknown variables. Increase your likelihood of successful validation of your new delivery system by first developing it with a drug with well-known safety and efficacy.

New Products in Development

It may appear obvious but before embarking on your own product development program, you must fully understand the market dynamics and status of all new potentially competitive products currently in development. The acid test of determining what competitive advantage your product will have perhaps 7-10 years from your starting point, is a critical factor to agree on with your development and commercial teams.

There are many new products with potential sustained-release technology, including new topical formulations in development, ranging from preclinical to Phase III. But, as yet, the Holy Grail referenced earlier has yet to be found, even with the four currently approved sustained release products available for the posterior segment.

The multi-billion dollar market opportunity for "new & innovative" ocular sustained-release products and other delivery systems, particularly to the posterior segment, therefore remains a significant market opportunity, as represented in the following areas and indications.

- Polymer-drug conjugate for neovascular AMD and glaucoma

- Microsphere and nanosphere systems for neovascular AMD and Glaucoma

- Encapsulated cell technology with extracellular delivery of ciliary neurotrophic factor for retinitis pigmentosa and geographic atrophy

- Cell based programs, including stem cells for neovascular AMD

- Pre-clinical novel adeno-associated viral variant technology for long-term protein delivery to the eye in DME, neovascular AMD, glaucoma and other conditions

- Latanoprost delivery system (L-PPDS) in subjects with ocular hypertension and open angle glaucoma

- Injectable drug delivery implant for glaucoma

- Proprietary hydrogel technology

- Suprachoroidal injectable suspension with triamcinolone acetonide for uveitis

- Topical peptides for neovascular AMD and corneal injuries

- Topical semi-fluorinated alkane delivery, enhancing drug solubility - posterior and anterior applications

- Topical anterior mucosal delivery for posterior treatment

The PEG medical device, which is compatible with a range of drug classes, can be customized to provide therapeutics on a schedule that can range from days to months.

There are device technologies currently in research that, pending regulatory approval, stand to be game-changers in delivering less taxing, more effective options for the increasing number of ophthalmic disease patients. These leading-edge technologies aim to address unmet need disease indications such as back-of-the-eye disorders, as well as underserved ophthalmology diseases such as dry eye, glaucoma and cataracts that are growing disease areas in need of improved drug and device therapies.

Innovators are researching therapeutic ocular films made of materials that are fitted over the cornea or applied to the eye in an otherwise more sustainable form, much like a contact lens or controlled-release solution, that would dissolve slowly enough to provide a sustained drug release, thereby creating a more stable therapeutic environment and increasing the duration window for efficacy.

GrayBug's proprietary controlled release intraocular drug delivery systems can be tailored to meet performance requirements of duration and rate of release for a diverse range of therapeutics. Two polymer based drug delivery platforms have been developed that can be customized for enhanced delivery and elimination of inflammation that can be associated with other delivery systems. GrayBug is also focused on its own proprietary product development portfolio for major eye diseases including w-AMD and glaucoma.

Clearside Biomedical is developing a micro-injection technology to improve posterior drug delivery through the suprachoroidal pathway. If successful, the technology could reduce side effects such as eye trauma, increase efficacy and advance a new series of drugs that target currently difficult-to-reach structures such as the retina and choroid.

Novaliq GmbH based in Heidelberg Germany are enhancing topical drug delivery by developing a superior generation of ocular formulations for poorly soluble drugs. The patented formulations are based on semi fluorinated alkanes (SFA's) which can be easily applied in the form of an eye drop or spray.

The companies and researchers working to improve ophthalmology patients' lives share an objective of commercializing products that allow patients to manage their chronic diseases with innovative pharmaceutical treatments combined with drug delivery technology, while abiding fewer physician visits per year or a far less arduous schedule of therapeutic applications than are the standard today.

The future for sustained-release ocular drug delivery lies in reducing the treatment burden by commercializing 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. Patient compliance will be a key driver in the pursuit of ocular drug delivery; however, a demonstration of improved efficacy for a new product will practically be essential if delivering competitive advantage is to be achieved.

Spotlight on:

Innovative Ocular Drug Delivery Companies

Unique Drug And Oxygen Delivery Systems

NOVALIQ

gray bug®

CLEARSIDE BIOMEDICAL

Improving the Delivery of Topical Ocular Drops

Using semifluorinated alkanes to transform poorly soluble drugs into effective therapeutics.

BY BERNHARD GÜNTHER, CEO, NOVALIQ GMBH

Novaliq GmbH, based in Heidelberg, Germany, is a drug delivery company that is developing a superior generation of ocular formulations for poorly soluble drugs. The patented ocular for mulations are based on semifluorinated alkanes (SFAs), which can be easily applied in the form of eye drops or an eye spray.

Since its establishment in 2007, Novaliq has obtained five rounds of funding totalling $35 million from its major shareholder, Dievini Hopp Biotech Holding (a venture capital company focusing on biopharmaceutical companies in Europe).

BUSINESS STRATEGY

To make full use of the vast potential of this novel drug delivery platform, Novaliq plans to continuously expand the range of ocular indications. The company will develop existing product candidates that it will guide through clinical Phase I/II testing. Due to the company's focus on superior drug formulations with well-estab lished drugs, Novaliq's pipeline projects have low failure risks and high projected values. For further development and commercialization, Novaliq intends to license these formulations to suitable partners.

> "SFAs are a special class of fluorocarbon compounds that have been used for more than 10 years in the posterior segment with an excellent safety profile."

In addition, Novaliq has just received CE mark for its first OTC dry eye product, NovaTears ®.
These drops make use of the excellent wettabilty and biocompatibility of SFAs on the cornea. The company also intends to seek partners for this product opportunity in the near term.

THE TECHNOLOGY

EyeSol®

EyeSol® is a novel topical ocular drug delivery system for poorly soluble drugs. Although the anterior segment of the eye is one of the most readily accessible organs of the body, drug delivery to the eye tissues is particularly problematic. This is reflected by the notoriously poor bioavailability of topical ocular drug formulations of 5% or less. A standard drop of water of approximately 40 to 50µL will activate the

blinking reflex, which washes away most of any topically administered dose within 15 to 30 seconds after instillation.

To further complicate matters, up to 75% of new chemical entities (NCEs) are considered poorly soluble, even for oral administration. In short, a drug is considered poorly soluble if the required dose cannot be dissolved in 250 mL of aqueous medium. An aqueous has a volume of 40 to 50µL, 5,000 times less volume. This exacerbates the solubility problem by several orders of magnitude.

Three major issues need to be addressed for ocular formulations: safety, bioavailability, and stability. EyeSol, Novaliq's proprietary ocular drug delivery technology, fulfills these requirements. EyeSol is based on an SFA platform. SFAs are a special class of fluorocarbon compounds that have been used for more than 10 years in the posterior segment in thousands of patients with an excellent safety profile.[2,3] Their low viscosity and surface tension result in much smaller droplets of around 15 µL, approximately three times less than a standard aqueous drop. Thus, SFAs avoid the spillover effect (and the subsequent loss of most of the administered dose), which obviously increases their bioavailability. In addition, the refractive index of SFAs is similar to water, so these formulations will not impair patients' vision like emulsions and oily drops tend to do. Due to their amphiphilic nature, SFAs dissolve a number of therapeutically relevant, poorly-water-soluble compounds such as cyclosporine A and Tacrolimus. Moreover, the aqueous-free environment of this delivery system increases drugs' stability by preventing oxidation and hydrolysis..

CyclASol®

CyclASol® is the first Cyclosporine A solution for dry eye disease. This proprietary SFA product is based on the EyeSol technology and therefore provided preserva tive-free in multidose units. The absence of surfactants and irritating preservatives that tend to blur patients' vision leads to improved tolerability and convenience.

Summary

Novaliq GmbH offers a compelling drug delivery opportunity to enhance the performance of topical eye drops. A new generation of products is possible through the unique and proprietary properties of SFAs as the delivery vehicle.

Novaliq welcomes invitations from interested par ties to enter discussions about significant additional development opportunities under a confidentiality agreement.

CyclASol and NovaTears are not approved for use in the USA.

1. Sahoo SK, Dilnawaz F, Krishnakumar S. Nanotechnology in ocular drug delivery. 2008;13(3-4):144-151. Drug Discov Today.
2.Kirchhof B, Wong D, Van Meurs J, et al. Use of perfluorohexyloctane as a long-term internal tamponade agent in complicated retinal detachment surgery. Am J Ophthalmol. 2002;133(1):95-101.
3.Meinert H, Roy T. Semifluorinated alkanes--a new class of compounds with outstan ding properties for use in ophthalmology. Eur J Ophthalmol. 2000;10(3):189-197.

FAST FACTS

LOCATION

Heidelberg, Germany; www.novaliq.de

PRODUCT

- Topical drug delivery technology
- CyclASol, a 0.05% clear, preservative-free, multidose Cyclosporine A solution

UNIQUE CHARACTERISTICS

CyclASol is a crystal-clear, preservative-free, multidose solution with no blurring. In rabbit corneas, it has shown long-term stability and superior wettability, superior pharmacokinetics, and superior biocompatibility compared with emulsions.

SFAs have the potential to create significant competitive advantages with multiple drug candidates in ocular conditions, primarily by enhancing the therapeutic effect of poorly soluble drugs.

APPLICATIONS

Dry eye disease and other ocular indications

MARKET SIZE POTENTIAL

$3 billion

REGULATORY STATUS

Phase 1 clinical development; preclinical trials completed. Not yet approved in the US or other countries.

MANAGEMENT TEAM & CONTACTS

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Overview

GrayBug is a new privately held ophthalmic pharmaceutical company pioneering breakthrough intraocular therapeutics through innovative drug delivery platforms. Our business objective is to build and implement two synergistic development strategies in major global disease segments:

1) **Proprietary Product Development Programs** with lead compounds in neovascular diseases including age-related macular degeneration (AMD) and glaucoma. Worldwide markets for AMD and glaucoma each currently exceed $4 billion with significant market need existing for product enhancements and innovation.

2) **Proprietary Polymer-Based Delivery Technologies** that deliver a wide range of drugs, including small molecules. Specifically,
   - Novel polymer-based drug delivery systems, formulated into drug-loaded nanoparticles, microparticles and biodegradable implants for intraocular injection.

Proof of concept has been demonstrated in animals for all five products in the pipeline and GrayBug's lead AMD and glaucoma candidates are being moved toward IND. The Company's proprietary controlled-release drug delivery systems can be tailored to meet performance requirements of duration and rate of drug release. GrayBug possesses the technical expertise, experience, and capacity to collaborate with select partners in areas of mutual interest.

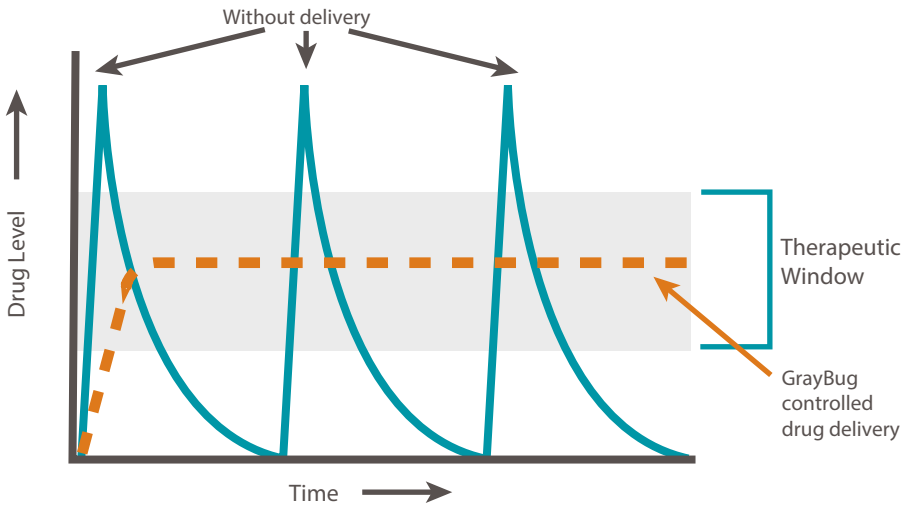
Technology

GrayBug proprietary technologies allow customizable sustained release of all therapeutic classes, including small molecule drugs, when delivered intraocularly. GrayBug's controlled-release technologies may reduce dosing frequencies to only 2-3x per year, which is expected to improve patient compliance and drug efficacy. GB-101, the lead AMD product, is a single agent that inhibits multiple pathogenic angiogenesis signals. Blockade of multiple signals was demonstrated more efficacious than inhibition of only one in clinical studies. Pipeline products include innovative glaucoma therapies, both for controlled-release of intraocular pressure lowering drugs and for long-term protection of the optic nerve to prevent blindness.

MILESTONES

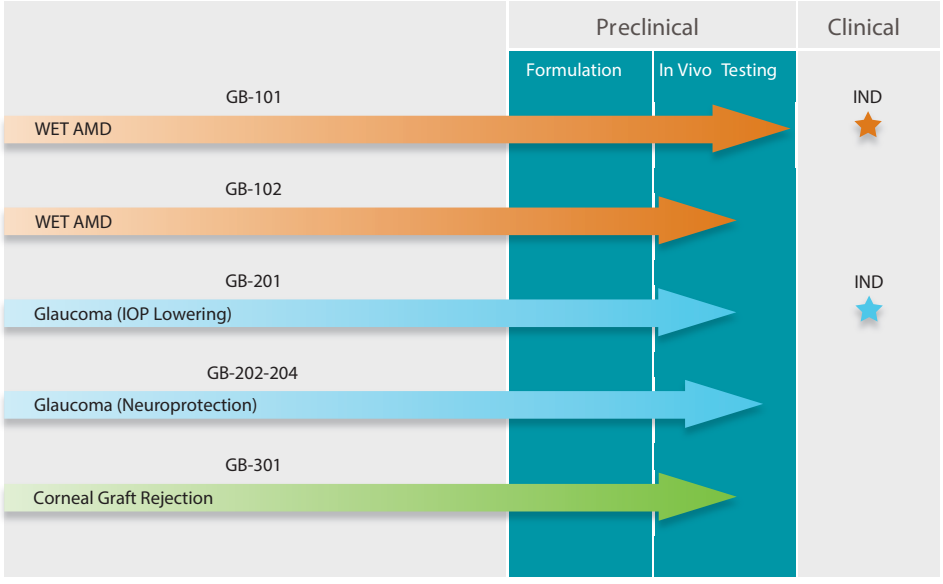
- Founded in 2011 as a spin-out of Johns Hopkins University
- >$2.5 million capital raised
- Strong intellectual property position. US and interna - tional patent application families protecting two drug-delivery platform technologies through 2031.
- GrayBug technologies allow controlled drug delivery with long durations of drug-release
- Proprietary pre-clinical product development programs in AMD and glaucoma
- Strong and experienced management team in ocular drug delivery development and commercialization
- World class advisory group

GrayBug Controlled-Release Drug Delivery



The GrayBug controlled-release drug delivery platform technologies allow constant sustained drug delivery to improve drug *efficacy.* Drug delivery rate and duration are customizable to maintain drug concentration within the therapeutic window for the desired duration.

Development Pipeline



GrayBug is Advancing the Treatment of Ocular Diseases Through the Development of Innovative, Injectable, Controlled-Release, Biodegradable Polymer, Drug Delivery Technologies and Proprietary Therapeutic Agents with Significant Competitive Advantage.

GrayBug welcomes invitations from interested parties to enter discussions about significant business development partnership opportunities under a confidentiality agreement.

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Exploiting a Physiologic Fast-Lane for Safer Drug Delivery to the Back of the Eye

Clearside Biomedical's investigational microneedle dosage form puts the suprachoroidal space within reach in an office visit

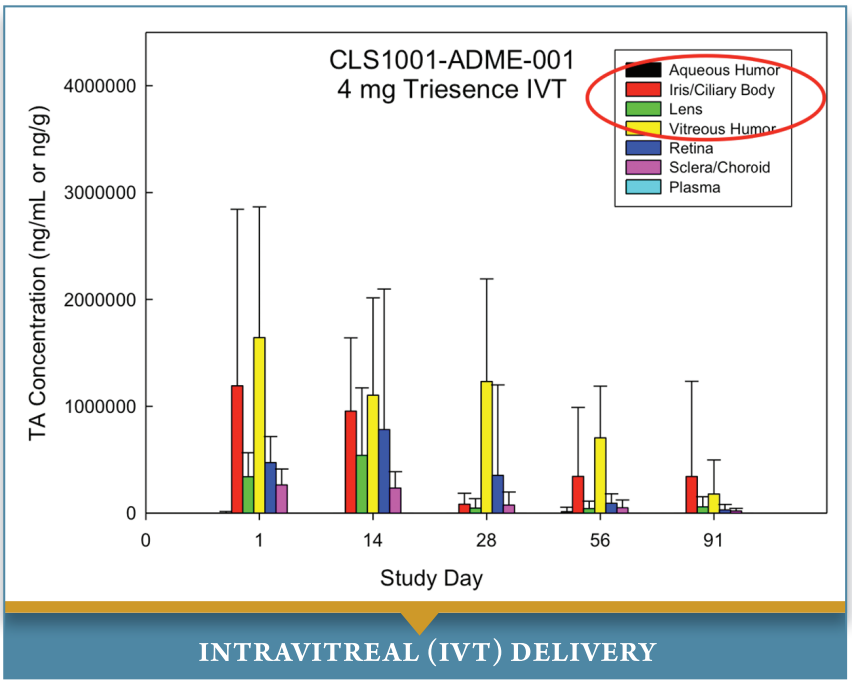
CLEARSIDE BIOMEDICAL

The retina and choroid are the sites of major vision-threatening diseases including wet age-related macular degeneration (AMD), diabetic retinopathy and diabetic macular edema (DME), retinal vein occlusion (RVO), and uveitis. At present, ophthalmic drug therapy only treats the end-stages of these diseases, often merely slowing their progression. Typically, these drugs are delivered by intravitreal injection with a traditional hypodermic needle. This is an indirect method of reaching key tissues involved in posterior eye disease, particularly the retina and choroid. Such non-targeted delivery allows drug uptake in other parts of the eye, possibly producing unwanted side effects. Additionally, intravitreal injections carry the risks associated with an invasive procedure and are very unpleasant for the patient.

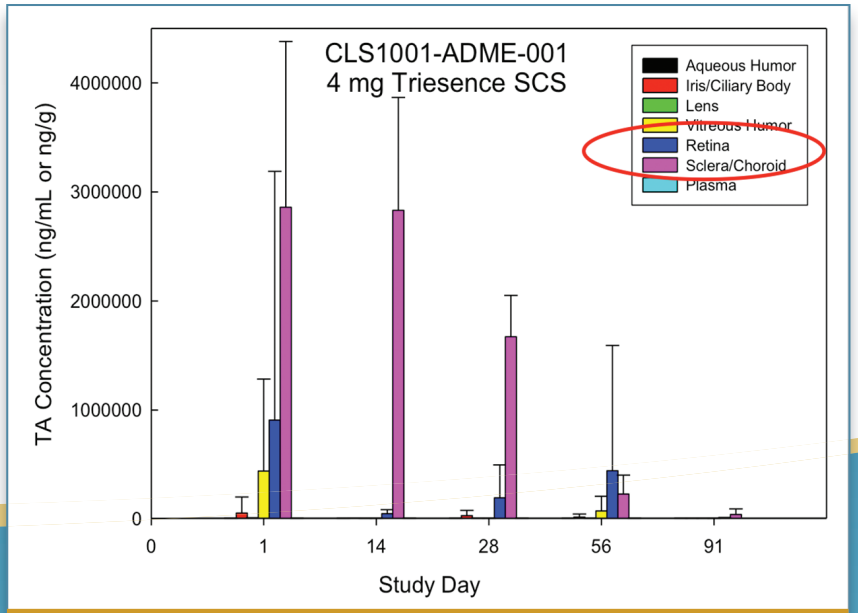
A Better Way to the Back of the Eye

Clearside Biomedical's proprietary microinjection dosage form is designed to reach the retina and choroid via a microneedle through the sclera into the suprachoroidal space to allow direct access to targeted tissues in an in-office procedure.

Compared to conventional intravitreal injections, microneedle delivery of corticosteroids through the suprachoroidal space increases the availability of drug to the choroid where inflammation originates while minimizing exposure of non-target tissues.[1] In this example, drug levels in target tissues are substantially enhanced with delivery through the suprachoroidal space, while negligible drug levels are found in the iris/ciliary body and lens, where intraocular pressure and cataract side effects associated with corticosteroids can occur.



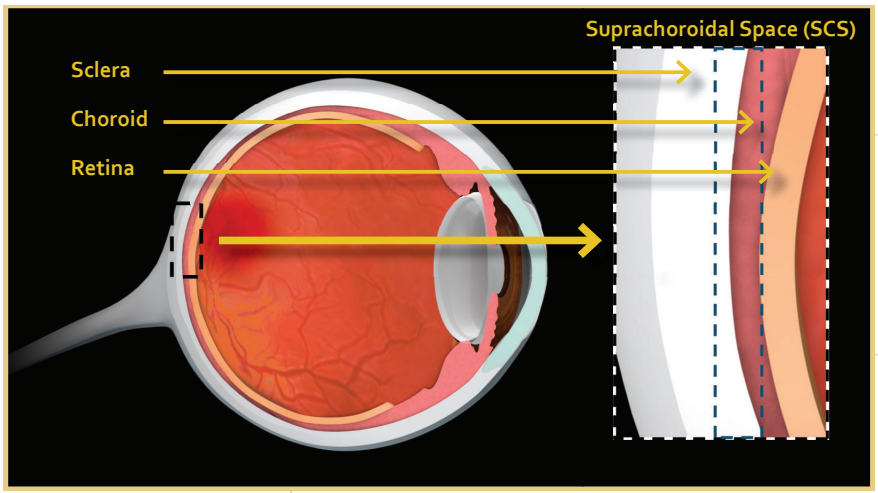
INTRAVITREAL (IVT) DELIVERY



SUPRACHOROIDAL (SCS) DELIVERY

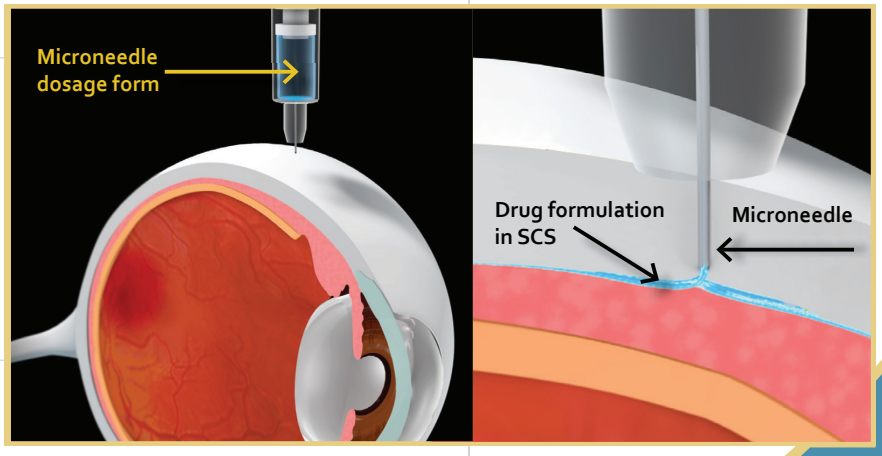
1. Edelhauser H, Patel S, Meschter C, Dean R, Powell K, Verhoeven R. Suprachoroidal Microinjection Delivers Triamcinolone Acetonide To Therapeutically-Relevant Posterior Ocular Structures and Limits Exposure in the Anterior Segment. ARVO Meeting Abstract 2013;5063-B0021

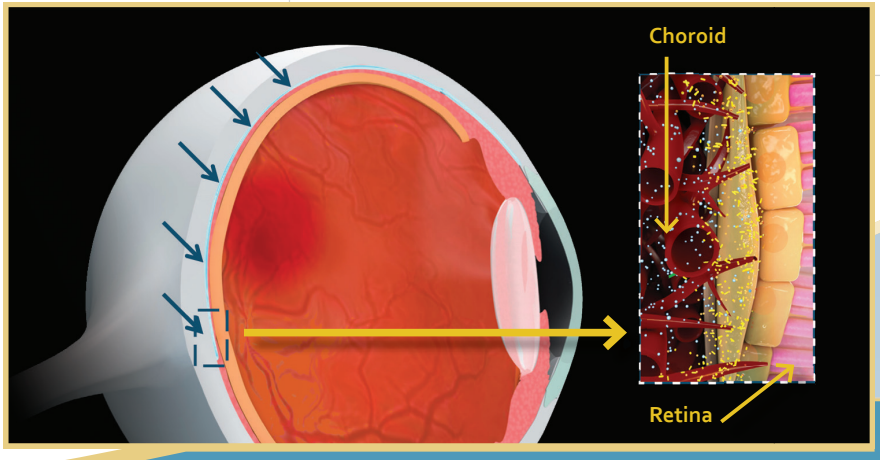
A Closer Look at Suprachoroidal Drug Delivery



In the eye, the suprachoroidal space (SCS) lies between the sclera and the choroid. This "virtual space" has a surface area of 17 cm^2 and has been shown to hold up to 200 µL of fluid.

Ophthalmic drug formulations can be injected through the sclera into the SCS with a minimally invasive microneedle dosage form. Traditional administration requires full penetration of the globe with a hypodermic needle to reach the vitreous.





The drug formulation quickly spreads around the back of the eye, directly reaching posterior segment ocular tissues involved in the disease process, including the retina and choroid, while limiting exposure to anterior segment tissues, and other non-target areas of the eye.

About Clearside Biomedical, Inc.

Clearside Biomedical is a privately-held ophthalmic pharmaceutical company dedicated to developing and commercializing therapeutics that safely treat diseases of the posterior segment of the eye like macular edema, wet AMD and inflammation. The Company's patented microinjection dosage form is the only non-surgical method for focal delivery of drugs to the retina and choroid through the suprachoroidal space. Clearside Biomedical is currently in the clinic studying uveitis and preparing clinical programs in macular edema associated with uveitis and following retinal vein occlusion which will initiate in 2014.

Clearside Biomedical was established with investments from Hatteras Venture Partners, Santen Pharmaceuticals Co., Ltd., Kenan Flagler Venture Fund, Mountain Group Capital and the Georgia Research Alliance Venture Fund.

More information is available at www.clearsidebio.com.

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