

Executive Summary

The eyes provide the human brain with more input than all other sensory organs taken together. While humans can eventually adjust to many severe physical impediments, loss of vision is devastating to anyone. The need to intervene effectively confronts ophthalmological medicine developers with a plethora of targets in a highly complex and immensely sensitive organ, from the easily accessible cornea and external mucous membranes to the retina and the optic nerve, which are protected against external agents—including drugs—by several effective barriers. Infections, diabetes, hypertension, blood vessel proliferation, degenerative disorders, genetic defects, malfunction of the glands producing the vital tear film, and injuries (inadvertent or caused by surgery) provide the multiple mechanisms that can endanger vision. In more ways than one, the eye is even more complicated to treat than the brain.

This report provides a cutting-edge review of the challenges, achievements, and perspectives that characterize the inseparable therapeutic triad of ophthalmological pharmacology, surgery of the visual tract, and implantable ophthalmological medical devices. At annual sales of less than \$10 billion, this is a niche segment by the standards of the drug industry; however, it is a highly prestigious and profitable field. Because nothing that concerns intervention with the visual system is trivial, highly innovative specialist companies dominate development on the pharmacological as well as on the drug delivery side, which is immensely important in ophthalmological medicine.

Based on a thorough analysis of the peer review and patent literature, this report provides a pipeline analysis showing how a very broad range of drug classes—from “simple” antibiotics and anti-inflammatory drugs to complex retinoids, monoclonal antibodies, cleverly designed siRNA strands, and gene therapy—are combined with advanced formulations and delivery devices to achieve the purpose of restoring unimpeded

vision, or at least to halt progression of vision loss. Scenarios and specific quantitative projections to 2015 are provided for the major areas of unmet medical need and for the major existing and advanced-stage development candidates.

The report also presents profiles of the players in the ophthalmological drug industry and their interactions with big pharma companies, on which the small corporate specialists mostly have to rely when it comes to marketing. Shifts that have taken place in the corporate landscape since 2000 are analyzed, and developments that are likely to decide what the scenery might look like by 2015 are discussed.

The ophthalmology market is not only a market for diseases of advanced age and lifestyle but also a market with an extremely high level of unmet medical need. Until antiangiogenic biotechnology drugs entered the market after the millennium, there was nothing medicine could seriously do to slow, let alone reverse, loss of eyesight in age-related macular degeneration (AMD). Other diseases of the posterior segment of the eye still defy all pharmacotherapy, with surgery being the only means showing some hope. Progression of vision loss in glaucoma can be slowed in many cases if the elevated intraocular pressure is lowered pharmacologically (or surgically), but degeneration of the optic nerve head that has already taken place cannot be reversed. Even restoring the impaired tear film in dry eye is not a task that the pharmaceutical industry has mastered to full satisfaction. The prosthetics that ophthalmologists can insert to replace a lens opacified by severe cataract are comparatively crude, and only the most recent and most advanced models are now beginning to offer a limited degree of focus variability. For a damaged cornea, transplantation from cadaver eyes is currently the only option.

With its complexity and sensitivity—and with its tremendous importance to the quality of human life—the eye offers a broad range of challenges to pharmaceutical, surgical, and prosthetic science. A host of highly focused research-driven specialist companies, many of them very small and fueling their cash burn rate on the basis of innovation-support funding programs, has risen to these challenges. Those select few of these innovators who have created effective and broadly applicable products had no trouble finding a marketing partner from the ranks of the top-5 pharmaceutical companies that made the drugs extremely successful. In many cases, big pharma will now fund the development of advanced products at ophthalmology companies instead of attempting to establish such R&D know-how in-house. And then there are the established stand-alone integrated ophthalmology and eye care specialist

companies such as Alcon (Fort Worth, TX and Hünenberg, Switzerland) or Bausch & Lomb (Rochester, NY), whose portfolios cover everything from the generic beta-blocker eye drop formulation to the discovery-stage gene therapy, and from the intraocular implant to the fully computerized LASIK laser surgery equipment.

The market for prescription drugs to treat eye disorders will experience considerable and consistent growth throughout the next 10 years. The table below shows some of the research and development programs that are part of the growing field.

Advanced Drug Candidates for Dry Eye Syndrome

Product Name and Developer	Active Principle	Stage
Rebamipide (Novartis)	2(1H)quinolone derivative	Phase III ongoing
Ecabet sodium (ISTA Pharmaceuticals)	12-Sulfodehydroabietic acid (natural phenantrene-type compound)	Phase IIb concluded
IDESTRIN (NP50301) (Nascent Pharmaceuticals)	17beta-estradiol ester	Phase IIb concluded
Prolacria (Inspire / Allergan / Santen)	Diquafosol (P2Y2 receptor agonist)	Phase III concluded in US; ongoing in Japan
Vekacia (Novagali Pharma)	Cyclosporin A	Phase III ongoing
Civamide (Opko Health)	Cis-capsaicin (zucapsaicin) TRPV-1 receptor modulator, neuronal calcium channel blocker	Phase III for nasal formulation in cluster headache (Winston Labs); rights for ophthalmological use acquired by Opko in October 2007
ST-603 (Sirion Therapeutics)	Cyclosporin	Phase III commenced April 2007
ALTY-0501 (Alacrity Biosciences)	Doxycycline	Phase II concluded
AL-2178 (FID 109980) (Alcon)	Rimexolone	Phase II ongoing since July 2006

Source: H.M. Pharma Consultancy/Insight Pharma Reports

