

<b>DRY EYE PIPELINE</b>		
<b>Drug</b>	<b>Class</b>	<b>Mechanism of Action</b>
Lifitegrast	LFA-1 antagonist	Lifitegrast is an ICAM-1 decoy, interfering with the homing of activated T cells to the ocular surface thereby, breaking the inflammatory cascade.
CF101	A3 adenosine receptor	This antiinflammatory steroid is A3AR mediated. Targets modulation of key signaling proteins, such as PI3K, PKA, PKB/Akt, IKK, and NF-κB, resulting in inhibition of inflammatory cytokine production.
RX-10045	Synthetic resolvins analog	Targets the on/off switch for cytokine production without immunosuppression in acute and chronic cases. Additionally, there is activation of proresolution functions to mediate the inflammatory cascade
MIM-D3	TrkA (tyrosine kinase) agonist	Targets the stimulation of mucin MUC 5AC secretion from conjunctival goblet cells. This potent mucin secretagogue may also have potential for regulating and improving neural function.
Rebamipide	Mucin secretagogue	Targets the increase in the level of mucin in the tear film covering the conjunctiva and cornea (goblet cells). It has illustrated, in gastric models, that it stimulates the migration and the proliferation of wounded epithelial cell monolayers.
R348	JAK/SYK (janus and spleen tyrosine kinase) inhibitor	Targets the underlying inflammatory components of dry eye by inhibiting beta cell and T cell receptor sites. Additionally, the drug could potentially block cytokine translocation pathways.
RGN-259	Tβ4 (thymosin beta 4)	Targets wound-healing attributes, including down-regulation of inflammatory chemokines and cytokines, promotion of cell migration, vasculogenesis, and promoting cell survival which decreases superficial keratopathy and inhibits matrix metalloproteinase 2 and 9 activity.
EBI-005	IL1 (interleukin 1) inhibitor	Targets inhibition of the inflammatory cytokine IL-1. EBI-005 has clinically demonstrated the ability to provide dual therapeutic action by safely blocking both the inflammatory cascade (signs) and the neuropathic pain (symptoms).
ESBA105	Antibody fragment	Targets the inhibition of TNF-α. Has the potential to modulate the inflammatory and immune response for severe dry eye.
Ikervis	Immunosuppressive (cyclosporine A)	An increased concentration of cyclosporine A (0.1%) with a novel cationic emulsion molecule, Nova22007 (Novasorb), improves penetrance and absorption within the corneal and conjunctival tissue.
Restasis X	Immunosuppressive (cyclosporine A)	An improved formulation of cyclosporine A further enhances penetrance and absorption within the corneal and conjunctival tissue .
ISV-101	Nonsteroidal antiinflammatory drug (bromfenac) in DuraSite delivery vehicle	Targets the inhibition of cyclooxygenase 1 and 2 pathways by blocking prostaglandin synthesis. The study molecule is a lower dose (0.01%-0.04%) due to the delivery system, which maximizes the residence time on the ocular surface.
0.25% LE-MPP	Glucocorticoid in mucus penetrating particle delivery system	Thought to target the induction of phospholipase A2 inhibitory proteins by antagonizing potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of arachidonic acid. The lower concentration is achieved by this novel delivery system, which improves the ocular surface penetrance of the molecule.
DA-6034	Synthetic flavonoid derivative (eupatilin)	Increases secretion of mucin-like glycoprotein and some mucin species in the conjunctiva and cornea and inhibits NF-κB activation to preserve ocular surface integrity.
KCT-0809	Antiplatelet agent	There is limited information, but by exerting influence on thromboxane-A synthase, the agent can inhibit platelet cyclooxygenase 1 in order to prevent the formation of prostaglandin H2. The website claims it will have restorative corneal and conjunctival properties.

*Editor's note: Michael S. Cooper, OD, assisted with this chart. Although care was taken in its creation, it is not a complete listing of every agent in*

Administration	Company	Phase/Status of Study
Topical	Shire	3
Oral	Can-Fite BioPharma	3
Topical	Resolvix/Celtic	2
Topical	Mimetogen/Bausch + Lomb	2/3
Topical	Otsuka	2
Topical	Rigel	2
Topical	RegeneRx	Phase 2, heading into phase 3. It has also been granted orphan status for neurotrophic keratopathy.
Topical	Eleven Biotherapeutics	Pivotal phase 3
Topical	Alcon	2
Topical	Novagali Pharma (Santen SAS)	European Marketing Authorization Application has been filed to the European Medicines Agency.
Topical	Allergan	2
Topical	InSite Vision	2
Topical	Kala	Exploratory 2014
Topical	Dong-A Pharmaceutical	2
Topical	Kissei Pharmaceutical/Teika	2

*development. Nor was it possible for the staff to obtain input from all manufacturers.*