



DROP-LESS THERAPY: A REALITY

Here, Chris Muller, Chief Commercial Officer, and Deepank Utkhede, Chief Scientific Officer, both of Mati Therapeutics Inc, introduce the company's Evolute® ocular delivery system, a non-invasive, sustained-release platform that combines a novel punctal plug with a sustained release drug eluting core.

Ophthalmologists are in agreement that a better option to administer ocular therapies rather than eye drops is needed for their patients since the lack of compliance is a serious and leading cause for concern.

When we consider the associated disorders that these medications treat such as glaucoma, inflammation, allergy or dry eye, each of these can be very problematic if not sight threatening if the treatment regimen is not followed. The therapeutic agents available for each of these conditions are very effective when prescribed and used appropriately. However, the problem is that they are rarely used appropriately or in accordance to the dosing regimen that is required and for diseases such as glaucoma, which is initially asymptomatic, this can lead to irreversible vision loss.

The ophthalmic community relies on the patient to adhere to the treatment regimen. However, due to a number of factors such as age of the patient population, the complexity of the dosing regimen or discomfort caused by drops, it is not realistic to expect that the majority of these patients will comply with the required treatment regimen. There have been many attempts to solve this issue but the sustained-release innovation by Mati Therapeutics may be the perfect answer for a majority of patients.

There are multiple approaches to the administration of sustained-release systems. One is invasive, where a physician either through incision or injection enters the anterior chamber of the eye to deliver the drug depot or creates an incisional pocket in the sclera or conjunctiva to house the depot. The problem with both of these methodologies is that because they are invasive in

nature they expose the patient to potential sight-threatening infection and decreasing the overall health of the eye by undergoing multiple surgical procedures per year. The repeated tissue trauma increases scarring over time and could complicate future surgical procedures needed to control the disease.

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Mati has developed a completely non-invasive sustained-release platform by combining a novel punctal plug with a sustained release drug eluting core (see Figures 1 and 2). This platform is known as the Punctal Plug Delivery System (PPDS) or Evolute®, as it will be known commercially. The Evolute® is inserted into the patient's punctal duct by a simple in-office, non-invasive proce-



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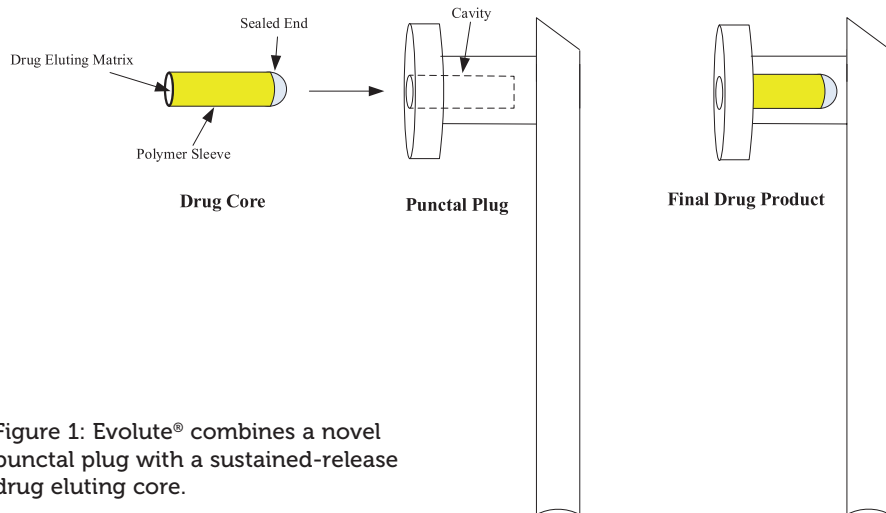


Figure 1: Evolute® combines a novel punctal plug with a sustained-release drug eluting core.

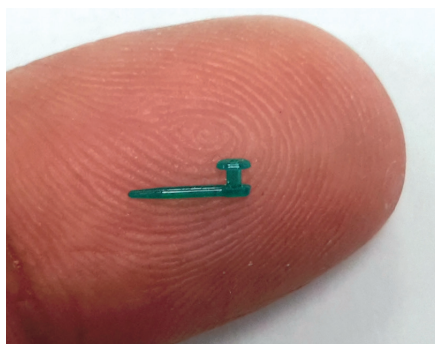


Figure 2: An Evolute® device, shown on a finger-tip for scale.

After placement, the Evolute® delivers therapy to the ocular surface or tear film over a predetermined period of time. At the end of the treatment period for acute conditions, Evolute® is removed from the puncta without any further follow-up. At the end of the Evolute® elution period for chronic conditions, the patient returns to the clinic

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to have the depleted Evolute® removed and a new Evolute® placed to continue treatment. The Evolute® has the advantage of being easily removed unlike the more invasive techniques previously described, which require a surgical procedure for removal.

The Evolute’s® unique configuration creates a unidirectional system that delivers therapy primarily to the tear film and ocular surface. This is a distinct advantage for any sustained release system because virtually all the formulated medication in the system can be directed to the targeted site rather than being absorbed by non-targeted tissue or lost down the canaliculus into the nasal cavity and/or systemically absorbed. Another advantage to the Evolute® is that both the punctal plug portion and the drug eluting core are non-bio-erodible and non-biodegradable. This leads to the ability to predict accurately when and how much of the formulated drug is delivered over the course of therapy. Also the punctal plug retention features will be unchanged over the treatment period which has resulted in very high retention rates for the Evolute®.

Clinical studies have demonstrated a reproducible and predictable retention rate in range of 92% to 96% over a 90-day targeted treatment period. Another advantage of a non-biodegradable and non-bio-erodible system is that if removal is required for any reason, the Evolute® is easily observable and removable with a pair of forceps. A bio-erodible platform will become smaller and/or weaker, during the implantation period potentially making removal more complicated.

The Evolute® is a platform technology that can be tailored to treat multiple front-of-the-eye conditions. Depending on the ocular condition, the elution rate and period of delivery can be adjusted for short-term, high levels (for example, in post-cataract surgery treatment), to long-term, low levels (for example, in glaucoma therapy) of drug delivery. Multiple products have been developed for the Evolute® including anti-inflam-

matories for post-cataract surgery, allergy medications, and glaucoma therapies.

Through extensive formulation development, Mati has developed the capability to adjust the elution profile for any of these therapies to potentially meet the needs of the ophthalmic community. For example, the Evolute® can be designed to deliver a high initial amount of medication followed by a consistent lower concentration over time or a much more limited initial delivery and increased delivery of medication over the treatment period.

There are several additional benefits to the Evolute® system, such as that it allows for the formulation of hydrophilic or hydrophobic compounds and it is a preservative free therapy so there is no need to worry about long-term exposure to preservatives such as benzalkonium chloride, which has been shown to cause ocular surface issues such as conjunctival inflammation, tear film instability, corneal toxicity, anterior

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chamber inflammation, and cataract development among other issues. In addition, since the Evolute® prevents loss of drug into the canaliculus, it will likely lead to less systemic absorption of the therapy in question, which may greatly reduce undesired systemic side effects associated with some ocular medications.

In clinical studies, the majority of patients preferred the Evolute® system to their usual eye drops. This isn’t surprising because of the passive nature of the system. The patient doesn’t have to do anything once the device is inserted. This may prove to be substantial benefit for ophthalmologists and their patients insuring better adherence and more consistent administration of the therapeutic agent leading to superior outcomes.