Elcam
Drug Delivery Devices

A REVIEW OF REUSABLE AUTO-INJECTORS FOR BIOLOGICAL & BIOSIMILAR DRUGS

In this article, from the perspective of the growing biologics and emerging biosimilars markets, Menachem Zucker, PhD, Head and Founder of E3D – Elcam Drug Delivery Devices (a sister company of Elcam Medical ACAL), showcases the company's mechanical and electronic auto-injector platforms, both of which are reusable devices with disposable cassettes.

A GROWING NEED FOR BIOLOGICS & BIOSIMILARS

When generic drugs began to be introduced 30 years ago, they revolutionised the pharmaceutical industry. Now, many ask if biosimilars will have the same impact. Since the approval of the first biosimilar drug in 2015 this approach is becoming ever more prominent in drug development. Healthcare Recruiters International (San Francisco, CA, US) suggest a figure of US$250 billion (£185 billion) in drug cost savings[1] if 11 bio-similar drugs are approved by the US FDA. The same source claims that biosimilars have been lowering healthcare costs globally since 2006 with no known safety issues. Another report, by SNS Telecom (Dubai, UAE), claims that by the end of 2020 approved biosimilar drugs will account for nearly $22 billion in revenue.[2] According to Dyadic (Jupiter, FL, US) the market for therapeutic biological drugs will soar to $287 billion by 2020.[3] These numbers are only a first indicator of the clear demand for, and true potential of, biologicals and biosimilars.

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Both biological drugs and biosimilar drugs are typically fragile proteins, calling for administration by injection. Auto-injectors therefore increase the therapeutic value of the drug. When these drugs are prescribed for people with chronic diseases – such as multiple sclerosis, diabetes or growth hormone disorders - requiring daily doses (sometimes multiple times a day) for treatment success, then reusable auto-injectors are the sensible solution. Reusable auto-injectors increase safety and ease of use, they reduce the volume of storage and waste footprint (and are thus more environmentally friendly) and they are also significantly more cost effective.

GENERATIONS OF REUSABLE AUTO-INJECTORS

E3D (a sister company of Elcam Medical) specialises in the development and production of high-quality, patient-compliant auto-injectors. The company sees its products as the next step in effective care. E3D offers two generations of reusable auto-injectors, which are currently under development.

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Figure 1: E3D Flexi-Q-mMU, reusable auto-injector.

Mechanical Multi-Use Auto-Injector

The E3D Flexi-Q-mMU comprises a reusable driving unit and a disposable cassette (Figure 1). The cassette is cost effective and can be used with standard prefilled syringes (PFS) and vials (using an adapter).

The Flexi-Q-mMU reusable auto-injector is designed with patient compliance in mind. The product is easy to use (with just one additional preparation step when compared with a fully disposable injector). All the patient has to do is:

1. Insert cassette into the driving unit
2. Remove safety cover
3. Press against skin
4. Press the INJECT button.

A two-step mechanism for enhanced safety was designed: drug delivery can only take place when both the skin sensor and the INJECT button are activated. This way only when the auto-injector is pressed to the skin (and when the patient is ready) can the button be pressed and the injection take place.

Safety is further enhanced as the patient will have two indications for the end of injection. Firstly, they will hear a click when the injection is completed and, secondly, the patient can monitor the process through the injection window.

The needle is hidden during the entire injection process. It only emerges when the auto-injector is touching the skin and the INJECT button is pressed. Injection is a quiet process and injection speed/time can be pre-set by the pharma company at assembly to further reduce patient anxiety, needle phobia and perceived pain. As soon as the patient lifts the injector from the skin the needle shield is lowered and the cassette jumps partly out, ready for disposal.

The disposable cassette design can be customised to incorporate standard glass PFS from different manufacturers, including dual-chamber syringes. A vial adapter is also currently in development, which will enable drug reconstitution and mixing.

The reusable injector is an environmentally friendly product on a number of levels (see Figure 2). The disposable cassette reduces the storage footprint for both manufacturing and delivering the product. The storage volume is also reduced at the patient's home, as is waste. In fact, the disposable cassette's waste footprint is four times (4X) smaller than that of a disposable injector. Due to its smaller size, the amount of plastic used is also reduced, the benefits of which in terms of production costs and the environment are clear.

Using a disposable cassette rather than a disposable auto-injector reduces the

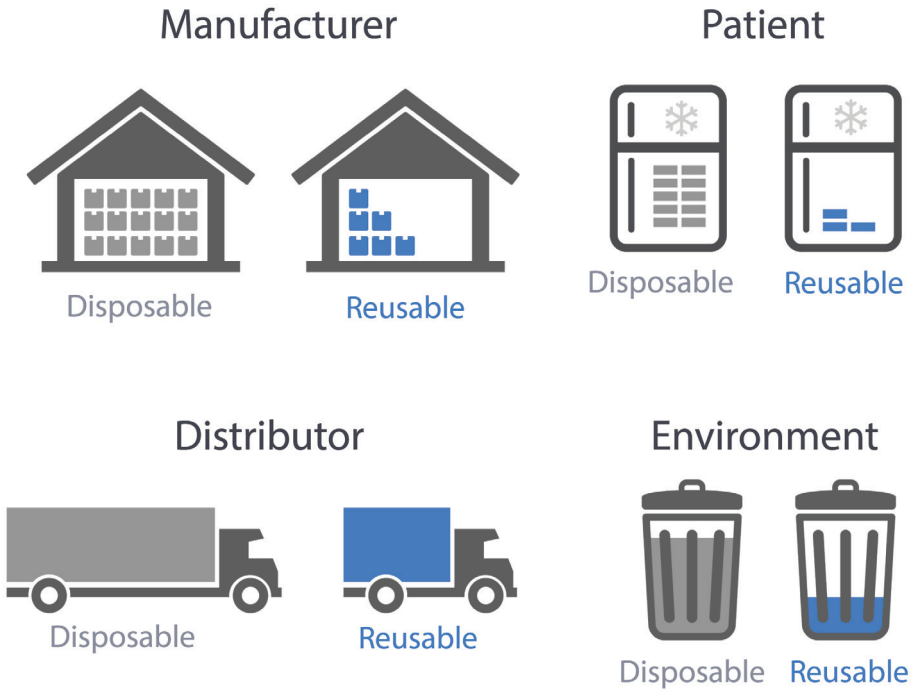

Figure 2: Footprint and environmental impact.

cost per injection. The cost ratio is 1:5, meaning a reusable auto-injector results in a saving of approximately 80%. The reusable unit is good for three years (approximately 1000 uses) and is easily disposed of. It thus has a negligible effect on the environment and operation costs.

Electronic Multi-Use Auto-Injector

E3D has taken all the advantages of reusable auto-injectors for effective care mentioned above another step further with its electronic version, the Flexi-Q-eMU-P (Figure 3). The electronic version works with PFS and E3D also offers a version that is suited for cartridges (Flexi-Q-eMU-C).

With Flexi-Q-eMU-P, self-injection is made even easier. The LCD screen provides the patient with a large display where each stage of the injection process is presented with clear instructions in real time. The patient is further empowered for effective care with reminders and injection history (Figure 4).

The disposable cassette also includes an RFID component, on which the pharma company can encode the expiry date, anti-fraud barcode, various permissions and definitions and, of course, the drug name and dose. If the drug has expired or is fraudulent the injector will warn the patient, and will not allow the injection to proceed.

The needle within the disposable cassette is protected and hidden at all times in this version as well. In the electronic version, injection is stopped as soon as the patient lifts the injector from the body (even if injection is not completed – so no drug is lost – but the cassette becomes void). Partial injections are recorded into the electronic log.

With a specialised mobile app (Figure 5), the data regarding injecting habits and patient compliance with the prescribed treatment programme can be enhanced and its delivery made even easier. The auto-injector can automatically send patients, as well as doctors and family members, reminders, logs and injection data.

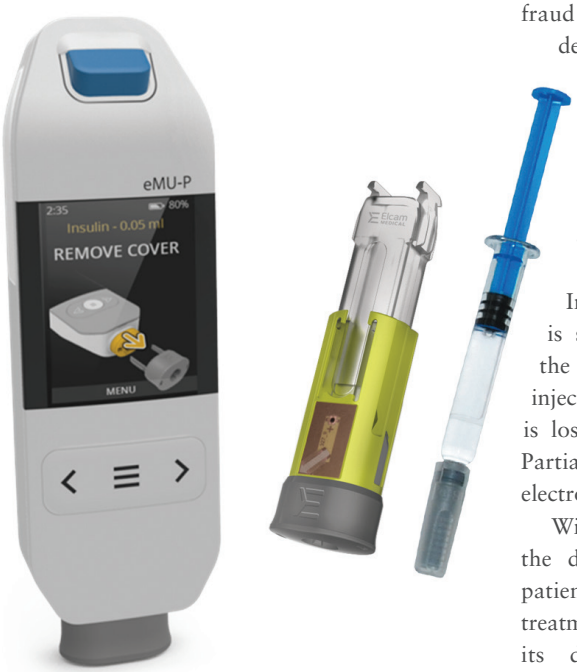

Figure 3: Flexi-Q-eMU-P, electric reusable auto-injector and disposable PFS-based cassette.

> "Time, quantity, drug type and whether a full or partial injection was delivered are all recorded and sent from the auto-injector via a wireless connection to the cloud, per the definition of the drug company at the filling stage of production."

This is especially useful for patients who are prone to forgetting their injection schedule.

Time, quantity, drug type and whether a full or partial injection was delivered are all recorded and sent from the auto-injector via a wireless connection to the cloud, per the definition of the drug company at the filling stage of production. The pharmaceutical company may also make use of injection data in order to improve its future products.

A five-question survey following the injection can be defined as optional or mandatory, helping to gather additional data regarding the injection process, patient symptoms and their reaction to the drugs in real time. This information is especially important for the physician follow-up and its collection has never been easier.

Further advantages of the electronic product include measuring drug temperature before injection is permitted and injection with a motor for better control of injection

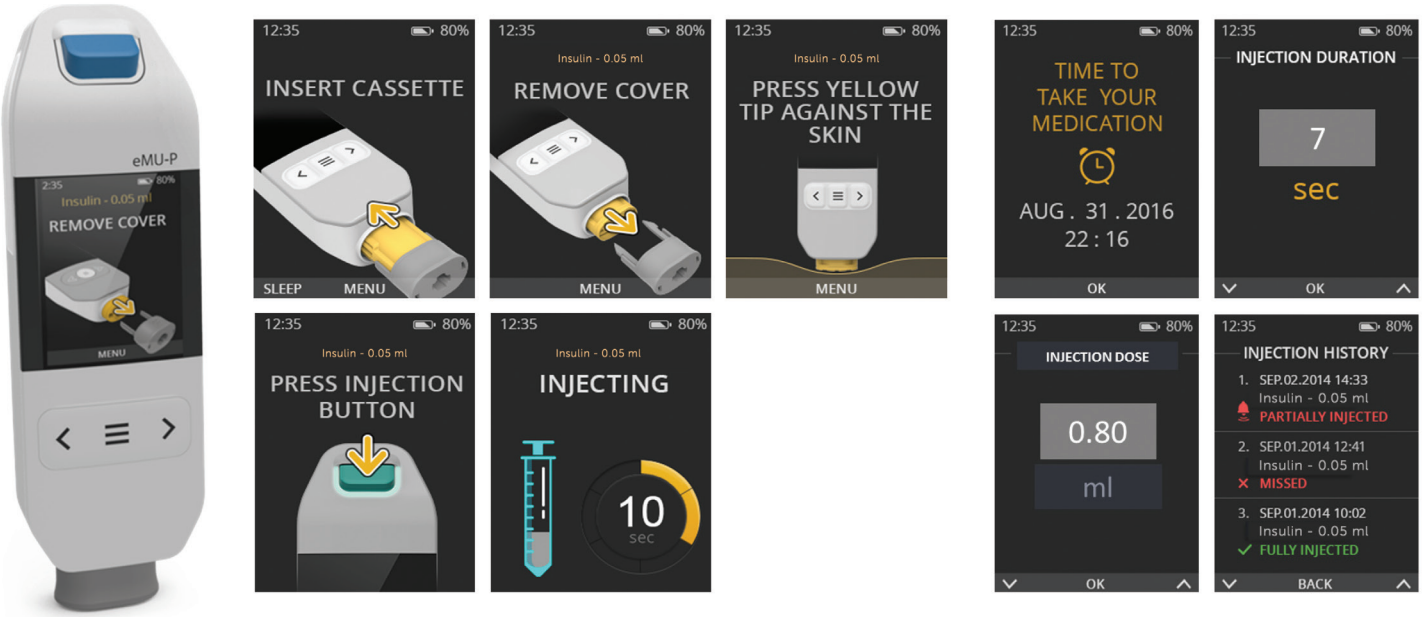

Figure 4: Injection stages and instructions on screen, reminders, data and history display.

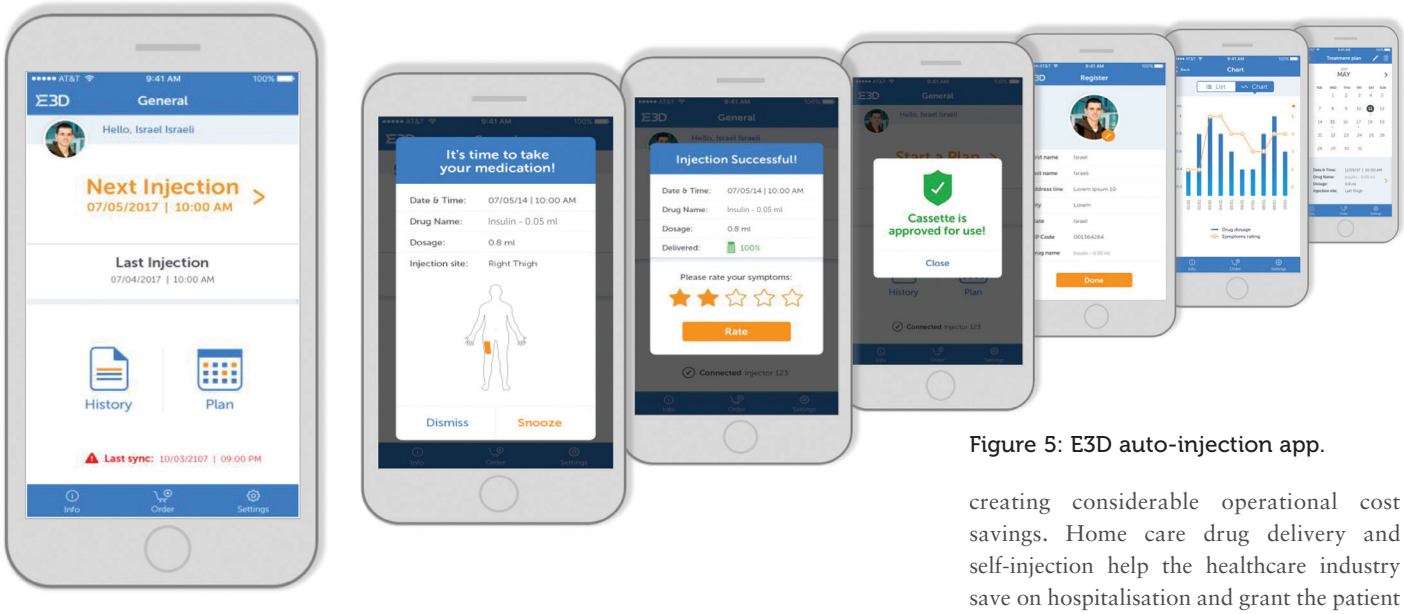

Figure 5: E3D auto-injection app.

speed and reduced pain. Out-of-date cassettes cannot be used. Drugs with high or low viscosity (or anything in between) can be all injected using the same platform.

The product can also be customised for marketing and commercialisation. The front panel is available in different colours and designs for branding purposes, as well as for fun. A music feature can be enabled for targeting younger users.

AUTO-INJECTOR SUPPLY CHAIN

At E3D we know that flexibility and customisation are keys to success (we even named our product line FLEXI). We know that the selection of drug delivery devices depends on several factors, including formulation, primary package, dosing and safe, effective usage. Our products are designed to suit varying needs so that each drug company can find the auto-injector best suited to its requirements.

E3D provides drug companies with all the components and machinery required to complete the assembly of the disposable cassette with the drug PFS (or cartridge), branding and labelling, all in accordance with the company's own requirements. The drug know-how and production thus remains fully under the pharmaceutical company's control.

E3D provides:

- Reusable auto-injector units
- Disposable cassette components
- Automatic final assembly machine for the cassette with the drug PFS (or cartridges)
- Software for electronic labelling (RFID chip on cassette).

Our products are designed in accordance with our belief that drug companies will have a growing need for auto-injectors that are customised to their products, their brand and to their user's needs and treatment programmes.

PHARMA GROWTH ACCORDING TO DRUG DELIVERY MARKET TRENDS

Three of the most significant demands driving the growth of drug delivery system development, in addition to increasing the commercial value (and lifecycle) of the drug, are:

- Demand for improved patient compliance and quality of care
- Growing awareness of production costs, both financial and environmental
- Self-administered drug therapy (another step towards precision medicine and telemedicine).

E3D reusable auto-injectors, of both generations, answer these trends. The products are designed to provide each patient with effective care according to their own specific treatment programme. By making the product safe and easy to use, reducing needle phobia, ensuring delivery of the full dosage and enabling better therapy follow-up, the quality of care, patient safety and patient compliance are all increased.

Reusable auto-injectors reduce both the storage and waste footprint, for both manufacturers and patients, thus reducing environmental impact. Disposing of only the cassette and not the entire injector reduces the cost per injection significantly, creating considerable operational cost savings. Home care drug delivery and self-injection help the healthcare industry save on hospitalisation and grant the patient enhanced independence via self-treatment.

The electronic generation of reusable auto-injectors takes these traits even further. By enabling full supervision of the amounts of drug used, injection logs, reminders to patients, reports to family members and physicians, every participant in the entire healthcare system can become more involved (even at a distance), thus providing enhanced and effective care.

The software enables control of dosage and other therapeutic factors, customising them to personal patient needs after a specific follow-up of injection logs and analysing the therapeutic results attained. This is just a step away from precision (or personalised) medicine. Adjustments can be made by patients, doctors or both, depending on parameters predefined by the drug company. This means that the highest quality treatment can be easily administered from a distance.

Throughout the development process for its auto-injectors, E3D conducted formative usability tests involving patients form various groups (gender, age, illness, disability, etc). Issues such as auto-injector shape, convenience and ease of use, location of buttons, size of display and ideal ratio between injector width and display size were tested and optimised. After integrating the test recommendations into the product design, repeated tests resulted in high satisfaction with regards to holding the injectors, display size and ease of use.

At E3D we develop and manufacture our products according to required regulations and relevant standards. With our sister company Elcam Medical's know-how in injection and moulding, plus its automated assembly capabilities, and by embracing

their business culture of partnering with clients, we can provide drug companies with the exact products they need.

ABOUT THE COMPANY

E3D is a sister company of Elcam Medical ACAL, developing and manufacturing auto-injectors and patch pumps for biologic and biosimilar drugs, utilising the moulding injection and assembly know-how, engineering and technologies of Elcam Medical as well as its well-established quality assurance and quality control. E3D believes in a growing need for customised auto-injectors that enhance the therapeutic and commercial value of drugs and their lifecycles. Customisation and flexibility are at the core of its product development.

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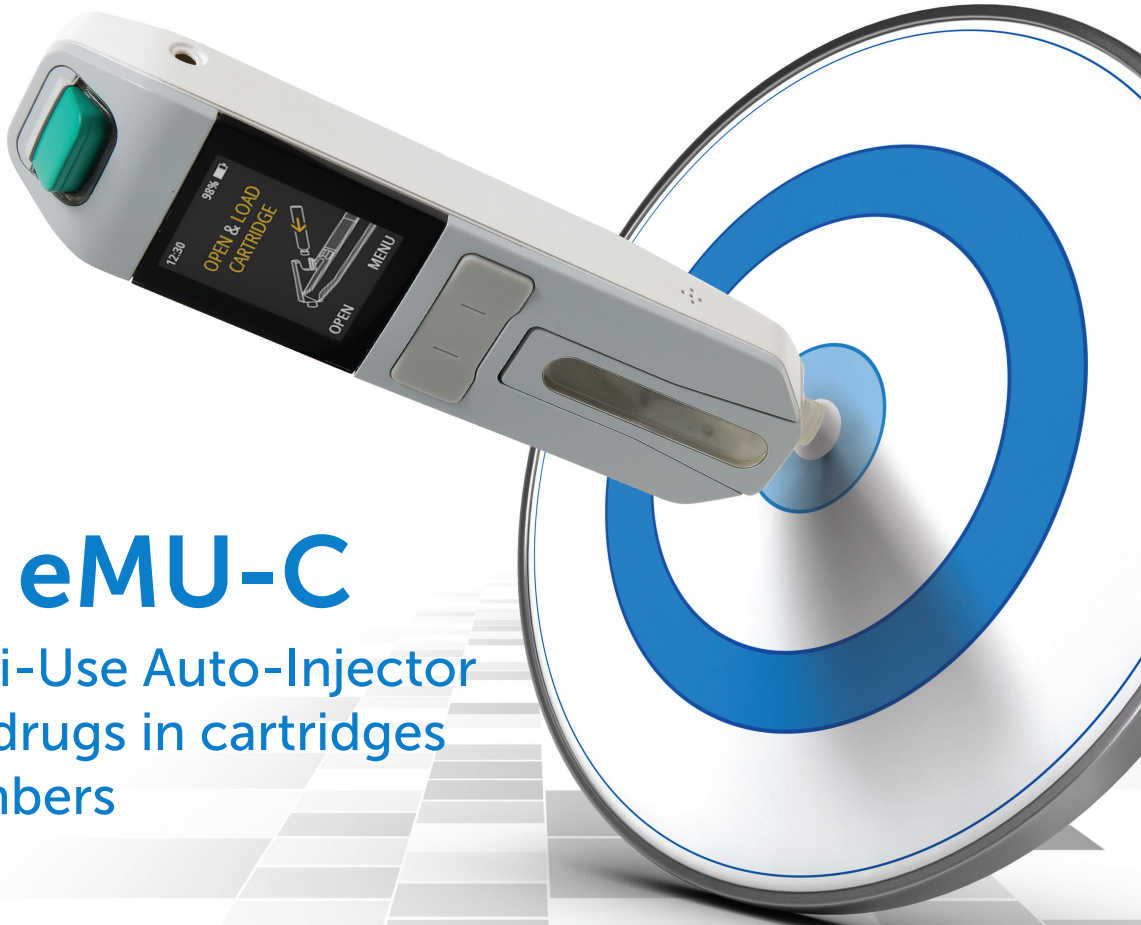
ABOUT THE AUTHOR

Joining Elcam Medical ACAL in 2002, **Menachem Zucker** served as Vice-President of Business Development, Marketing and Sales. In 2010, he initiated the E3D activity and since then serves in the role of Vice-President and Head of E3D. Previously the Chief Executive of Opgal Medical (Israel), he led the development of simulation products for cardiac surgery. He also founded a company for catheterisation closure devices. Dr Zucker holds a PhD from Imperial College London, which he obtained in 1990.

ON drugDELIVERY

2017/18 EDITORIAL CALENDAR

Publication Month	Issue Topic	Materials Deadline
Nov 2017	Pulmonary & Nasal Drug Delivery	DEADLINE PASSED
Dec 2017	Connecting Drug Delivery	Nov 13th 2017
Jan 2018	Ophthalmic Drug Delivery	Nov 20th 2017
Feb 2018	Prefilled Syringes & Injection Devices	Dec 22nd 2017
Mar 2018	Skin Drug Delivery: Dermal, Transdermal Microneedles	Jan 20th 2018
Apr 2018	Pulmonary & Nasal Drug Delivery	Feb 19th 2018
May 2018	Injectable Drug Delivery: Devices Focus	Mar 19th 2018
June 2018	Connecting Drug Delivery	April 23rd 2018
July 2018	Novel Oral Delivery Systems	May 21st 2018
Sept 2018	Wearable Injectors	July 23rd 2018
Oct 2018	Prefilled Syringes & Injection Devices	Aug 27th 2018
Nov 2018	Pulmonary & Nasal Drug Delivery	Sept 24th 2018
Dec 2018	Connecting Drug Delivery	Oct 29th 2018



Flexi-Q eMU-C

Electrical Multi-Use Auto-Injector for biological drugs in cartridges and dual chambers

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Our wide ranged auto-injectors portfolio, customization capabilities and in-house manufacturing & assembly, ensure your drug is delivered exactly as planned

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