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TERIPARATIDE MICRO-PATCH™: A SOLID MICRONEEDLE PRODUCT NEARING CLINICAL TRIALS

In this article, Faz Chowdhury, PhD, Chief Executive Officer, Nemaura Pharma, details a Micro-Patch™ solid formulation of the parathyroid hormone analogue, teriparatide, for the treatment of osteoporosis. Teriparatide Micro-Patch™ is the company's first microneedle product selected to advance to clinical development, due to begin this year.

With estimates of the cost of developing and launching a new drug ranging up to US\$2.6 billion (£1.9 billion), and the process taking ten years in many instances, there are clear clinical and commercial advantages in successfully developing a truly superior formulation of an existing drug, where the costs are far lower and the time to market can be four years or less.

Delivery via the skin is increasingly viewed both by patients and physicians as an attractive method of choice and, as such, the skin drug delivery market is growing rapidly, being expected to reach \$40 billion this year.

Microneedle patches represent a particularly attractive class of skin drug delivery system. They can reduce or even eliminate many of the challenges and disadvantages of self-administration by needle and syringe, the route by which most

biologics currently have to be administered. Such challenges – including that self-injection can be difficult, often requires training and is perceived as unpleasant and painful – reduce compliance. Microneedles represent a safer, easier-to-use, non-invasive and more convenient format.

However, many existing microneedle patches have their own drawbacks, including: slow delivery requiring the patient to wear the patch for up to 30 minutes; incomplete and variable dose delivery; and local skin irritation. These can all be problematic when it comes to market approval.

In contrast, Nemaura's microneedle patch, Micro-Patch™ (Figure 1), overcomes these barriers, delivering the complete dose two seconds after application, painlessly and with a single needle. Additionally, liquid formulations of biotherapeutic products for injection often have stability issues at room temperature, meaning that they need to be refrigerated during shipping and storage. Micro-Patch™ comprises a solid dose which is stable at room temperature and does not require refrigeration.

A UK-funded proof-of-concept for the technology (Reference: 710437) has been successfully completed with a solid dose vaccine, demonstrating efficacy compared with a liquid vaccine. Now Nemaura is taking its first product, a hormone analogue for the treatment of osteoporosis, forward.



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"Having selected teriparatide Micro-Patch™ for further development and secured £5 million in private investment in 2017, Nemaura is advancing the product, with clinical trials planned for this year."



Figure 1: Micro-Patch™ delivers a complete solid dose of teriparatide two seconds after application, painlessly.

TERIPARATIDE: ADVANCING THE FIRST PRODUCT CANDIDATE

Nemaura Pharma has developed a Micro-Patch™ solid-dose teriparatide microneedle product, to prevent fractures in vulnerable elderly osteoporosis patients. Having selected teriparatide Micro-Patch™ for further development and secured £5 million in private investment in 2017, Nemaura is advancing the product, with clinical trials planned for this year.

Osteoporosis is a disabling and painful condition where bone strength is lost. It affects men and women over 50 and there are approximately 75 million people suffering from the condition in Europe (>3 million sufferers in the UK alone), US and Japan. It affects over 200 million women worldwide.

First-line treatments for osteoporosis are bisphosphonates such as Merck & Co's Fosamax® (alendronate sodium). These first-line treatments do not reverse bone loss, only prevent it and thus do not pose direct competition to teriparatide products. They are also associated with significant adverse effects including gastro-intestinal side-effects.

Exogenous teriparatide, a parathyroid hormone analogue, is the only anabolic (stimulating bone formation) available for the prevention of fracture or further fractures in postmenopausal women and men at high risk of fractures. Eli-Lilly's Forteo®, for example, is a liquid formulation presented in a syringe pen. The patient must self-inject each day, dispose of the needle and keep the medication at 2-8 °C to avoid loss of potency.

The logistical issues of this route and injection-site pain lead many to discontinue

medication, and consequently suffer further fractures, resulting in hospitalisation, significant secondary health issues, and loss of mobility and independence. A US report indicated that at 12 months 67% of patients discontinued treatment. The consequences of another fracture can be devastating.

Despite its drawbacks, subcutaneously injected teriparatide is a clinically established treatment and Forteo® is expected to generate revenues of \$5.2 billion in major markets by 2021, according to Roots Analysis. Thus, a substantial market opportunity and unmet clinical need exists for a simpler, more accessible teriparatide product. There is considerable interest in avoiding the problems associated with the subcutaneous route by seeking an alternative delivery mechanism.

The delivery of teriparatide using microneedle patches is being pursued by several biotech companies. None are yet marketed and, with the exception of teriparatide Micro-Patch™, all those in development are multi-needle (>50) arrays, which face the significant hurdles mentioned previously (longer delivery times, dose variability, incomplete dosing and local skin irritation).

MICRO-PATCH™ ADVANTAGES

Micro-Patch™ does not suffer from these disadvantages. Its patient-centric design, with simple “press on, peel off and dispose” user steps, delivers the complete dose, quickly and painlessly (Figure 2). Teriparatide Micro-Patch™ comprises solid hormone coated onto a single microneedle, and is designed to be stable at ambient temperature. Thus, it negates the need for needle-based self-injections. Patient benefits include greater safety and independence, and a reduction in fractures through improved compliance.

It also avoids the costs, inconvenience and risks posed by keeping an unstable liquid formulation of teriparatide refrigerated for a month. According to data analysed by Pharmaceutical Commerce for its annual Sourcebook, cold-chain logistics spending in 2017 was expected to be more than \$13 billion worldwide, in an \$80 billion overall pharma logistics market. By 2021, cold-chain biopharma logistics spending will expand to more than \$16 billion. Conventional liquid formulations of biologics such as teriparatide, and vaccines, carry stability

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Figure 2: The patient-centric Micro-Patch™ enables self-administration via three simple user steps: “press on, peel off and dispose”.

risks, especially if they aren't stored at the correct temperature. In addition to being costly, this is potentially dangerous. In solid-form, the drug can remain stable for several months without loss of potency.

The innovation in Nemaura's product lies in the development of an aseptic process for formulating the solid dose – teriparatide 20 µg – and mounting it on a single needle patch to form a shaped dose which remains in the skin when the patch is pressed on and removed. This is the Micro-Patch™ platform and, in addition to teriparatide, it is suitable for the delivery of other solid formulated biomolecules, vaccines, and low-molecular-weight drugs.

Micro-Patch™ is designed to transform the way vaccines and biologics are administered through the skin in a single-use, disposable, user-friendly device format costing just £0.10-£0.20 per unit. A releasable drug coating/sleeve of solid drug dose is applied around 1-5 stainless steel microneedles, which deposit the entire dose through the skin immediately, as shown in Figure 3.

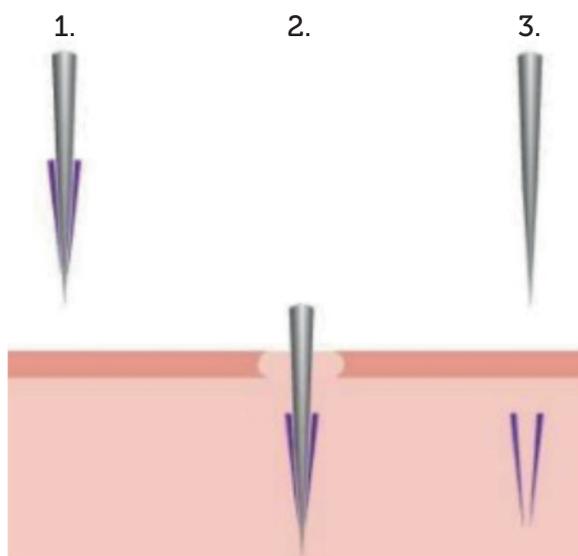


Figure 3: A releasable drug coating/sleeve of solid drug dose is applied around 1-5 stainless steel microneedles, which deposit the entire dose through the skin after which the device retracts the needle.

“The dose volume administered is a fraction of the equivalent liquid dose, reducing the cost, enhancing stability in the solid form, improving control over drug release and absorption, and reducing pain whilst enabling safe self-administration.”

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The dose volume administered is a fraction of the equivalent liquid dose, reducing the cost, enhancing stability in the solid form, improving control over drug release and absorption, and reducing pain whilst enabling safe self-administration. The device fully and immediately retracts the microneedles so needle-stick injury is impossible, and the device is disposed of. Disposal costs are low.

Micro-Patch™ is protected through multiple global granted and pending patents (e.g. EP3052087) meaning Nemaura can confidently claim freedom to operate in the area.

SUMMARY

Nemaura Pharma is developing a microneedle teriparatide product for the treatment of osteoporosis, using its Micro-Patch™ platform, comprising a solid dose, less than 1 mm in size. Both stability at room temperature, and mechanical properties that allow the drug to be inserted into the skin as a solid dose, have been demonstrated.

Teriparatide Micro-Patch™ is clearly differentiated, in terms of patient convenience, cost and other factors, from both the existing teriparatide product on the market, which is injected subcutaneously, and also overcomes the challenges faced by other microneedle versions of the drug in development.

The global market for this product is very large and the commercial opportunity substantial. Teriparatide Micro-Patch™ is expected to enter clinical trials later this year and dossiers will be submitted next year.

ABOUT THE COMPANY

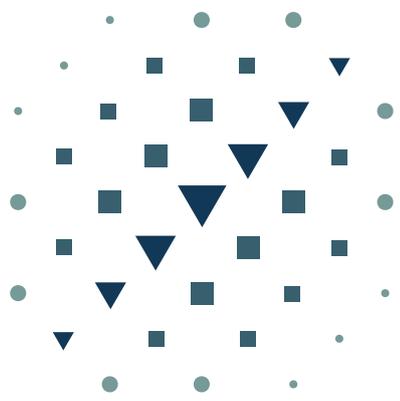
Nemaura Pharma has spent several years working with private investors to transform the way drugs are delivered through the skin. The company has made significant progress in the reformulation of traditionally injected liquid biotherapeutics using its solid dose delivery system, Micro-Patch™, for delivery through the skin. The device works by depositing the drug under the outer layer of the skin using a metal needle which then retracts completely, minimising the risk of needle-stick injuries.

Nemaura's specialism is drug delivery through the skin and the company has completed or is completing programmes involving a large number of product formats including:

- Topical gels: developed ibuprofen and diclofenac sustained-release gels
- Transdermal patches: developed patches for Alzheimer's and Parkinson's diseases
- Simple injectable drugs for subcutaneous, intradermal and intramuscular delivery using liquid micro-injectors: successfully developed insulin aspartate and insulin Glargine formulations
- Complex injectables: successfully developed risperidone and octreotide formulations

Nemaura now has patents secured or pending across multiple patent families, is ISO9001 and ISO13485 accredited, and has an in-house cleanroom for cGMP manufacture of investigational medicinal products, under aseptic conditions. It has a controlled drugs licence from the UK Home Office, and also holds an IMP licence for the manufacture of sterile solid injectable doses, sterile liquid injectables, transdermal patches and topical gels.

It has partnered with commercial manufacturers with state-of-the-art facilities for transdermal patch manufacture. Nemaura additionally has an in-house design and prototyping facility for medical devices, using medical grade materials.



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**Enhanced delivery of
almost any drug, old or
new, through the skin**



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