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Pioneer's Startlingly Innovative Biologics Portfolio

By Robin R. Young

Pioneer Surgical's CEO and Founder, Matt Songer, M.D., has been trying to tell anyone who'll listen that he's got not one, but two potential game-changing biologic technologies in his portfolio.

With its acquisition last month of Angstrom Medica, we decided to take a closer look at Pioneer and from what we've seen, we think he's probably right.

Pioneer Surgical is a spinal implant manufacturer located in what is often referred to as "God's Country"—Marquette, Michigan. There are portions of Minnesota, Wisconsin, and Michigan—particularly the Upper Peninsula (UP)—with deep forests, clear streams, large cold water lakes, and air that is so clean and refreshing that breathing it makes you feel as though you are in a Grizzly Adams movie. That's "God's Country" and Pioneer Surgical lives there.

Sales for Pioneer are running about $80 million per year and growing fast. Dr. Songer is also a practicing spine surgeon and serves on the company's medical advisory board. From its earliest days, Matt Songer has defined Pioneer as a "surgeon's company," and more than most, it is. Pioneer is Matt's company and its products and philosophy reflect his hands-on perspective of spine surgery.

Looking at his recent purchases in biologics, it is clear that Matt also has a strong and especially insightful vision of what is and what isn't a valuable biologic material. Clearly, he does not follow the crowd. Never has. And, for the sake of his customers, shareholders and patients, may he never.

In just the past nine months, Matt has purchased two highly differentiated and leading biological technology companies—Encelle, Inc. and Angstrom Medica, Inc.

Encelle, the company purchased earlier this year, has a vast portfolio of intellectual property regarding compounds that accelerate tissue and bone healing. While Encelle never got off the ground with its original business plan (islet cell generation and diabetic foot ulcer treatment), it did manage to create E-Matrix™, a material that some studies indicate can grow bone as well as or better than morphogenic proteins.

Angstrom Medica has a portfolio of nanomaterials based on hydroxyapatite that appear to deliver implant performance comparable to or superior to allograft spacers.

With these purchases, Matt and Pioneer Surgical have put their flag in the ground in two, billion-dollar markets. What is so interesting about this is that both product families are highly unique and will clearly help Pioneer differentiate its offerings in the marketplace.

Pioneer Biologics (Formerly Encelle, Inc.)

Pioneer purchased Encelle earlier this year. Last we checked, Encelle had 13 patents issued and 7 more pending for its unique E-Matrix—a porcine collagen gelatin-dextran combination that has been shown to stimulate rapid, nearly scarless tissue or bone growth.

E-Matrix is a co-polymer of a high molecular weight protein and a high molecular weight carbohydrate that appears to actually mimic mesenchymal connective tissue. Mesenchymal tissues are the core materials in bone and are composed primarily of single-stranded molecules as opposed to triple-stranded molecules found in mature, slow growing tissues of most adults. In other words, E-Matrix acts like young, new (even embryonic) tissue and is designed to grow.

The key to E-Matrix is the production method. In it, Pioneer Biologics obtains triple-stranded porcine collagen and then processes it into an open, monomeric single-stranded form.

In the monomeric form, polar binding sites are in effect exposed, and that allows for the E-Matrix to bind *in vivo* with host cells responsible for initiating the tissue or bone growth process. It is this physical interaction between E-Matrix and the host cells that initiates the growth cascade. Polar sites on the host cells are exposed through the disruption caused by the injection process, and E-Matrix binds to these polar groups.

OK; the chemistry lesson isn't done just yet. Researchers who've studied the mechanism of action on E-Matrix have concluded that it is this polar binding interaction between E-Matrix and host cell surfaces that, in turn, alters the gene expression of those cells. ***One of the genes that E-Matrix up-regulates is transforming growth factor-beta 3 (TGF-beta 3).*** In addition, an E-Matrix treatment produces cells in the wound bed that are "mesenchymoid" in morphology.

E-Matrix has been shown to rapidly increase bone and other tissue growth as well as to improve the vascularity in the injected area so **that the vascular response is sustained**. (That, by the way, is in contrast with growth factors, which do NOT sustain their effect.)

There are lots of potential applications for E-Matrix including dermal healing of diabetic foot ulcers and other cutaneous wounds, soft tissue augmentation in cosmetic surgery, and supplying a three-dimensional scaffold for cosmetic surgeries. But the application that attracted Matt was bone repair—obviously for spine fusion but also for non-union fracture repair and dental surgery.

NanOss™ (Formerly Angstrom Medica, Inc.)

NanOss™ is the material that Pioneer acquired when it bought Angstrom Medica last month. Six years ago Dr. Edward Ahn and two fellow classmates from the Massachusetts Institute of Technology (MIT) in Cambridge, Massachusetts, founded Angstrom. Its core intellectual property is based on Dr. Ahn's MIT thesis research entitled, "Nanostructured Apatites as Orthopedic Biomaterials," which he conducted at the Nanomaterials Research Laboratory in the Department of Chemical Engineering at MIT.

For his work, Dr. Ahn won the 2001 Grand Prize from *MIT's 2001 $50k Business Plan Competition.*

Angstrom's technology entails forming crystals of hydroxyapatite at the atomic or "nano" scale. The resulting material is a kind of calcium phosphate substance that has the strength of stainless steel.

The crystals in what was to be called NanOss are so small that they can only be measured in billionths of a meter (there are 10 Angstroms in a nanometer). What gives NanOss its strength is that cracks have a more difficult time forming between the nanocrystals than they do between the larger, haphazard grains of traditional hydroxyapatite.

Bottom line: NanOss is like a resorbable stainless steel implant. It is structural, weight bearing, and will remodel into human bone! It can also be injectable, endothermic, AND weight bearing in the form of a bone cement.

In addition to inventing the material, Angstrom's founders also had to create a new process for forming these nanostructured calcium phosphates. While all of the details of the process are a trade secret, we do know that the nanocrystals are retrieved from the solvent and when consolidated into fully dense, nanocrystalline, transparent monoliths, they can form such complex shapes as screws, pins and interbody cages.

In many ways, NanOss is the first synthetic material with a good chance for replacing allograft structural implants in the spine surgeon's armamentarium. Finally, since the underlying material is hydroxyapatite, the material allows living cells to grow between and latch onto the nanocrystals. These cells then engulf the crystals, break them down and remodel them into real bone. Over time, therefore, implants made of NanOss should become indistinguishable from normal, living bone.

Combined, NanOss and E-Matrix represent two of the most innovative new biomaterials we've seen in a long time (with the exception of stem cells like Trinity™ or Osteocel®). And we find it more than a little amazing that these two materials are now in the hands of a single company—Marquette's own Pioneer Surgical Technology.

How significant will this be for Pioneer? Well, a lot depends on Matt's ability to build awareness for his technologies. It's a crowded marketplace right now, and at the end of the day execution will tell the story. Still, having two highly differentiated and effective products that can replace and potentially improve on the standard of care is the best starting point any company could hope for.

Pioneer Surgical Technology's first product was the Songer Spinal Cable System, which was introduced to the market in 1992. Since then Matt has cobbled together a fine line of spinal implants and instruments nestled within 100 million acres of forest and woodland otherwise known as God's Country.

With these two acquisitions, Matt may also be adding another sobriquet to the UP: Emerging Biomaterials Center of the orthopedics industry.

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