

SPECIAL FEATURE: Part 3

**INSULIN INJECTIONS, NO MORE! ...**  
**STOPPING THE DIABETES PANDEMIC-PART III**

*Too Good To Be True?*

*“Too Good to be True”*, that’s what most people say when they hear of the INGAP research. If in science you have a major break-through that people don’t understand and you cannot explain how and why it does what it does people will discount it before they buy in. Especially if it goes against some of the prevailing theories,. This according to Tom Finn VP of Strategic Planning for P&G Pharmaceuticals, when I asked him, “Is This Too Good To Be True”



P & G is well known for their cleaning and health and beauty products but they have also been in the pharma business for over 20 years. With over \$1 billion in global sales, their marketed drugs include Actonel for osteoporosis and Asacol for ulcerative colitis. Beyond that, they look for opportunities to leverage their long standing expertise in endocrinology. So, P & G set out to find a product that would be considered break-through technology in the treatment of diabetes.

Over a year ago, the GMP Companies approached P&G with the INGAP research. They took a serious look at the research and the more they checked it out, the more interested they became. INGAP met their goal of being a possible break-through in the treatment of Type 1 diabetes and for all insulin users.

Eli Lilly originally had a license agreement for 100 million dollars and they let it expire. If this research looked so good to P&G, why did Lilly drop out? There could be many reasons, but from conversations with GMP and P&G, the simplest answer was that, Lilly did not have the same information 2 years ago that P&G had when they made their decision to get involved.

This was not the first research that P&G had looked at. They had seen a lot, but none with the potential of INGAP to make a major impact in the field of diabetes. They wanted something that was unique and not just another me too treatment. They also didn’t want to go head to head with similar or existing technology.

P&G invested 5 million into the INGAP research and another 24 million into the GMP Companies because they felt it was a good business model.

P&G has always included licensing and acquisitions as part of their strategy to bring new products to market. Their appreciation of good relationships with the academic community led P&G to realize GMP could become a liaison between Pharma, and places such as McGill University and Eastern Virginia Medical School to get P&G exposure to new technology.

Just how committed is P&G to the INGAP research? According to Mr. Finn, the collaboration with GMP

Tom added “As we progress to making this available we will also be answering the questions as to how will we help to educate the patient with diabetes.”

“Because diabetes is a unique disease, which requires the patient to manage their care, we will need to develop new monitoring and managing techniques. We will require new protocols, behaviors, training tools and methods to educate not only the patients but also the medical community. With INGAP in early stage development, it is too soon to be making specific plans.. But we know that medical and patient education programs will be necessary and P&G has the deep expertise and commitment to make it happen when ready..

Besides having a sales force of more than 1500, they are also very committed to have the pharmacist be part of the process. P&G feels pharmacists would be key to the success of a product like INGAP. “Pharmacists are the front line players, whether it be compliance, side effects, or just knowing which patients have diabetes. We will be dedicated to a pharmacist program, which will be a key aspect to the INGAP program.”

As to the future of INGAP, “at this point in time, we are not comfortable saying that we might have the cure for diabetes but, we feel that we are looking at a very exciting therapy with a lot of questions that still need to be answered. It might provide an insulin holiday rather than a cure, we only can hope and work diligently to answer the needed questions.”

When asked about INGAP by those people with diabetes, Tom tells them that we have a potentially game changing breakthrough product that could ideally eliminate their need for insulin by growing new fully-functioning islet cells in their own bodies. But we still have a lot to learn about this new drug and how the body will respond to it. P&G, GMP and the key investigators are working hard to generate this learning as fast as possible.

### **Prior to INGAP**

In 1929 a surgical procedure was used on two juveniles with type 1 diabetes. They performed surgeries which tied off the tail of the pancreas in both individuals. In both cases the islets increased in size and quantity and improved both insulin sensitivity and control. Sixty years later we find that INGAP might have played a role in the success of the early surgery. “*THE EFFECT OF LIGATING THE TAIL OF THE PANCREAS IN JUVENILE DIABETES*” was published in [Surg Gynecol Obst 53:45-5 in 1931.](#)

### **Diabetes and INGAP: Where do we stand now**

According to **Dr. Vinik**, the animal studies showed the drug was well tolerated in mice and dogs. Therefore, it was concluded that it was safe to give animals and likely to be safe to give to humans. Then, on February 12, 2001, GMP companies met with the FDA for a preliminary review of the program. In July the application was received at the FDA and approval given in September. On December 5, 2001, the human trials began.

Part one of Phase I/2A, looking at just the safety issues was finished this summer and Part 2 of Phase I/2A trials are now beginning and will be conducted in two stages.

Stage 1 is comprised of administering increasing single doses of INGAP Peptide to 30 insulin deficient patients, both Type 1 and Type 2.

**Dr. Vinik** says, “The INGAP Peptide represents a potentially novel anti-diabetic therapy directed at the basis of the disease because it stimulates the growth of insulin-producing cells in the pancreas, rather than treating the metabolic consequences of diabetes such as high blood sugar.”

Optimistic about the translation of development of the research with animals to humans, **Dr. Vinik** explains, “It is very encouraging that INGAP in humans appears to be remarkably like that in hamsters, and the antibodies that we have made to different portions of the hamster INGAP molecule cross-react very well with INGAP in the human and other species.”

He continues, “We have been able to synthesize the gene down to a small peptide made up of a string of 15 amino acids that is responsible for inducing new islet production in the pancreas. The simpler the compound when administered for treatment, the less likely complications will occur in other areas. In our research with small animals, we experienced no complications, and we saw a reversal of diabetes when INGAP was administered at an adequate dose and for a sufficient period of time.”

Although researchers were testing for safety, not efficacy, in large animals, they found that when they administered the INGAP Peptide, it was not only safe, but it also caused the production of new smaller beta cells within the islets responsible for secreting insulin. They were encouraged that when the Peptide was administered in the peritoneal cavity, it went directly to the pancreas and did not concentrate elsewhere in the body.

Also encouraging is the fact that researchers have the ability to synthesize as much of the INGAP Peptide as they need for therapeutic treatment. Humans will be receiving the same Peptide that was administered to the animals. The ability to create the necessary quantities of the INGAP Peptide for therapeutic treatment gives scientists a wide potential for application. This is a marked difference from the islet cell transplantation approach to treating diabetes that is acutely limited by the number of islets that become available from donors.

**Dr. Vinik** explains, “There are only a limited number of pancreases that become available for islet transplants, and even if all were harvested for the purposes of islet transplantation, then only a few hundred people with diabetes would benefit. In contrast, every person with diabetes, even if they have had diabetes for a long time, may have precursor cells in their pancreases that can be trans-differentiated into islets, and there appears to be no limit in the capacity.”

These researchers believe that islet cell regeneration has the potential for treating Type 1 and Type 2 diabetes. People with Type 1 diabetes probably have had their beta cells destroyed by an autoimmune assault in which the body recognizes its own beta cells as being foreign. Though the beta cells are destroyed, other cells within the islets that produce hormones and the precursor cells appear to survive the assault. In Type 2 diabetes the beta cells don't function effectively. In both cases, the body may harbor precursor cells in the pancreas that can be turned on to become beta cells with the administration of INGAP.

“For people with Type 1 diabetes, the good news is that after a person has had diabetes for many years, the autoimmune process seems to die down. It seems that the body has to see foreign material to keep the autoimmune flames alive. When there is sufficient destruction of islets that have been damaged by the process, then the body possibly no longer recognizes these as foreign and loses interest in further destruction,” says **Dr. Vinik**.

He continues, “In people with Type 2 diabetes, the beta cells do not function effectively. It was once thought

reverse diabetes. The interesting thing is that one needs only about 2% of the total islet mass to be free of diabetes. Say we were to stimulate the formation of a reserve mass, then that would be equivalent to plugging the hole in part. We could always go back to the well if necessary.”

GMP Companies is working with the Strelitz Diabetes Institutes(SDI) to develop INGAP into a pharmaceutical application for diabetes treatment. It is not yet known what form of therapy this will take. And it is not known whether treatment will be needed for a defined course of time, as was the case in studies with small animals, or whether a person will need the INGAP Peptide therapy at certain intervals to induce the regeneration of beta cells.

**Dr. Leon-Paul Georges**, Director of the Strelitz Diabetes Institutes and Chairman of EVMS's Department of Internal Medicine, explains, “Much research lies ahead, but the most exciting thing is that we are now working with humans; a goal that **Dr. Vinik and Dr. Rosenberg** have been working toward since 1983 when they first discovered that the pancreas could grow new islets. For years, **Dr. Vinik's and Rosenberg's** research was considered too “avant garde” to attract federal research support. I've been a believer, and I remain a believer in INGAP's potential.”

While GMP Companies and P&G work in the pharmaceutical arena, P&G, GMP Companies and the Diabetes Institutes Foundation continues to fund SDI research work on the basic science of islet cell regeneration.

Researchers at the SDI continue to investigate how INGAP turns on the receptor of the beta cell to produce insulin and what other factors may be necessary for INGAP to work effectively in allowing the beta cells to create the insulin. They are also seeking to identify people at risk for developing diabetes and are looking at who may benefit from the INGAP Peptide's regeneration of islet cells.

With Part 2 of Phase 1/2A trials now underway they will be able to begin to answer many questions that remain:

What Controls INGAP?

What are its factors - because they may be able to use these factors to stimulate an individual's own production of INGAP?

What does INGAP control – because somewhere down the line they may find another molecule that INGAP turns on and then we can use that molecule or a smaller molecule or even find the receptor – the key to the lock?

Then there will be the need to establish who INGAP can help.

Who in the general population has a genetic susceptibility. The methods need to be developed and acquire the technology to evaluate this.

Who is deficient in INGAP so that it can be replaced?

A closer look at Type 1 and Type 2 diabetics, those people who don't have insulin and those people who don't have enough insulin.

Learning about the antibodies. People with Type 1 diabetes have antibodies that destroy the islets. There may be other elements that may be required to use with INGAP.

Will INGAP be given by itself or in combination with other factors? In order to make insulin, a pancreatic beta cell requires multiple different signals that are very carefully coordinated and regulated. Maybe INGAP can stimulate the formation of islets, but maybe it is going to require a lot of refinement down the road.

To read the Feature in it's entirety [click here](#)

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**For information on participation in the INGAP human trials, please call GMP Companies at 954-745-3537.**