ImmuCell

First Defense

Historical Review of ImmuCell's Core Technology

An Excerpt from our Q1 2022 Financial Results Conference Call

Michael Brigham

I'm very excited to introduce Dr. Joseph H. Crabb to you. Joe is our Former Chief Scientific Officer and VP of Product Development. He is now serving in a consultancy role to ImmuCell. So thanks for joining Joe. I have two questions for you. First Defense was first approved by the USDA back in 1991. Take us back to that time, please. How did you come up with the idea of purifying antibodies from milk to make a scours prevention product for newborn calves?

Dr. Joseph H. Crabb

Okay. Thanks a lot, Michael and Joe and everyone, I appreciate the opportunity to have a little discussion. Well, I wasn't the first one to come up with the idea, but I did ultimately develop the product First Defense. It starts with the differences between ruminants and primates, believe it or not. Human infants get almost all of their immunity in their first days of life through the placenta of their mom, the antibodies transfers across the placenta to the baby. In ruminants, the infant calf receives all of its maternal antibody not from the placenta but from mother's milk or colostrum. So it's always been known to be a very good practice in the dairy industry to feed your calves one gallon of high-quality colostrum, which contains a lot of antibodies for that developing calf.

And there was a lot of literature in the 1980s regarding using bovine colostrum to treat or prevent gastrointestinal illnesses. In the '70s, work by Norden, Mebus and others primarily at the University of Nebraska identified several different types of viruses that cause gastrointestinal problems in calves. And Norden established the value of using vaccines for the dam. In other words, vaccinate the mom so she can provide specific immunity to the developing calf. Right around that time in the late '80s, ImmuCell, I came on board because I had a vaccine and an antibody purification background. And we were working with Mead Johnson, an infant formula company, researching the addition of adding bovine anti-rotavirus antibodies into specific formulas for human infants. And while that work never went forward too far, we retained the animal health rights to the technology, and we began working on First Defense. Our reasoning here was that if we could make a convenient dosage form of these antibodies that are strong against the gastrointestinal pathogens, we might have a good product to easily prevent this illness in calves.

So we focused on developing subunit or otherwise novel vaccines, and we also focused on antibody purification technology so that we could boost the antibody levels in colostrum, to the point where we could offer an efficacious protective dose against multiple pathogens in a single orally delivered capsule. Also, we found that freeze drying, which is our main method of drying these purified antibodies, turned out to be the most gentle way to preserve the antibodies. And so that was basically the beginning of the First Defense franchise.

Michael Brigham

Wow, Joe, that's really interesting. I learn something new every time you speak. That's great history. Thanks for reviewing that. Let me switch over to Re-Tain. So as we know, Re-Tain has a much longer development path with the FDA than what we did experience with the USDA for First Defense. Take us back to the 2000s, what was it about Nisin that interested you? And how did you come up with the purification technology to make a pharmaceutical drug preparation of Nisin at commercial scale?

Dr. Joseph H. Crabb

Sure. Thanks, a lot. Well, then so to transition here, after several years of working on human applications of these bovine antibodies at ImmuCell, such as travelers' diarrhea, Clostridium difficile and Cryptosporidium, and a lot of that was funded through SBIR grants from the NIH, in the late '90s, we made the strategic decision to focus on only animal health applications, to focus in and be successful with animal health products. Mastitis was our obvious market because it's the largest animal health market. It's responsible for approximately $2 billion worth of losses in the US every year. I became interested in bacteria as potential mastitis treatments, looking at some of the literature and through the work of Phil Sears, who at the time was in Cornell and later MSU and some of the pioneering work of the company called Applied Microbiology, who became AMBI and then ultimately became N21.

After discussions with AMBI, we were able to secure animal health rights to their Nisin technology. And we started off by purchasing their product already on the market, it was a Nisin based pre-milking teat wipe called Wipe Out. Our reasoning here was that we could establish the proof of concept of Nisin being useful against mastitis pathogens by having some experience with this teat wipe, and we also gained experience in manufacturing Nisin. Well, ultimately, though Wipe Out was a good product, it never really could compete on a cost basis with the iodine and chlorhexidine based products that were already on the market. But we were able to leverage the Nisin technology and develop Re-Tain. And in doing so, we developed a novel purification method that ended up with pharmaceutical grade Nisin, i.e., 95% pure Nisin.

And since Nisin was used for many, many years in the food industry as a food preservative, a much cruder form of Nisin, we felt that we would have a clearer path through the FDA to develop this product for mastitis applications as an intramammary because of its long use and history as a safe product in food. That ended up not being totally true. We ended up going down pretty much the standard drug pathway for Re-Tain. But thankfully, we were able to secure the zero milk discard, which is a critical difference between Re-Tain and the other intramammaries, which are primarily based on antibiotics. So hopefully, in the coming months, we're going to meet the goal and be able to launch the product. Is there anything else I can add to that, Michael?

Michael Brigham

Well, I'm just so glad you joined the call. You've captured 30 years or so in a few minutes, and I've traveled that road with you and boy, it was really good to hear a concise summary like that. I hope that was of interest and benefit to our investors. So thanks for sharing that, Joe. I really do appreciate it.

About ImmuCell

ImmuCell Corporation's (Nasdaq: ICCC) purpose is to create scientifically-proven and practical products that improve the health and productivity of dairy and beef cattle. ImmuCell manufactures and markets First Defense®, providing Immediate Immunity™ to newborn dairy and beef calves, and is in the late stages of developing Re-Tain®, a novel treatment for subclinical mastitis in dairy cows without a milk discard requirement that provides an alternative to traditional antibiotics. Press releases and other information about the Company are available at: http://www.immucell.com.

About First Defense

First Defense® is the only USDA-licensed, orally delivered scours preventive product on the market for calves with claims against E. coli K99 and coronavirus (two leading causes of scours). First Defense® products provide bovine antibodies that newborn calves need but are unable to produce on their own immediately after birth. Our milk antibody products provide Immediate Immunity™ during the first few critical days of life when calves need this protection most. Studies have shown that calves that scour are more susceptible to other diseases later in life and under-perform calves that do not contract scours. The direct, two-part mode-of-action of First Defense® delivers specific immunoglobulins at the gut level to immediately protect against disease, while also providing additional antibodies that are absorbed into the bloodstream. These circulating antibodies function like a natural timed-release mechanism, as they are re- secreted into the gut later to provide extended protection. A single dose of First Defense® products provide a guaranteed level of protection proven to reduce mortality and morbidity from two major causes of calf scours.

Forward Looking Statements

This document contains “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Forward-looking statements can be identified by the use of words such as “expects”, “may”, “anticipates”, “aims”, “intends”, “would”, “could”, “should”, “will”, “plans”, “believes”, “estimates”, “targets”, “projects”, “forecasts”, “seeks” and similar words and expressions. In addition, there can be no assurance that future developments affecting us will be those that we anticipate. Such statements involve risks and uncertainties, including, but not limited to, those risks and uncertainties relating to: difficulties or delays in development, testing, regulatory approval, production and marketing of our products (including the First Defense® product line and Re-Tain®), competition within our anticipated product markets, customer acceptance of our new and existing products, product performance, alignment between our manufacturing resources and product demand (including the consequences of backlogs or excess inventory buildup), uncertainty associated with the timing and volume of customer orders as we come out of a prolonged backlog, adverse impacts of supply chain disruptions on our operations and customer relationships, our reliance upon third parties for financial support, products and services, our small size and dependence on key personnel, changes in laws and regulations, decision making and delays by regulatory authorities, a recurrence of inflation and its impact on our customers’ order patterns, currency values and fluctuations and other risks detailed from time to time in filings we make with the Securities and Exchange Commission (SEC), including our Quarterly Reports on Form 10-Q, our Annual Reports on Form 10-K and our Current Reports on Form 8-K. Such statements involve risks and uncertainties and are based on our current expectations, but actual results may differ materially due to various factors, including the risk factors summarized herein.