

# THE WALL STREET TRANSCRIPT

Questioning Market Leaders For Long Term Investors

## Hollis-Eden Pharmaceuticals, Inc. (HEPH)



RICHARD B. HOLLIS founded Hollis-Eden Pharmaceuticals, Inc., in August 1994, and currently serves as Chairman, President and Chief Executive Officer. Mr. Hollis has over 29 years' experience in the healthcare industry, has a proven track record of launching and marketing important new medical products, and a distinguished career of managing the growth and operations of companies in a variety of senior management positions. Mr. Hollis began his career in product sales with Baxter Travenol (today Baxter International), where he specialized in launching and marketing parenteral, enteral and intravenous solutions to hospitals and nursing homes. Mr. Hollis next joined Imed Corporation, a world leader in drug delivery devices in the 1980s, where he rapidly advanced through numerous sales, marketing and managerial positions.

After leaving Warner Lambert, Mr. Hollis joined Genentech, Inc., as the Bay Area biotechnology revolution was unfolding. At Genentech, Mr. Hollis was instrumental in the launch of two blockbuster pharmaceutical products—Protropin (human growth hormone) and Activase (tissue plasiminogen activator).

**TWST: May we start with a short history and would you give us your scientific mission?**

**Mr. Hollis:** The Company was founded in 1994, and we went public in 1997. The founding vision we had for the company then is the same as it is today, and that is to discover new chemical entities that are based on the biochemistry of endogenous adrenal steroid hormones. It is our belief that these adrenal steroid hormones have many other metabolites that are converted by tissues in the body, and that have their own unique signaling properties that regulate biology to maintain health. Being able to identify these metabolites, understand their chemical structures, signaling pathways, and their biological effects, allows us to determine if they are involved in particular diseases. The goal of our novel drug platform is to develop those active metabolites or their synthetic analogs as pharmaceuticals to restore hormonal signaling pathways dysregulated by disease or the process of aging.

**TWST: Would you elaborate on how you are using your knowledge to translate into product candidates and what is the mechanism of action of these candidates?**

**Mr. Hollis:** Adrenal steroid hormones are all converted from cholesterol in the body and there have been many successful pharmaceuticals that have been developed from the metabolome of these steroid hormones. For instance products derived from similar hormones in the body are pregnenolone, glucocorticoids and the androstenedione series that converts into androgens and estrogens for hormone replacement therapy or birth control pills. This is about the extent to which the pharmaceutical industry has evolved in regard to developing steroid hormones as pharmaceuticals. We were looking at a new and different class of steroid hormone metabolites that are converted by the body, identifying those unique chemical structures and then screening them in biological assays to determine their role in the body.

We have two candidates in the clinic right now, but we have other steroid hormone structures that we've identified in the metabolome that are still in our broad preclinical pipeline. The two product candidates that we should be talking about today are TRIOLEX and APOPTONE. TRIOLEX comes from a metabolite off this adrenal steroid hormone conversion that takes place in the body. We optimized

the chemical structure of the compound and then screened it in our *in vivo* animal models. The result of our work and knowledge is, we believe, TRIOLEX is an orally active optimized pharmaceutical that possesses potent anti-inflammatory properties, such as regulating NF-kappaB without the immunosuppressive side effects of the currently approved anti-inflammatories. We believe its role in nature is to restore stress / inflammatory immune response back to homeostasis.

TRIOLEX is a drug candidate that we are using in diseases such as ulcerative colitis and rheumatoid arthritis in autoimmune conditions, and in type 2 diabetes, where we are looking at inflammation as the root cause of disrupting insulin signaling and therefore creating insulin resistance. Our hypothesis in type 2 diabetes is, if you can use this chemical structure to down-regulate the inflammatory signaling pathways to restore insulin signaling, you should improve insulin sensitivity and be able to lower hemoglobin A1c, a clinical endpoint necessary for approval in type 2 diabetes. So it's a very nice indication to demonstrate the anti-inflammatory activity of the compound without the side effects of the currently approved drugs.

Our second drug is APOPTONE, which is a compound that we are now prosecuting in a Phase I/II clinical trial for prostate cancer. The reason we are involved in prostate cancer is because there are many hormone sensitive cancers, including breast cancer, which could be ideal indications for our class of drug candidates. We have an open IND for breast cancer, but focusing our clinical efforts right now in prostate cancer because that is where most of our preclinical experience is. The mechanism of action for APOPTONE is that it is an androgen receptor-targeted drug that down regulates the androgen receptor and causes cell apoptosis, or planned tumor cell death. So both these compounds are very exciting and we are looking forward to announcing data from our ongoing clinical trials in the months ahead.

**TWST: As far as TRIOLEX is concerned, are you currently pursuing the diabetes, colitis and rheumatoid arthritis indications?**

**Mr. Hollis:** Yes, we are. Currently, we are in a Phase II clinical trial for type 2 diabetes, where, by the end of this year we will have completed enrollment of 90 patients that are type 2 diabetics. We should have a clinical data release point sometime in Q1 2009 and no later than early Q2. For ulcerative colitis, by the end of the year we should have enrolled at least 27 patients. We are looking at doing an interim data release sometime in Q1. For rheumatoid arthritis, we will complete our safety combination trial with methotrexate by Q1 as well. In ulcerative colitis, we are looking at treating flares, and if TRIOLEX is effective in treating flares in ulcerative colitis, that would give us the data we need to accelerate a Phase II clinical trial in rheumatoid arthritis, while we are going for the acute indication of treating flares, which is a much quicker pathway to the market than other forms of rheumatoid arthritis.

**TWST: What is the current market for type 2 diabetes drugs?**

**Mr. Hollis:** The oral drug market for type 2 diabetes is currently about \$12 billion per year, and it is projected to grow in the com-

ing years. This is the epidemic of the 21st century in all developed countries. Actos and Avandia are the two insulin sensitizers that are approved, and they dominate the market. They garner about 50% of the annual sales in the oral anti-diabetic market; their combined sales in past years have been approximately \$6 billion annually. Both those products have recently been given Black Box warnings by the FDA because they are associated with increased cardiovascular events. And just recently, as of last week, Avandia was removed from the treatment guidelines both in the United States and Europe for its recommended use. So this really demonstrates the need today for a better insulin sensitizer, which we believe TRIOLEX represents. If we can actually demonstrate that we can regulate these inflammatory signaling pathways, improve insulin signaling, improve insulin sensitivity and show an improvement in hemoglobin A1c with a better safety profile than the currently approved drugs, we have the potential to dominate those markets. So this is a very big marketplace that we're entering with incredible opportunity for TRIOLEX to possibly become a new and safer insulin sensitizing drug.

**TWST: What are you targeting for TRIOLEX as far as diabetes is concerned? Does it have equal efficacy with less side effects than Avandia and Actos?**

**Mr. Hollis:** That is what we believe. I think the safety profile is very important and that's where the FDA is really concentrating. As in a chronic indication like type 2 diabetes, safety will be a major factor, and these two currently approved drugs have major issues. Now, I think what we should stress here is the fact that the currently approved drugs are associated with increased cardiovascular events. We believe not only in the safety of TRIOLEX compared with those other products, but also that our treatment could demonstrate cardiovascular improvement because it is anti-inflammatory in nature.

One of the key inflammatory biomarkers for cardiovascular disease is high levels of C-reactive protein or CRP. We've been able to demonstrate in our initial Phase I/II trial that we lower C-reactive protein, which could translate into cardiovascular improvement. So not only will we have a safer drug in regard to managing blood glucose levels, but we will also potentially be able to demonstrate the cardiovascular benefit. So I think if that plays out in our clinical trials, it will really have the ability to dominate the market for drugs that are currently approved, and even competitive drugs that are in the pharmaceutical pipeline. We have a unique approach to type 2 diabetes by treating the disease at the root cause, and the root cause in type 2 diabetes is obesity-induced inflammation. Obesity-induced inflammation is what causes the insulin signaling disruptions that eventually develops into insulin resistance. TRIOLEX is treating the obesity induced inflammation, so we are treating the disease at the root of the problem.

**TWST: It seems that the early driver for your company is going to be TRIOLEX. Can you elaborate further on APOPTONE?**

**Mr. Hollis:** APOPTONE is equally important to us; however it is not as advanced in the human clinical trials. But we believe that during 2009 it will catch up to TRIOLEX, and it is extremely important because we have a lot of expertise in steroid hormones and

hormone-sensitive cancers are using hormones as growth factors. Through our expertise in steroid hormone structures, and also in medicinal chemistry, we believe we've identified a compound in APOPTONE that is going to play a major role in hormone-sensitive cancers targeted at prostate cancer initially. Those markets are also very significant. The prostate cancer market is approximately a \$7 billion market, and we've chosen late stage prostate cancer because it is a quicker time to market and where we believe we can demonstrate progression-free survival. We will be using MRIs and CT scans also to demonstrate the activity of decreasing tumor size. We'll also be looking at the decrease in circulating tumor cells (CTC's), so there are a lot of markers we will be looking at with APOPTONE. But the primary clinical endpoint is improvement in progression free survival. We believe that if APOPTONE can demonstrate activity in late stage prostate cancer patients, that will bode well for testing the drug in earlier stages of the disease. So this is a very important program to us, it's just that it's a little earlier in development than TRIOLEX.

**TWST: Any other product candidates or other disease indications in the pipeline to note?**

**Mr. Hollis:** That is a very interesting question because if we show efficacy for TRIOLEX in any of the inflammatory diseases that we are looking at, it will allow the drug to be expanded into multiple other anti-inflammatory indications. It also opens up the opportunity for us to explore the use of other similar drug candidates in our pipeline in a variety of other inflammatory conditions. The currently approved corticosteroid hormones that are being used today as anti-inflammatories are based off cortisone. There are nearly 70 million prescriptions written a year for glucocorticoids. They are used in multiple diseases of inflammation and autoimmunity, and we believe that if we can demonstrate that we are just as efficacious as those products without the side effects of immune suppression, then we can expand TRIOLEX into many other indications. It could potentially replace the glucocorticoids, and potentially the biologics as the first-in-line anti-inflammatories.

We currently have a relationship with The Cystic Fibrosis Association which has selected TRIOLEX as a candidate for treating CF, which could lead to its development for other respiratory lung inflammation such as asthma and COPD. The product can expand into other autoimmune markets as well if it shows any efficacy in humans in these initial indications associated with inflammation. So that is a vast pipeline in itself. And if you look at prostate cancer with APOPTONE, that can move into other hormone sensitive cancers as well such as breast cancer, which is another enormous market opportunity for us. So just these two compounds can expand in many other indications and we have two or three other candidate compounds that we are moving along pre-clinically, but we haven't accelerated those discoveries into the clinic yet because we are preserving our resources to demonstrate activity on our initial four clinical trials. So until the point comes where we can establish the safety and efficacy in humans in these clinical trials, we will not accelerate the development of those other indications or products.

**TWST: What is the company's burn rate currently and how does the liquidity look to you?**

**Mr. Hollis:** Our capital structure is really good from the standpoint that we've been public for 11 years, and we only have 29 million shares outstanding. So we have really managed our capital judiciously and leveraged it into some major indications. Moreover, we've done all this in just the last two years with a quarterly burn rate of about \$5 million. For the past couple of years, we have had approximately a \$20 million annual burn rate. Our fixed burn rate is between \$12 million and \$13 million annually without clinical trial expenses. So our capital right now is being infused into these clinical trials.

**TWST: Do you have the management team in place to achieve your goals?**

**Mr. Hollis:** Our management team has been in place since the company's going public in 1997. This is an experienced management team that has been very stable and very committed and dedicated to our science. This has provided the continuity and consistency to move this technology forward. If you look at the backgrounds on most of our senior scientific team, they all have a combination of Big Pharma experience and also biotech experience in smaller companies. The team has several decades of experience in this area. Personally for myself, this is my 33rd year in the industry, and I have been able to gain most of my knowledge in this field by being in several other successful companies such as Genentech, where I was in the early and mid-1980s. We believe we have a management team that is not only well experienced, but very committed to being able to deliver these compounds as eventual treatments for major diseases.

**TWST: How do you feel about where your stock is trading? Do you feel you are getting enough credit for how far you have advanced as a company?**

**Mr. Hollis:** It's a very interesting question being asked at a time when our markets are at historic lows, and most biotech companies that are pre-earnings are not getting a lot of technology value or intrinsic value. Most of the companies are trading basically near or at cash. So the marketplace is not operating efficiently in this sector right now from the standpoint of giving value to companies that have future growth and revenue potential in regard to the products that they are developing to bring to the marketplace. So this is a very difficult time in our economy, and it's extremely difficult in the biotech sector, which is normally a high growth but a high risk area, and investors today are moving to safe stocks and are really not into risk.

There is not a lot of premium priced into our stock today and we are not happy about our stock price. We've spent 15 years and \$300 million approximately to bring our drug candidates to these indications. These indications represent enormous markets, such as type 2 diabetes and rheumatoid arthritis where combined annual drug sales exceed \$25 billion. These diseases are currently served by products in the marketplace today that have value, but still fall short of optimally treating these conditions. So these are unmet medical needs and we believe we can bring a better product to the market, and we are in our human clinical

trials now with data inflection points occurring within the next three to six months. So with the potential revenue opportunity that our products represent, and then you take a look at our stock price, there is a huge disconnect. But that's currently on par with the entire sector.

What we believe we have to do is stay very focused on executing our clinical trials demonstrating the safety and efficacy of our products in humans and being able to give investors the confidence that this data and the clinical trial results will bode well for success and potential commercialization. I think at that point in time, investors will be able to do the economics in regard to return on investment for our molecules. I believe at that point in time, we are going to become a very compelling investment story that possibly could be historic from the standpoint of a company with only 29 million shares outstanding, currently in Phase II clinical trials in major indications, and just a few months away from potentially compelling data that may demonstrate our proof of concept in humans. I think when you do the math here the economics are really compelling, and I think if we can demonstrate our products' efficacy, that we will survive this economic climate where investors are not inclined to put their money in right now.

**TWST: Any thoughts about partnerships?**

**Mr. Hollis:** Well, those are only considerations at this point. Partnerships would have to provide two things. Number one, an infusion of capital that's non-dilutive, and number two, synergy with our company with the science, the distribution capabilities and the chemistry where both companies share the same common vision with the compounds. If these things materialize, that could potentially happen. We are in various stages of discussions with multiple pharmaceutical companies around the world, and if we have to license some particular rights away to monetize some of our assets during this economic down trend, we would certainly consider that. This is just one of the strategies that we will be looking at very closely here as we evolve into the future.

**TWST: Any final thoughts?**

**Mr. Hollis:** I guess my final thoughts would be that in economic downturns like this, there are always opportunities. There is smart money and the ability to discriminate between technology and products that can succeed or fail. We believe we are a very compelling investment for these particular reasons. We've discovered novel innovative first-in-class drug candidates that are based on endogenous adrenal steroid hormones, and since these are nature's products, they are basically designed to perform certain functions that can be used in treating human diseases. So the probability of translation from pre-clinical animal models to humans is very high because the products originate out of our own metabolome.

I think we are poised for success in major indications and we've done extensive pre-clinical studies that project that there should be a high probability of success. Clinical endpoint data is due over the next three to six months and any inflection points that show that our

technology is safe and efficacious in those indications will also allow us to expand into several other additional indications, which increases our economic opportunity even more. We own all of our intellectual property, and when you do the economics in regard to the markets that we are pursuing with our compounds, the return on investment could be historical, if we are correct. I think we are at the inflection points where we'll be able to demonstrate that probability in the first half of 2009.

I have to believe that we represent a very compelling investment that is going unrecognized right now in this very tough economic environment. But those investors who do their due diligence will better understand what we are doing and the probability of success in delivering a better product in current markets that have a vast opportunity. If you take the time to learn what we are doing at Hollis-Eden, I believe you can't come away with any other conclusion than it could be a compelling investment.

Finally, I believe that there actually is much more at stake here than delivering better pharmaceutical products to medicine for specific indications. Our scientific vision rests on a fundamental platform that I believe could alter the length and quality of human life for generations to come. The longevity revolution is upon us and as we age our biochemistry changes, and we die from diseases related to the process of aging itself. If we can restore hormone signaling involved in pathways that maintain biology and health, I believe we can prevent or delay diseases associated with aging such as cardiovascular disease and various forms of cancer, as well as many autoimmune disorders. This vision is what drives us at Hollis-Eden every day, and it is what I have committed my life to achieving. All of the employee/shareholders of Hollis-Eden Pharmaceuticals share this passion to serve humanity. We are a company that you should want to be right, and I would hope invest in, not only for a return on investment but for your health as well. Thank you for the opportunity to discuss our company with you.

**TWST: Thank you.**

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