Neothetics
IPO Roadshow[1]
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George Mahaffey, President and CEO

Good morning. Neothetics is a Phase 3-ready, specialty pharmaceutical company developing therapeutics for aesthetic medicine. Our lead product, LIPO-202, is a first-in-class, injectable drug that reduces bulge in your central abdomen, or so-called body contouring.

What we've done is developed a drug that patients desire when they want to look thinner and not have the difficulties of current treatment options — namely liposuction and mid-devices. What we believe is that with LIPO-202, being able to give surgery or body contouring through a needle will not only expand this already large and growing market, but in fact will transform it, similar to what BOTOX did for the facial surgery market, circa 15 years ago.

I will be making forward-looking statements today. I'll call your attention to the safe harbor statement and the overview of the deal. We're looking to raise, at this point, $60 million with a price target of $13-15.

At Neothetics, we've been able to assemble a very seasoned management team. We have experience in companies both large and small. What attracted me to the company about four years ago was an asset of products that gives compelling and consistent data across clinical trials, and also a target to market that is large and very much ripe for transformation.

Dr. Ken Locke, our chief scientific officer, has about 30 years in the business, mostly in small companies from development through commercialization. Susan Knudson, our CFO, has about 25 years in the business; again, mostly small-company focused with a specialty of licensing and M&A. Lastly and certainly not least, we have a very strong group of investors that have taken us to this point.

We're excited about our prospects. LIPO-202 — the active ingredient in our product is salmeterol, a long-acting beta-2 agonist, that when injected reduces fat in the localized area of injection. We've seen across, now, six trials, very consistent and compelling data and safety data almost identical to placebo, which is important for an aesthetic drug. And because salmeterol is also the active drug in Advair and now has been used in millions of patients — and our dose is so much lower than Advair — we are on a 505(b)(2) pathway which lets us get to market more rapidly and less expensively.

However, we've been able to build a very strong wall of patent protection around our asset and we have no relationship with any other company. We own the asset outright. The market, which I described earlier, is large; it's growing; but it has yet to be transformed with that truly novel, changing product that can take it to the next level [and] what happened with the neurotoxins in facial surgery.

This market, now, is a cash-pay market. Our drug will be the same and we know who the patients and the physicians are, so that we can target them in a very efficient manner with a sales force of manageable size.

[1] IPO Candy transcripts are formatted and lightly edited for readability. We also highlight portions we believe are of greater interest to readers.

It's safe to say that nearly everyone wants a flatter belly. That's why we diet, and this notion of attaining and maintaining the ideal appearance has led to this creation of this huge and rapidly growing cosmetic-procedure market. But embedded in that procedure market is the cosmetic-injectable drug market. That's the area of most rapid growth. There is a flight from surgery or devices to cosmetic-injectable drugs. And if we furthermore drill down into this procedure market, there's the body-contouring market; and this, again, is a large and rapidly growing market. And while it's been incrementally expanded over the last several years, it has yet to be transformed similar to what BOTOX did, making it a mainstay-type treatment.

Now, when we assessed the beginnings of our commercial opportunity, we went to cosmetic-injectable patients. These are people already getting facial fillers and neurotoxins. And we asked them — hundreds of them — where on your body do you have an area of fat that you would like to change? What they told us, resoundingly, is it's the belly. It's the abdomen. It's one of the reasons that we all diet, is to get a flatter belly. And there's other areas of the body that are of great interest to us, but our initial focus on the abdomen is the right focus with [this] data and common sense about why people diet and where they want to improve their appearance.

This body-contouring notion has been around for decades. In fact, it was first addressed when liposuction came to the U.S. in the late seventies and early eighties. While it works, liposuction has weaknesses. It's real surgery. General anesthesia. A difficult recovery period. It takes months to see the effect, etc. So, it is not the perfect solution for this high demand of body contouring. However, liposuction is still the number one cosmetic surgery done in the United States. It is still a huge, surgical procedure when it comes to incidents.

To address the weaknesses of liposuction, several devices have entered the market over the last several years, and these non-invasive solutions are an improvement over liposuction, certainly. They're more safe — but they still have significant drawbacks — one being economics to the doctors. Second, it takes patients several hours to complete their treatment, and it still takes months for them to see the effect, etc. This is an expansion to the market, not a transformation.

Our solution to this — by giving surgery or body contouring through a needle — we believe will totally take this large market and transform it to the next level. We can have our drug injected through a tiny, half-inch 30-gauge needle in less than five minutes by the physician, and shrinking fat cells rather than killing fat cells helps a patient have no recovery period. They see the effects within a month or less, and this meets the need of what they've been trying to get out of body contouring for decades.

These are some examples of our typical patients. We don't make big people small. We make thin people thinner. Our average patient loses about three-quarters of an inch in circumference around their belly over a two-month period with no change in lifestyle, and that three-quarters of a belt loop to a belt loop is a clinically meaningful and noticeable change for these otherwise thin, not obese people; most of whom exercise and eat right and can't get rid of that area of bothersome fat. And when given LIPO-202, they lose about three-quarters of an inch, on average, as I mentioned.

Now, if we look at our drug in a little more detail, I mentioned that the salmeterol is the active ingredient. Salmeterol is a long-acting, beta-2 agonist and our target population is, as I described earlier, the non-obese subjects with stable weight and a good lifestyle. The drug is given once a week for eight weeks and how it's actually given is each week, the patient gets twenty small shots across their central abdomen.

You can see the patient on the right here has a temporary tattoo applied. This is done in a manner of seconds by the physician like my kids get at the fair, and then the clinician or the nurse injects 1 milliliter of drug into each one of those twenty targets. This is what takes them about five minutes or less. The needle is a half-inch, 30-gauge needle. It's a couple of human hairs in thickness. We don't use a numbing agent. The patients don't have any complaints of significant pain. The physician or the nurse can go across this field and complete the injection in about five minutes or less. Importantly, the safety profile of this drug is nearly identical to placebo, and that is a key piece for an aesthetic drug.

Undoubtedly, the safety profile is explained by the mechanism of action. The fat cell — the key to fat burning — is the beta-2 receptor. Once it is activated, it cleans the fat or the triglycerides in the cell. The triglycerides are released from the cell, and the cell shrinks in size. That's normal metabolism — the natural metabolic process that we are all having at the moment.

Whether it is the body's own metabolic process or LIPO-202, which is a beta-2 agonist, the result is the same. There's an activation of the beta-2 receptor; the fat is released from the cell; the cell shrinks in size; and that's what is observed. Because we give the drug across the grid on the central abdomen, we focus the drug's effect in the area of injection, and when the cells shrink in size, en masse, across the injection zone; that's what patients observe as having a flatter abdomen. Another way to think about our drug is spot diet. Instead of losing volume throughout our body while we're dieting; we lose the volume at the grid where the drug is injected.

We've completed six clinical trials, to date, with over 800 patients. We see very consistent results, trial to trial. As I mentioned, the safety is nearly identical to placebo, which is a key for aesthetic drug development. And from an efficacy standpoint, it's important to note that the volume change patients get with LIPO-202 is roughly the same volume change they get post-liposuction surgery. So, here [is] this most commonly done cosmetic surgery that has weaknesses; [yet] the effect that our patients get on LIPO-202 is about the same as what they get after liposuction surgery.

We've defined the right dose, and in fact, when we started the company we started at high dose; and as we came down in dose, we saw efficacy increase. That's an expected finding, because beta-2 agonists, like other agonists, if given at too high of a dose or given too frequently, can cause downregulation of the target receptor; in this case, the beta-2 receptor. As we gave the drug at a lower dose and spread the dosing to one week apart, we actually saw efficacy increase; until, through clinical trials, we optimized the dose at being a 0.4 microgram dose per week. This is a very small dose and, in essence, we're just tickling the beta-2 receptor very similar to the body's own metabolic process. We cull the mechanism, and that's what the beta-2 receptor is the most responsive to — is that small stimulation.

This is a new indication and it requires new endpoints. Under rigorous FDA guidance and regulation, we're developed endpoints to address this indication. We've used them successfully in the most recently completed RESET trial we'll describe, and we know that these tools are appropriate as we move into Phase 3 targeted for the first half of next year.

Now, aesthetic drugs have a road map or a framework that has been developed by FDA for approval; the primary endpoint of which is a composite of patient assessment and clinician rating. That means that a subject that comes into the study — they themselves must show or report the change by using tools developed for this indication — and the clinician must see that change in the patient. If they hit both, they're a responder. If they miss one or the other; they're not a responder.

What we do at the end of the study is we look at drug responders versus placebo responders. If there's a statistical difference, that's the approvable endpoint. So, in this case, to address this road map, we've developed the patient verbal scale called P-GAPS, and we've developed this photonumeric scale. A subject comes in, [and] we use these scales with both patients and clinicians to determine before and after; again a composite where they have to win on both.

Now, the Derma Division goes one step further. They tell us, and all aesthetic companies, that their interpretation of approvable requirement is that a subject must have a 2-point change on the patient scale and a 2-point change on the clinician scale; roughly a 40% improvement over eight weeks. That 2-point and 2-point change is the approvable endpoint. Our Phase 3 studies are designed to accommodate the regulatory hurdles, and we are comfortable that we'll meet that. However, in the Phase 3 studies, we will also capture the data that are relevant for the commercial market; and that is what our data shows are clinically meaningful. In this case, it is a composite of a 1-point change on the patient scale and a 2-point change on the clinician scale. We'll capture that data.

Now, one further thought that is key for aesthetic drugs is aesthetic drugs, unlike blood pressure-lowering drugs or cholesterol-lowering drugs, don't have a tool that the clinician uses to objectively measure success. What the measurement of success is for aesthetic drugs is how the patient feels about how they look after the treatment. That's why they come in for treatment. That's how they measure success. While the physician's input in interesting, it's all about the patient. And we know from our data, both qualitatively and quantitatively, that a 1-point change on the patient scale is a clinically meaningful change and we furthermore know from our data that the majority of patients have a 1-point or greater change on that 5-point scale over an 8-week period and therefore the majority of patients have a clinically meaningful response to this treatment.

FDA asks that companies like ours define, develop, and validate the secondary endpoint — the endpoint used for a physical measure. The physical measure should then explain the outcomes that patients and clinicians are reporting. In our case, we've developed a sophisticated, laser-guided manual tape technique. We run manual tape around the circumference of a patient. This sounds easy, but in clinical practice, it's not so easy, because you have love handles. Do you go up, around them, over them? What do you do [with] the crevice in the back? There's a practical reason this was not as easy to do as it seems.

To meet that challenge, we've actually developed a technique where we project a laser line onto the patient's belly, as you see in this slide here. The clinician, then, uses a specialized, sophisticated manual tape. They apply it right to the laser line around the circumference of the patient. The tape is sophisticated in that it is a constant-tension tape. Doctors don't worry about how tight to pull the tape. They can put it on the same tension every time. So, by doing that, we can apply the tape in the same way, at the same tension, each and every time, and we get very tight data when it measures the physical change which in our data set matches and tracks with the reported outcome tools we get from patients and clinicians.

Kenneth Locke, Ph.D., Chief Scientific Officer

Good morning. For those on the line, this is Ken Locke, the chief scientific officer for the company. George has introduced the primary and secondary endpoints that have been validated to examine changes in central abdominal bulging. What I'd like to do, today, is show you how LIPO-202 performs on those tools in a large clinical trial. That large clinical trial we called RESET, and RESET was a double-blind, placebo-controlled trial in 513 patients. The data that I'm going to show you today is from the placebo

arm of that trial, as well as our best-dose arm of the trial. Each of those groups have about 125 subjects in them.

Talking first about the primary endpoint measures, what we saw was significant and clinically meaningful changes in these tools with LIPO-202 that occurred more frequently than with placebo. That was true whether or not it was the 2-point patient and 2-point clinician change as mandated by FDA, or whether we include the 1-point change in the composite that we know is clinically meaningful to patients. Regardless, we saw significantly more LIPO-202 responders than placebo responders. These response rates are very similar to other aesthetic treatments as applied to these types of endpoints, and if we can replicate these findings, which we are confident we can do in Phase 3, this should make the drug approvable to FDA.

Not only did patients and clinicians see the change, but we could also measure that change with our laser-guided tape measure procedure. In RESET, we saw significant reductions in treatment-area circumference and volume with LIPO-202. This was true whether we measured a mean change from baseline, or whether we looked at numbers of responders to a threshold response.

What I'm showing you here on the left is the percent responders to a 1.83-centimeter change in circumference, or about three-quarters of a belt loop, and we know that this is clinically meaningful to patients. And we saw significantly more responders to LIPO-202 meeting this hurdle than placebo responders. Similarly, we know that about a 300 cc reduction in volume — about a can of Coke's worth of volume — coming from this anterior abdomen is significant to patients. And again we see significantly more responders on LIPO-202 than to placebo, so we can measure the change that patients and clinicians report.

Now, to give you a little bit of perspective on how big the LIPO-202 treatment effect is, we can compare it to a published study on limited-volume liposuction. On the left-hand side of the figure is data from RESET, where the mean change in our best-dose group was about 200 ccs in volume. Now, in the published study, 23 subjects underwent limited-volume liposuction over essentially the same treatment area as we used in RESET, and these are patients who would also qualify under the inclusion/exclusion criteria for that study. And what was found, 10 weeks after the surgery, was about the same 200 cc reduction in treatment-area volume. So, despite the caveats of cross-study comparisons, we're very encouraged that we can produce the same volume reductions with LIPO-202 as with limited-volume liposuction, without all the side effects, pain, and recovery associated with the surgery.

Now, safety, safety, safety. An aesthetic drug has to be safe, and we have consistently seen, across all trials including RESET, a very favorable safety and tolerability profile of LIPO-202. What we typically see in our trials are transient, mild, injection-site reactions — a little bit of pain. Maybe a redness. An occasional bruise. But these local reactions occur with the same frequency with LIPO-202 as they do with placebo injections, which says to us it's more about the local reactions to the needle sticks than what's contained in the syringe itself. So, this safety profile will be extremely important, not only to FDA and their establishment of [a] risk-benefit profile, but certainly in the marketplace having this great safety profile will be very important.

We believe we had great success in RESET, so we are going to design our Phase 3 pivotal trials in much the same way. We're going to use essentially the same non-obese patient population. We're going to use the same endpoints I just described from RESET. There will be two pivotal trials — 800 patients per trial

— 400 on drug [and] 400 on placebo. We're going to use the same treatment paradigm — 20 1-cc injections each week for eight weeks.

We're confident that with this many people in each arm compared to the RESET — 400 versus 125 — we should be able to replicate that data that we saw in RESET. In addition, we'll be conducting six additional trials to fill out the NDA package, including the required one-year safety follow-up, in which we'll also look at durability of effect. We'll also look at the safety of retreatment, and we'll also be doing some pilot trials in other areas of the body, including the submental or under-chin fat, as well as in lipomas.

George Mahaffey, President and CEO

Let's examine the market and the opportunity in a little more detail. I mentioned, earlier, that the cosmetic-procedure market is large and rapidly growing. In fact, in 2013, the spending in the United States alone exceeded $12 billion dollars for cosmetic procedures. But I also told you that the cosmetic-injectable drug market was the stimulus for this growth of the overall procedure market and you can see from this slide, here, that that spending is approaching $3 billion per year in the U.S. and is growing at about a 35% clip per annum. Clinicians and patients are moving away from surgery and devices as they expand into the cosmetic-injectable drug market.

How we think about our opportunity, in particular, is the following. On the left side, there are three-quarters of a million patients in the United States currently getting cosmetic-injectable drugs, neurotoxins, and fillers; and these people are the natural place to start for us as we come to market. We do that because, to the patient, they're already intervening to improve their appearance. They're not afraid of needles. They have adequate funds to pay for these types of treatments. They found a physician who does these injections, etc. It's kind of common sense. For the clinician, these doctors are already used to using cosmetic-injectable drugs and you saw, from the prior slide, their growth rate of cosmetic injectables is exceeding 35% per year. It's a natural place to start.

But the area of transformative marketing will be to the million-plus patients who are not currently getting cosmetic-injectable drugs, but are interested in looking thinner and will not go do liposuction or devices today. Many of these patients are too young to get cosmetic-injectable drugs because they don't have wrinkles, so they're in this separate bucket. But by coming to market with a drug where we can give surgery through a needle and body contouring through a needle, it's these people that we'll bring into the body-contouring market as we transform it to the next level.

If we think about this million and three-quarter people as available patients, and we assume that our price to the doctor for [eight weeks] of treatment is $1,500 U.S., we know that the doctor will charge the patient $3,000. That's what they do with cosmetic-injectable drugs. That cost to the patient is about roughly the cost of a device treatment for body contouring to the patient. Furthermore, it's about a half to a third of the cost of liposuction to the patient. So, it's a pretty good estimate and placeholder for price to the clinician and eventually to the patient.

So, we have one and three-quarter million people; we have a placeholder of [a] $1,500 price to the clinician; and if we assume a peak of 5-10% into this market; you can see this is a multi-hundred-million dollar product. And yet, we've assumed no off-label use, which may happen; we've assumed no growth in the male market, which will probably happen; and yet, still, it's a sizeable market opportunity that is done through transforming the market.

Why we think this will happen in the market is for the patient, I've described the benefits here, which are clear, especially compared to other treatments; but, more importantly, they may come in to body contouring for the first time. To the clinician, this is a natural. It fits their cosmetic-injectable drug market [and] they get a touchpoint with the patient, once a week for eight weeks, so they can upsell their other procedures and services. That's what they do when they build their practice. There's no up-front capital expenditure. Obviously, this is a buy and bill. This matches what the clinicians do and want to do more of, and we have a drug that gives patients what they want and more patients want more of that. It's a natural fit as we look to transform the market.

Susan Knudson, Chief Financial Officer

We have a number of compelling milestones and value-inflection points over the next two years. Post completing the IPO, we plan to initiate our Phase 3 program and other studies in support of the NDA filing in the first half of 2015. Importantly, we expect to deliver top-line data from our Phase 3 pivotal studies by the end of 2015. Driving that NDA filing in the second half of 2016 are two things — the one year safety and durability study, as well as the multi-cycle retreatment study. Post the NDA filing, we've allowed a one-year standard trajectory for what could be approval and possible launch of LIPO-202 in the second half of 2017.

We have a strong IP portfolio and I remind you that we own the assets worldwide except for Russia and a few of the Commonwealth of Independent States. To date, we have three issued patents in the U.S. and abroad. These patents are formulation, methods, and use. The strength of the claims of these patents include the broad coverage of the long-acting beta agonist and the low dose at which LIPO-202 is administered, and specifically, that is to injectable fat as well as an injectable formulation. I'll point out that these patents will provide us with three years of data exclusivity. They're "Orange Book" listable and will provide us coverage through 2026 and 2030, respectively.

To date, we've raised just over $74 million to bring us to a Phase 3 readiness and complete the IPO. Our most recent financing was the Series D which we completed in September of this year. It was a $6 million raise with all new venture investor money. I point out we have $116 million post-money at this point in time, and cash on hand of $19.5 million which includes a $10 million debt facility.

George Mahaffey, President and CEO

We're pleased with where we are and we're excited for our future. We have a drug, LIPO-202, that works with consistent, compelling data and addresses a large and untapped market. We have good IP. We have a regulatory pathway that's affordable. And we can reach this group of patients and clinicians in a very efficient manner. For these reasons, we believe we will be the company on the frontier of the next great company in aesthetic medicine. Thank you.

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