

Edgar Filing: NUVELO INC - Form 425

NUVELO INC
Form 425
October 08, 2008

Filed by Nuvelo, Inc. Pursuant to Rule 425

Under the Securities Act of 1933

And Deemed Filed Pursuant to Rule 14a-12

Under the Securities Exchange Act of 1934

Subject Company: ARCA biopharma, Inc.

Commission File No. 000-22873

The following is a transcript of a presentation made by Nuvelo, Inc. and ARCA biopharma, Inc. on October 6, 2008.

Nuvelo, Inc.

JMP Securities LLC Healthcare Focus Conference

October 6, 2008

<<Unidentified Speaker>>

Okay. Well good afternoon. It is my pleasure to introduce the next, well really at this point companies, soon to be company, Nuvelo and ARCA. We actually used to cover Nuvelo and we've never had an opportunity to cover ARCA, ARCA is a private company and they have recently decided to merge. And so it is my pleasure to introduce a large panel of guests. Mr. Dick Brewer who is the CEO of ARCA, long day here, who is the Chief Medical Officer I believe of ARCA and Dr. Ted Love who is the CEO of Nuvelo. So it is a pleasure to introduce these folks, very interesting story, ARCA and Nuvelo. Thanks.

<<Richard Brewer, President and Chief Executive Officer, ARCA Biopharma>>

Well thanks Charles and we appreciate the opportunity to be here. Again my name is Dick Brewer and to my left is Dr. Mike Bristow, Mike is the Founder of our ARCA Biopharma. He was also one of the founders of Myogen recently was sold to Gilead. Mike is a heart failure specialist and a scientist. He's been spending the last decade of his life really understanding the genetics heart failure. And of course he was prominent in developing the story that I'm about to tell you.

Dr. Ted Love is a cardiologist also, President and CEO, Chairman of Nuvelo. Ted and I go back 20 years when we worked together at Genentech in developing TPA and involved in the GUSTO trial and all those things that maybe some of you remember. This is the first time in about five years that I've ever made a public presentation, referencing a public company. So I need to do this. And this Safe Harbor statement is something that you've all seen before, so I won't read it to you. But be aware that at least I showed it to you as I'm supposed to do.

Let me tell you a little we have fairly intricate story. It is pretty straight forward, but it can be involved. And what we're going to try to do today given the time constraint is to

give you a pretty broad overview. First talking about the merger and what it does for us and there are lots of points here to consider. But the most important is that we will with this merger create a late stage cardiovascular company. We have a product Gencaro which is the ARCA product, that's bucindolol hydrochloride, which we already is developed for heart failure and is now going to the FDA.

We have a PDUFA date of May 31 2009 and that's what makes this a very late stage company with a product that's going to be approved, if all goes well in a year or so. In addition this merger provides us with another product that we are very enthusiastic about and that's Nuvelo's product called NU-172, a very short acting anticoagulant that we see a lot of potential for. And both of these products, Gencaro our product for heart failure and NU-172 address large market opportunities. We have done this before. I was the CEO of Scios before this and we introduced a drug for acute decompensated heart failure. It was the first one in about ten years actually and the physician audience that we address when we introduced NATRECOR is essentially the same audience that we'll be addressing when we introduce Gencaro.

So the funding from the Nuvelo merger which we hope will close at the end of the year, provides more than just dollars. It also provides us with a product and with people to help us build out our company. So this a little bit different from reverse mergers that you've all seen and talked about no doubt in the past where there is just a reverse into some cash, that's not what this is about. There is cash, there is product and there is people.

We have near-term milestones that can drive value, the first is our NDA acceptance by FDA. We filed sorry we submitted our NDA in July of this year, FDA informed us on September 19th that they have filed the NDA which is important to the whole process of prosecuting this particular application. The merger should complete in the fourth quarter, probably December/January of 2009 and at that point we will initiate a Phase II trial probably in coronary artery bypass grafting for NU-172. LabCorp is our partner and LabCorp has developed a companion genetic test that I'll talk about in just a minute and will Mike Bristow, that is integral to our offering of Gencaro. Because you need to be able to identify in advance which patients are likely to be the best responders to our drug and this test will allow that to happen.

We don't have any say in whether or not there is a Cardiorenal Advisory Committee Meeting on this application, that's strictly up to the FDA, but we will believe there will be one, not so much to talk about beta blockade and heart failure, that's pretty well established. But the genetic piece attached to this is something new, it's something that's of great interest to FDA. As you know they have their own initiative for personalized medicine and we imagine if there is Cardiorenal Advisory Committee Meeting that that's what the meeting will be all about. And that's just fine with us, we actually hope that happens. The FDA decision on Gencaro as I mentioned is 53109 and then we'll launch as soon thereafter as we can.

So let's talk a little bit about Gencaro, bucindolol hydrochloride and this product has the potential to be the first personalized treatment for heart failure. This drug is a unique beta

blocker, the pharmacology attached to this is completely different than that, that you see for carvedilol or metoprolol, two beta blockers that we approved about ten years ago for heart failure and have been extremely successful products, they're really great drugs. Ours is a little bit different. And that difference allows for genetic targeting that the other drugs simply can't do.

As I mentioned the companion test to identify which patients are going to be really good responders to Gencaro and which patients should not take the drug necessarily, is being developed by LabCorp and is going to be submitted to the agency under a 510(k) or a 510(k) with PMA. I'll get back to whether that makes a difference in just a second.

Frequently in personalized medicine the wrap on personalized medicine drug development is that the market opportunity is sometimes perceived to be too narrow, in other words just a small fraction of the large market, 5%, 10%. What I want to make clear to everybody today is that the very favorable genotype that we can identify with the LabCorp test represents about 50% of all patients diagnosed with heart failure. So it's a very large slice of a very large market. Gencaro has also been evaluated via the Phase III trial for heart failure in other ways and we've determined actually that the drug has a very strong signal for efficacy in certain types of atrial arrhythmias which we could pursue as second indications for the drug.

I mentioned that heart failure is a large market. Well right now there is 6 million patients who are diagnosed and living with heart failure in the United States alone. There are about 0.5 million new cases of heart failure diagnosed every year. Beta blockade is the standard of care. And the quote there makes that clear. This is from ACC/AHA guidelines which say beta-blockers should be prescribed to all patients with stable heart failure do to reduced left ventricular ejection fraction. It hardly gets more direct than that.

Yet only 60% of heart failure patients are actually on a beta-blocker. 40% still aren't experiencing beta blocker therapy and there are lots of reasons for that, but the reason I mention this to you is that there are a large number of patients out there who represent an opportunity to go on Gencaro as patients who have never experienced beta blockade before.

So what's personalized medicine all about? And every hears a lot about it. It's really designed to do two things. First is to maximize the response to a drug and second to minimize side effects, that's really all there is to personalized medicine. And if you could do those two things, that's a real winner. If you could reduce cost to healthcare system, and we think we can do that with Gencaro as well because of the pharmaco-economic studies that have been conducted in the Phase III trial, then you really have a lucky strike X-ray here and we think we can do all three.

So the point here is to improve outcomes for patients with heart failure and we can do that by understanding the common genetic variations which predict an individual patient's response to the drug. The test as I mentioned by LabCorp is easy to use and it's relatively inexpensive compared to some other genotyping test that are done for oncology patients for example. This is just a buckle swab, you put it in the tube and you send it off to LabCorp central office and the results are back to the physician via fax, e-mail and telephone call within 48 hours.

LabCorp has been a really great partner for us. I must say, they developed the test, the turnaround time right now is about 48 hours, which is fine for this particular audience. As I mentioned this test will identify not only the most favorable responders but also patients who might not do well on Gencaro and that's equally important to know. This drug will go through a diagnostic test will go through a 510(k) path at FDA. It is not under CLIA or the home brew and I Charles had mentioned, I heard that you were talking about that earlier with the last speaker and it's important for us to go down this path with FDA. Whether it's a PMA or just a straight 510(k) really doesn't matter. And FDA told LabCorp that they shouldn't worry about it and even if it was under a PMA they would not have to do additional clinical work as they can simply reference our clinical section in the new drug application.

So with that I'd like to ask Mike to come up and talk to you about the science briefly. Mike?

<<Michael Bristow, Chairman and Chief Science and Medical Officer, ARCA Biopharma>>

Thanks Dick, thanks Charles. Ladies and gentlemen fasten your seat belts we're going to get into the molecular genetics of this and so let me just identify this pointer if I can if there is one, there we go. All right, so the interaction here is within two kinds of adrenergic receptor polymorphism, two sets interacting with unique pharmacology of bucindolol. The first and arguably most important interaction is a polymorphism of the beta-1 adrenergic receptor. This receptor is what is on cardiac myocytes and essentially drives adrenergic response of the heart to adrenergic stimulation and long-term there is too much adrenergic stimulation which creates a problem basically creates more cardiomyopathy and the idea is to interrupt that.

This receptor comes in two flavors, one is the wide side, the beta-1 arginine homozygous, shown here and this receptor remarkably has four times the functional activity of its counterpart which is glycine at position 398. It turns out that not only is the function higher as a beta-1 arginine receptor, but also a much higher percentage of those receptors are in a constitutively active state, meaning they are signaling all the time, even in the absence of adrenergic stimulus, in the absence of norepinephrine, not only that but norepinephrine has a much higher affinity for these constitutively active receptors and it also turns out that bucindolol uniquely inactivates, blocks that receptor and then activates the active state of that receptor and no other beta blocker does this. And we believe this is the basis for the selective clinical effects of bucindolol on patients with this receptor. AS Dick said 50% of the general population has this receptor.

The other receptor polymorphism that interacts with bucindolol is the alpha-2C receptor, there is wild type version of this receptor and a four amino acid deletion of this receptor in a business into this receptor positions 322 and 325 which basically destroys the

function of that receptor and causes dysregulation to anything that effects norepinephrine release and another unique property of bucindolol compared to other beta blockers is that it is sympatholytic. We think that s through beta-2 blockade, but in the presence of this alpha-2C deletion receptor you have a situation essentially where you have dysregulation and when you have this deletion polymorphism you have too much norepinephrine lowering. It shuts down norepinephrine release and too much lowering. And so in the case of the wild type you have a mild ideal femoral lowering, which actually enhances therapeutic response, in the case of this deletion you have too much lowering which basically interferes with responses.

So here s a slide looking at clinical results across various beta blocker Phase III trials and it s divided into results in the US, shown here trial location versus rest of world. The first point is that US beta-blocker trials are basically conducted in patients that are actually sicker than patients in Europe, have results that are less positive. And so this is the best trial an NHLBI VA cooperative studies funded trial. This is the entire cohort, all 2,708 patients results. This is reduction in clinical endpoints, they re all statistically significant with the exception of all-cause mortality reduced by 13% with a P value of 0.053. Here is what happened in the only two other Phase III clinical trials intention to treat trials of beta blockade in US patients, a 5% increase in mortality and a 20% decrease in copernicus compared to the US data.

Over here our results are varied in copernicus in all the patients now diluted out three to one by patients from Europe essentially. The results are much better than in US for married and copernicus. And then finally here are the results of the very favorable genotype which is that high functioning beta-1 Arg, Arg genotype regardless of alpha-2C status and here are the reduction in clinical endpoints and in every case obviously you exceed what occurred in US trial results and you actually exceed by 20% to 25%. The average results across multiple clinical endpoints in the European trials as well.

So you put these two sets of polymorphisms together and you come up with this algorithm and we ve been referring to the very favorable genotype, this is beta-1 Arg, Arg high functioning receptor, it doesn t matter what the alpha-2C is. If you have norepinephrine lowering but you still have a high functioning receptor, the heart can be supported by adrenergic activity and you get an excellent clinical result. And these are the reduction in major clinical endpoints.

And over here you have the so called unfavorable genotype which is a combination of the alpha-2C deletion, too much norepinephrine lowering and the hypofunctioning beta-1 Gly receptor. There is no adrenergic support to the heart in this setting, it completely wiped out efficacy. These patients should be treated, should not be treated, these patients should be treated.

And so here is some milestone pathways to the market that Dick will handle.

<<Richard Brewer, President and Chief Executive Officer, ARCA Biopharma>>

So it's pretty straightforward from this point forward. Here we are with the submission, the filing took place last month. LabCorp will coordinate its 510(k) PMA with us at FDA's request. So that both product and companion test may be approved at the same time next year. As I mentioned there's a possibility for the Cardiorenal Advisory Committee to meet. Again we don't know if it's going to, it's not in our control to make that happen. But it's likely from our perspective that it would. If it does it can't really happen probably until March timeframe next year given the timing for all of this and FDA's need to do the review and then pull the book together with a bunch of questions, it's pretty time consuming as you know. PDUFA date 5/31/09, so less than a year from now we could have a significant product approved by the agency and then we will begin our commercial launch.

We are going to do this ourselves. That is we're going to commercialize Gencaro in the United States by ourselves. And I'll talk to you about what we need to do there in just a second. We believe that that's the best way to enhance shareholder value is to hang on to this asset and we intend to do that. As I mentioned the merger for us is with another product NU-172. And I'll briefly go over this because this is a very interesting product from our point of view particularly with regard to an anticoagulant for medical surgical procedures.

First of all there's a large population that we're looking at right now. For study that population is CABG patients or Coronary Artery Bypass Grafting and there are about 400,000 of those procedures done in the US every year. There are other opportunities we could expand into, but CABG is the first opportunity clinically. Now the standard of care today is Heparin as the anti-coagulant. When patients go on the pump they are heavily anti-coagulated and they are throughout the entire operation. But then when the surgeon's finished his or her work the idea is to turn off the Heparin. Otherwise there's lots of bleeding into the wounds as the patients go upstairs to the SICU or whatever part of the hospital they go into.

So there has to be an antidote to Heparin administered usually in the operating suite and that antidote is called Protamine. Now this has been done for years and years. And now is the time to come in with something better and we think we have that. So if you ask cardiothoracic surgeons what might be an ideal profile for a short acting anticoagulant. What they tell you is from an administrative point of view they want something that's got a predictable dose with a very rapid onset and a very rapid onset without the need to give another drug as an antidote, as is currently the case, Heparin, Protamine as the antidote.

If you had an anticoagulant that could be turned on, maintain anticoagulation throughout the procedure and then turned off and have that anticoagulant go away, that's the ideal from their perspective. From a safety point of view reducing bleeding is obviously the number one goal. No drug induced thrombocytopenia which you see with Heparin and of course Heparin has as you all know gotten something of a black eye over the recent past and frankly if Heparin would go away, that wouldn't necessarily be a bad thing. From an efficacy point of view it has a potent anticoagulant, it has to be active against clot bound thrombin and it has to be effective in static blood. These are all things that we would have to prove in our upcoming clinical trials.

So the proof of concept in the Phase Ib has really established that NU-172 has a very rapid and predictable onset and offset of anticoagulation. And I'll show you that rather than go through a bunch of words, we'll I guess that's not here, but there's a slide that actually will show you that within five minutes you can take out the activated clotting time of four times from base line within five minutes by turning this drug on, maintaining that anticoagulation for the duration of the procedure by a slower infusion and then when the drug is turned off, within 15 minutes it goes away. And it goes away because this drug is an aptamer, a little piece of DNA and it's metabolized in the blood, that's important because lots of patients who go through these types of procedures have poor kidney function and kidneys don't count in this particular circumstance, because the drug is metabolized in the blood. And that's different from Heparin. So we believe that this represents a very exciting opportunity for further development and we plan to initiate with Nuvelo of course a Phase II trial late this year or early next.

So, I'll end this presentation by talking about the milestones upcoming. Number NDA acceptance by the FDA, that's happened. Completion of the merger. At the end of this year we have planned to initiate the Phase II trial in CABG for 172 as an anticoagulant. LabCorp submission up there, PMA/510(k) oh by the way I wanted to mention that FDA said don't worry about it LabCorp, it doesn't matter if it's a PMA or 510(k), as I mentioned, but the difference is the rigor of the audit, and that's all. In other words if it's a PMA with a 510(k) LabCorp will go through a more rigorous audit which they are prepared to do.

An anticipated CRAC meeting if happens probably won't happen till around March and then there'll be decision on Gencaro with a PDUFA date in May of next year and then we'll launch. So there's lots and lots of near-term value driving milestones coming up with the merged company that we're very enthusiastic about.

So with that I'll stop and Charles I think we may have Q&A.

Q&A

<Q>: Yes, we have just a few minutes for questions. But thank you for that broad overview. I had a quick question for Mike. Why was it that the other beta-blockers do not antagonize 389 Arg?

<A Michael Bristow>: It has to do with inverse agonist activity of bucindolol in human cardiac beta-1 Arg receptors versus Gly, it's the only beta blocker that has inverse agonist activity which is the assay that basically detects inactivation of the constitutively active receptors. It's the only beta-blocker that has that molecular property is the answer.

<Q>: So it's the only one that shows as an inverse agonist?

<A Michael Bristow>: To human beta-1 Arg or human cardiac beta-1 Arg receptors, that's right.

<Q>: So the others don't interact with that?

<A Michael Bristow>: They don't have that particular molecular interaction which we haven't determined what that is, but just in an empirical sense they don't give that molecular signal in isolated hemin Arg preparations which we published that a fact that carvedilol doesn't have it in PNAS in 2006, we now know that metoprolol doesn't have it. We presented that at the Heartcare Society a couple of weeks ago.

<Q>: Okay. And then the other question is the, really this kind of genetic variation, is that seen pretty much across different ethnic groups?

<A Michael Bristow>: Yes. So it turns out that both of these receptor polymorphisms have a racial predilection or a racial difference in African Americans versus non-African Americans. So the alpha-2C deletion is ten times more common in African Americans. The beta-1 Gly hypofunctioning receptor is also slightly more common, statistically significant more common in African Americans and these two observations or two factors are part of the explanation for why African Americans don't respond as well or didn't respond as well to bucindolol in best. On the other hand 32% of African Americans have the very favorable genotype in can be treated and do give an enhancement of efficacy.

<Q>: Okay. I have one more quick question. But are there any questions from the audience at this point? Dick you mentioned commercialization, can you touch on that a little bit more? What are your plans for that?

<A Richard Brewer>: Sure. We expect to launch with a sales force of about 125 reps.

<Q>: Yes.

<A Richard Brewer>: And these reps will be covering 1,800 short-term hospitals, which account for 80% of all the hospitalizations for acutely decompensated heart failure patients. And therefore they are the hubs if you will for physicians and patients. They will also call on the 5,000 to 7,000 heart failure specialists, because this drug is not going to be promoted to all the cardiologists initially. That'll be promoted to the heart failure specialist and then those people will, if we're successful and use this drug and diffuse the use of the drug down into the cardiology community and even to the high volume leaders in internal medicine.

<Q>: And then my other question is with regard to the availability test. It's my experience that LabCorp is really good at selling tests to the laboratory and to know that they need to test. But I'm wondering if they have sales force that can help you be can be an effective partner in convincing folks they need to take the test. What's your strategy?

<A Richard Brewer>: Well we think they can. They have 1,000 reps.

<Q>: Yes.

<A Richard Brewer>: Those reps are going to be focused solely on their tests. We would not ask them nor would LabCorp want us to ask them to sell our drug.

<Q>: Yes.

<A Richard Brewer>: They'll be knowledgeable about it of course. But they won't sell our drug. But they will go out and make it clear to those same group of specialists that the test is now available, what it's for and how it can be used. And they'll make sure it's not only available in those physicians offices.

<Q>: Yes

<A Richard Brewer>: But also in the hospitals that I just referenced.

<Q>: So they are going to make sure they are going to cover the institutions, you're really going to sell the test?

<A Richard Brewer>: I mean that's a good way to put it. We're going to be doing both.

<Q>: Okay.

<A Richard Brewer>: The test and the drug.

<<Unidentified Speaker>>

Good. Well thank you everyone for coming all this way to talk to us.

<<Richard Brewer, President and Chief Executive Officer, ARCA Biopharma>>

Thanks for the invitation.

About Nuvelo

Nuvelo, Inc. is dedicated to improving the lives of patients through the discovery, development and commercialization of novel drugs for acute cardiovascular disease, cancer and other debilitating medical conditions. Nuvelo's development pipeline includes NU172, a direct thrombin inhibitor which has completed Phase 1 development for use as a potential short-acting anticoagulant during medical or surgical procedures; and NU206, a Wnt pathway modulator in Phase 1 development for the potential treatment of chemotherapy/radiation therapy-induced mucositis and inflammatory bowel disease. In addition, Nuvelo is pursuing research programs in leukemia and lymphoma therapeutic antibodies and Wnt signaling pathway therapeutics to further expand its pipeline and create additional partnering and licensing opportunities.

Information about Nuvelo is available at our website at <http://www.nuvelo.com> or by phoning 650-517-8000.

About ARCA biopharma

ARCA biopharma, Inc. is a privately held company focused on developing and commercializing genetically targeted therapies for heart failure and other cardiovascular diseases. The Company's lead product candidate, Gencaro (bucindolol hydrochloride), is an investigational pharmacologically unique beta-blocker and mild vasodilator being developed for heart failure and other indications. ARCA has identified common genetic variations that predict individual patient response to Gencaro. The companion genetic test for Gencaro is in development by ARCA's partner, Laboratory Corporation of America. For more information please visit www.arcabiopharma.com.

Forward-looking statements

This press release contains forward-looking statements which include, without limitation, statements regarding the completion of the proposed merger transaction between Nuvelo, ARCA and Dawn Acquisition Sub, Inc., the transaction's anticipated benefits, timing, progress and anticipated completion of the combined company's clinical stage and research programs, including possible regulatory approval, the potential benefits that patients may experience from the use of the combined company's clinical stage compounds, and the cash position of the combined company, which statements are hereby identified as forward-looking statements for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. Such statements are based on our management's current expectations and involve risks and uncertainties. Actual results and performance could differ materially from those projected in the forward-looking statements as a result of many factors, including, without limitation, failure of Nuvelo or ARCA's stockholders to approve the merger, the ability to complete the transaction contemplated by this communication in a timely fashion, the risk that Nuvelo's and ARCA's business operations will not be integrated successfully; the combined company's inability to further identify, develop and achieve commercial success for products and technologies; the risk that the combined company's financial resources will be insufficient to meet the combined company's business objectives; uncertainties relating to drug discovery and the regulatory approval process; clinical development processes; enrollment rates for patients in our clinical trials; changes in relationships with strategic partners and dependence upon strategic partners for the performance of critical activities under collaborative agreements; and the impact of competitive products and technological changes. These and other factors are identified and described in more detail in Nuvelo's filings with the SEC, including without limitation Nuvelo's quarterly report on Form 10-Q for the quarter ended June 30, 2008 and subsequent filings. We disclaim any intent or obligation to update these forward-looking statements.

Additional Information and Where to Find It

Nuvelo intends to file a registration statement on Form S-4, and a related proxy statement/prospectus, in connection with the merger. Investors and security holders are

urged to read the registration statement on Form S-4 and the related proxy statement/prospectus when they become available because they will contain important information about the merger transaction. Investors and security holders may obtain free copies of these documents (when they are available) and other documents filed with the SEC at the SEC's website at www.sec.gov. In addition, investors and security holders may obtain free copies of the documents filed with the SEC by contacting Nuvelo Investor Relations at the email address: ir@nuvelo.com or by phone at 650-517-8000.

In addition to the registration statement and related proxy statement/prospectus, Nuvelo files annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any reports, statements or other information filed by Nuvelo, Inc. at the SEC public reference room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for more information. Please call the SEC at 1-800-SEC-0330 for further information on the public reference room. Nuvelo, Inc.'s filings with the SEC are also available to the public from commercial document-retrieval services and at SEC's website at www.sec.gov, and from Investor Relations at Nuvelo as described above.

This communication shall not constitute an offer to sell or the solicitation of an offer to sell or the solicitation of an offer to buy any securities, nor shall there be any sale of securities in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such jurisdiction. No offering of securities shall be made except by means of a prospectus meeting the requirements of Section 10 of the Securities Act of 1933, as amended.

Nuvelo, ARCA and their respective directors and executive officers may be deemed to be participants in the solicitation of proxies from the stockholders of Nuvelo in connection with the merger transaction. Information regarding the special interests of these directors and executive officers in the merger transaction will be included in the proxy statement/prospectus of described above. Additional information regarding the directors and executive officers of Nuvelo is also included in Nuvelo's proxy statement for its 2008 Annual Meeting of Stockholders which was filed with the SEC on April 23, 2008 and its Annual Report on Form 10-K for the year ended December 31, 2007, which was filed with the SEC on March 12, 2008. These documents are available as described above.