

Edgar Filing: NUVELO INC - Form 425

NUVELO INC
Form 425
November 13, 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. 333-154839

The following is a transcript of a presentation made by ARCA biopharma, Inc. on November 12, 2008.

ARCA biopharma (definitive merger agreement with Nuvelo, Inc.)

Rodman and Renshaw 10th Annual Healthcare Conference

November 12, 2008

<<Unidentified Speaker>>

Okay, I would like to introduce our next presenting company ARCA biopharma and Dr. Michael Bristow, the Chairman and Chief Scientific Officer, and Founder will be giving the presentation.

<<Michael Bristow, Founder, Chairman and Chief Science, and Medical Officer>>

Okay. Good morning. As some of you know, ARCA and Nuvelo are in the process of merging, and that merger will likely be completed by the end of the year. Safe Harbor Statement. And so why are these two companies merging? For one thing, it creates a focused, cardiovascular company with late-stage potential. Will go into that in great detail. Perhaps somebody could shut that door there.

There is a near-term commercial opportunity related to a filed NDA on the lead product from ARCA, Bucindolol. The inclusion of Nuvelo in the combined company provides a long-term opportunity, which we'll be discussing. Both these compounds and development, we single all and NU-172 provide major market opportunities. These are big cardiovascular markets.

One of the characteristics of the company is the experienced leadership. Dick Brewer, the CEO, Ted Love, who will remain on the Board from Nuvelo, myself, the pedigree of the leadership in this company runs through Genentech, Scios, and Myogen. And the combined cash reserves of the two companies will allow funding of all the programs through 2009.

So there are lot of near-term milestones coming up in 2009 in this combined company. We have an NDA on file that's undergoing a very active review right now at some point till the next year, or some time around the middle of the year. I will get a decision on that. The merger is on the process of been completed as we said, there is a Phase IIa study

with the short-term anticoagulant designed to replace Heparin NU-172 beginning shortly after the first of the year. ARCA does pharmacogenetic drug development and we have a companion genetic test, that accompanies our drug and that is being codeveloped with The Laboratory Corporation of America, the submitted PMA for that will go in about 30 days.

We anticipate getting a Cardio-Renal Advisory Committee Meeting because bucindolol or the trade name being Gencaro was the first pharmacogenetically targeted, cardiovascular drug that's going to create a certain amount of uproar if you will at the FDA or certain amount of interest, let's say at the FDA, and so we anticipate a meeting, but we'll see about that. PDUFA date is May 31 '09 and the launch has slated for very early in 2010.

So, what is bucindolol the trade name have being Gencaro, let's say third or fourth generation now, beta-blocker which unique pharmacology, we'll talk about that in detail. It's going to be the first genetically targeted cardiovascular drug for the companion, the first drug ever at the FDA, were the companion genetic test and a drug coming out it should have approved at the same time.

The potential market, the pharmacogenetic market, the genetic variant that were marketing comprises around 50% of the heart failure population. So, this is not a niche target population. Within that 50%, which we call very favorable genotype, essentially what that does is create a best in class situation for this drug in heart failure. We have several potential follow-on indications with the Phase II data look very promising from the pharmacogenetic standpoint, prevention of atrial fibrillation and prevention of VT and VF, we planned to do fully developed programs in both those areas after approval for heart failure.

So heart failure is a, as most of you know, a very large market. There are over 6 million to 7 million patients in the U.S with this disorder. It's the only cardiovascular disease that's increasing at incidents and there are around 550,000 newly diagnosed patients per year. The class of drug that single [indiscernible] and beta-blockers is probably the single most effective drug class within heart failure.

It's one, A, approved by all the guidelines and there are two approved beta-blockers out there right now in this class. But this class has some difficulties in administration for one thing, you have to start at very low doses and then slowly up titrate. This is tedious not all patients respond, some patients actually do or else you have to periodically determine that and so the pharmacogenetic testing makes all this easier unless you increase the probabilities of who's going to respond, think some of the guess work out of treating with this class if you will.

So we are in the personalized medicine space at ARCA and of course that's, personalized medicine is designed to improve the therapeutic index meaning better efficacy, fewer adverse events, all of these with better efficacy and fewer adverse events translating to reduce cost. We have very powerful pharmacoeconomic data behind bucindolol in this

regard. And so outcomes will be improved essentially by avoiding treating certain patients and then singling out other patients for therapy.

In order to do that obviously, you got to have a genetic test. So this is the genetic test being developed by Laboratory Corporation Of America, literally we call the Gencaro test. This will have a turn around time of 48 hours; will be available everywhere in the U.S. It will identify favorable or very favorable responders and as I mentioned earlier the approval for this is warped up in this 510K/PMA that's about to be submitted.

The basis for the pharmacogenetic interaction of Bucindolol that has to do with the direct and indirect interaction with certain adrenergic receptor variants and so going over here on the right we have two specific properties that are unique of Bucindolol that interact with these genetic variants of adrenergic receptors.

The first is in the Beta-1 adrenergic receptors and this comes in two flavors as a high functioning receptor with a high percentage of receptors at a constitutively [ph] active state that's the [indiscernible] version of the receptor Beta-1 Arg/Arg being the genotype that constitutes the this very favorable subgroup and the Bucindolol has specific unique properties on this Beta-1 Arg/Arg receptor, it essentially inactivates the receptors that are in the constitutively [ph] active state in addition to blocking them competitively.

And that property of inactivation of active state receptor is known as inverse agonism, Bucindolol is the only drug in the Beta block of class of being able to identify that actually does that. Another unique property Bucindolol, is its ability to lower norepinephrine, it's fairly powerfully sympatholytic, the idea there is it, a little bit of this property is good in heart failure, a lot of that is not good.

It turns out that norepinephrine lowering is under genetic control, under genetic control by the Alpha2-C receptor, a receptor that sits on adrenergic neurons and there is a deletion of polymorphism of this receptor and when that is present there is too much norepinephrine lowering by Bucindolol and so impacts on responses or outcomes and will be talking about that.

So there are two interacting of polymorphisms of adrenergic receptor. The direct target of Bucindolol, the Beta-1 adrenergic receptor, I just told you there are two types of, two genetic variances of that. That is the Beta-1 Arg/Arg, which amounts to the wild type version of the receptor, the high functioning, high constitutive activity receptor, and there's a glycine version with about 25% of the function and about 25% of the constitutive activity.

And so here's the Bucindolol coming in, it will block both receptors but it activates the active state of this receptor. The norepinephrine lowering of Bucindolol comes in through beta-2 blockade but it's regulated by pre-junctional alpha 2c receptors. And so when you have got this deletion polymorphism, there's too much norepinephrine lowering, when you've got the wild [indiscernible] ideal smaller amount of norepinephrine lowering.

So these are clinical results, comparative clinical results with Bucindolol and other beta-blockers in Phase III placebo controlled trials. So over here, it's the sum total of data that's been generated in US patients and it turns out that US patients in heart failure clinical trials have more advanced heart failure and the results are somewhat better than in patients enrolled in Europe. The less sick you're with a beta-blocker, the better opportunity you have to see efficacy.

But here is the Bucindolol results in a Phase III trial called Best. These are event rate reductions with the exception of all-cause mortality where the P value is 0.053. All these P values and all these major clinical endpoints are statistically significant. Some have very low P values such as less than four zeros and a number.

And so basically long story short, this trial produced major benefit for secondary endpoints and a nominal benefit on all-cause mortality. The trial was actually stopped early for loss of investigator equipoise.

So here's the comparative data in US patients, Metoprolol a 5% increase in mortality in this trial, some reduction in this end point, not significant. Here's Carvedilol with patients in the US enrolled in Copernicus, 20% non-significant reduction in mortality. Here is the data, in Merit and Copernicus from European patients, these are all the patients, four times the patients in the US, mostly enrolled in Europe and you can see these large reductions in endpoints, these are the most positive trials yet in beta blockader, heart failure.

And here is the very favorable genotype, the beta 1-adrenergic genotype that will be sent to all, you can see the event rates in every case, numerically exceed those found in Merit and Copernicus, despite the fact that these are U.S patients. And all these P values are statistically significant and we believe all these endpoints will be enough to generate labeling in favor of a pharmacogenetic approach and we are going for approval based on these data on the entire co-work, we are going for labeling based on pharmacogenetics.

So here are the three sub groups or the three genetics groups created by putting together the beta-1 and alpha-2 C receptor. If you got the beta-1 Arg, is a high functioning receptor that's the group you wanted to treat. And so these are some major clinical endpoints. These are the reductions, this hospital days per patient is very end of the curve measure of hospitalization and so it generates a favorable pharmacoeconomic data and there's nearly a 50% reduction.

Over here is the unfavorable so, if you don't have the beta-1 Arg by definition, you got some glycine at the 389 position, I mean who has a 389 that creates a low functioning receptor, constitutively be constitutively inactive be similar has no special effect on that receptor and the response is here are much less and so when you have that low functioning receptor and you drop a lot of norepinephrine, you lower norepinephrine through the alpha-2 C receptor, you basically lose all efficacy.

And so these patients call the unfavorable genotype should not be treated, what's left over is the alpha-2 C wild-type, a favorable genotype for efficacy. Some efficacy coming in through the Gly-carrier patients and these responses are on the average about the same as non-targeted therapy with standard beta-blockers.

So here are the milestones that are coming up, NDA submitted, filings accepted, PMA going in, cardio renal advisory committee meeting anticipated, not clearing that is going to happen [indiscernible] and then launch. So this is a big market and we have elected to commercialize this our selves, the reason for that is, the heart failure market is heavily driven by heart failure cardiologist, there are few thousand of these in the US, they influence what is done in the heart failure market and you can cover them with smaller number of sales and marketing people numbers like 115 for example which is where we are going to start.

So it's a large market, but it can be covered with [indiscernible] sales and marketing people. Pricing and reimbursement, we believe that we will be able to get to tier 2 and perhaps to tier 1 in Medicare part D with the drug, we have reason to believe that based on the discussions we have had with CMS people and part B will be what covers the genetic test.

So here is the long term growth which is coming in by ND 172, this is a nucleotide DNA aptamer, generated by Larry Gold's [indiscernible] technology. And this is licensed into Nuvelo by [indiscernible] and basically this is a design for the replacement of [indiscernible] concept. The world would be a better place if [indiscernible] were to go away, we all believe, all of us in cardiology believe. And so this is for short term [indiscernible], the first indication we are going for is coronary artery bypass surgery, [indiscernible] surgery.

Long story short, this DNA aptamer, posses the unique profile for short term anti coagulation, predictable dosing rapid onset, rapid offset and we expect his based on studies done in animal models and phase I studies that have a good efficacy and safety profile. So proof of concept for this we believe it has been achieved in Phase 1A and 1B study. Actually this is the design of the 1B study. And this was a 2.0mg/kg IV bolus followed by an infusion and I will show you just in data in terms of ACT values.

This is the Inlab or in operating suite measure of anticoagulation used for heparin or any short acting anticoagulant activated clotting time. The drug has given as a bolus rapid achievement of what you sort of target anticoagulation that you want with an ACT comes the infusion is very stable. The ACT remains stable over the entire period of study of 200 minutes. The minutes essentially that the infusion has stopped anticoagulation goes away. There is no antidote needed for this and that's a major advantage to this product.

So in summary, these are the value driving near term milestones essentially for the combined company. NDA acceptance next year, completion of merger, initiates the Phase II trial, LabCorp submission, CRAC meeting FDA decision and then launch. Thank you very much. Questions? Time for questions.

Q&A

<Q>: [Low Audio].

<A Michael Bristow>: Well, there are over 4000 patients that have been exposed to Bucindolol, we've got preclinical CRAC data and animal model as well. So we have all of that. We have a full board thesis for Bucindolol; we have a full board of carcinogenicity studies, which submitted in the NDA.

<Q>: [Low Audio].

<A Michael Bristow>: Long time. The immediate follow-up actually in the best trial was two years, which is twice as long as other beta-blocker trials. And there are other trials that went fairly long but not as long as that. So we've got long-term data. Yes.

<Q>: [Low Audio]

<A Michael Bristow>: Yes, yes, good. Very good question. The pharmacogenic substudy didn't have time to go into it. But we did invest, I was actually on my academic side in charge of the substudies invest. So we set up the first DNA bank and we're set up in a hard and fair clinical trial. And how you got DNA out of that bank was you had to write a grant application and in that grant application, you had to have hypothesis, a sample size calculation and some ability to fund what you wanted to do and then we would give you DNA. So Steve Leggat actually who is sort of the Founder of Adrenergic Receptor Polymorphisms, the pioneer in this field submitted a grant application in 1998, while this study was still go on, that application was reviewed and approved. And the leading hypothesis of that grant application was at the beta-1 adrenergic receptor would be associated with more favorable clinical responses in the Gly counterpart and then hypothesis was hit in that grant application, in the DNA substudy. DNA substudy was 1040 patients out of the total of 2,708 it was a separate consent form and so on, but there is a large number of clinical endpoints in that DNA substudy as many endpoints as in your standard phase [indiscernible] trial. The reason for that in turn is sick patients very sick patients in a long duration of follow-up.

<Q>: [Low Audio]

<A Michael Bristow>: Everything submitted, everything ever done would be sent along was submitted in the NDA, yes. Yes.

<Q>: [Low Audio]

<A Michael Bristow>: Yes.

<Q>: [Low Audio]

<A Michael Bristow>: Filing date is officially September 29. We have received words September 19th and it was accepted. The official filing date, typically 60 days after submission is September 29th.

<Q>: [Low Audio]

<A Michael Bristow>: That's typically when they log you in, if they're going to accept it.

<Q>: [Low Audio]

<A Michael Bristow>: Yes we have the 70-core data letter. The response we got, we are working on.

<Q>: [Low Audio]

<A Michael Bristow>: Well they said submit it and we will review it. That's what said of course. They're not going to say anything until they review the NDA. But they basically agreed with our strategy of what we were doing. It makes no sense of doing other trial. Short story here is, it makes no sense doing the trial because you can't do a placebo control. And so they wanted us to do a placebo control, if they did another trial, we can't do it. You will never get through the IRB, unless they realize the extent of the data we had the fact that was prospective substudy and the fact that we are not going for approval based on the pharmacogenetic results, based on the entire cohort results and other results. Once they understood all of that, they said submit your NDA.

<Q>: [Low Audio]

<A Michael Bristow>: The message is yes the message is that because everybody from CMS to third-party other types of third-party payers to PBMs wants to see pharmacogenetics arrive. They're all heavily committed to this. There is a big political movement going on now at multiple levels as many of you know and there is very little action and there is so there is a lot of interest in this. In fact, there is a very large PBM, I won't name has been sort of in discussions with us for a long time and they are very excited about this, they think this is the way with a future, they've actually created a huge department of pharmacogenetics to deal with this kind of thing. So we think the uptick on this for various reasons including the hard data. But there is sort of a political wind behind the sales here right now as well I would say. Okay, thank you.

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 potential market for the combined company's products, 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 has filed a registration statement on Form S-4, and a related proxy statement/prospectus/consent solicitation, in connection with the proposed merger. Investors and security holders are urged to read the registration statement on Form S-4 and the related proxy statement/prospectus/consent solicitation. Investors and security holders may obtain free copies of these documents 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/consent solicitation, 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 is included in the proxy statement/prospectus/consent solicitation 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.