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#### CORPORATE PARTICIPANTS

#### Dr. Michael Bristow

ARCA biopharma, Inc. Founder, Chairman and Chief Science and Medical Officer

#### PRESENTATION

### **Unidentified Speaker**

ARCA biopharma Nuvelo is a biopharmaceutical company developing genetically targeted therapies for heart failure and other cardiovascular diseases. Presenting today is Dr. Michael Bristow will be the presenter. Thank you, Michael.

## Dr. Michael Bristow ARCA biopharma, Inc. Founder, Chairman and Chief Science and Medical Officer

Thank you. As many of you probably know, the reason there are two names up there is these two companies are in the middle of a merger. I come from the ARCA biopharma side. Safe Harbor statement arising out of the Nuvelo publicly traded aspect of the merger.

So this merger creates, we think, a quite valuable company. First of all, it s a late stage, now cardiovascular company, the focus is cardiovascular. At a time when big pharma is in retreat from the cardiovascular space, we believe there s substantial opportunity remaining in this space and the senior management and the board of this combined company are comprised largely of people with extensive experience in cardiovascular drug development.

The Company has near term commercial opportunity by virtue of a filed NDA, we ll talk about that. It has an attractive portfolio for long term growth by virtue of the asset that comes from Nuvelo that s ready to start Phase II, we ll talk about that. We re in major cardiovascular markets that is heart failure and anticoagulation for various cardiovascular indications.

The leadership in this Company stretches back literally decades. The pedigree runs through Genentech, SCIOS and Myogen. And we believe that there will be ample opportunity for increased valuation through various value creating milestones that will be arising in the next year which will enhance the funding opportunities.

So, here are the near term milestones in the combined Company. NDA was filed and accepted on were notified on September 19th for a compound called bucindolol, or Gencaro. The merger will be completed by the end of year or early in 2009. NU172, which is a short acting, short-term anticoagulant for the bypass surgery indication, will begin a Phase II trial end of year or early next year.

There s a companion genetic test for the drug whose NDA is filed, that PMA will be submitted in about a month or so. We anticipate that bucindolol/Gencaro will have a cardio renal advisory meeting that will likely occur sometime mid first quarter 2009. The PDUFA date for Gencaro is May 31st, and the launch date for Gencaro is targeted for early 2010.

Gencaro or bucindolol will become the first personalized treatment for heart failure and the first pharmacogenetically targeted cardiovascular drug. It is a next generation either third or fourth generation, depending on how you define generations, beta-blocker with unique pharmacology. Again, it will be the first genetically targeted cardiovascular drug with the companion genetic test that will be the first simultaneously developed companion genetic test and drug ever at the FDA.

It has the potential through its pharmacogenetic targeting to be indicative for 50% of the heart failure population. As you know, this is a very large market. There are several important potential follow on indications that also exhibit pharmacogenetic enhancement of response. Two of them are important, arrhythmias, atrial fibrillation, and VT/VF. And it also has potential in the hypertension space through pharmacogenetic targeting.

So, the market opportunity for bucindolol/Gencaro is great. There are lots, millions, 6 million to 7 million, in fact, heart failure patients in the US. 550,000 new patients join this club annually. Beta-blockers are arguably considered to be the best, most effective drug class in chronic heart failure, but they are actually somewhat difficult to administer.

You have to take your time, in terms of up titrating after starting at a very low dose. Not every patient responds. There s fairly marked [heterogenative] response. And we believe that the pharmcogenetic targeting will help in terms of being able to deliver this beta-blocker; or would help, essentially, for any beta-blocker. Although this is the only beta-blocker that exhibits the pharmacogenetic profile that we re going to be describing.

Personalized medicine, you re all familiar with. The idea here, is to improve the therapeutic index by targeting a response as subpopulation. The subpopulation would have less potential for adverse affects. And if you do improve the therapeutic index, working from both sides of the TI equation, you will improve cost of the heath care system.

In fact, the pharmaco economic data surrounding this drug is quite impressive. I m not going to have time to show it. And so, the idea here is basically to improve the efficacy of the drug, the safety of the drug and reduce costs.

So, it turns out that the response of subpopulation for Gencaro comprises 50% of the US population. And so this is not a small niche subgroup we re talking about here. And it turns out that the genetic tests that are being developed is actually easily done and will be widely available. And the turnaround time will be conducive to rapid decision making.

So, this is about the genetic test it s being developed in collaboration with Laboratory Corporation of America. We decided to partner this, as opposed to retain this, for various reasons. There ll be a 48-hour turnaround time on this test. They ll be unique platform of genotyping coming from third wave technology. And again, there is a 510k/PMA that will be submitted in a month or so and it s on track to be reviewed in the same time frame as the NDA for the drug and the approvals will come out at least contemporaneously if not simultaneously.

So, the basis for the pharmacogenetic targeting of Gencaro actually is due to the unique pharmacology of the bucindolol interacting specifically with pharmacogenetic variance or genetic variance of adrenergic receptors. So, over here, on the right, they re basically two unique properties, pharmacologic properties of bucindolol that are relevant to this.

One is that bucindolol is the only beta-blocker, at least the only one that we have tested in our laboratory that exhibits inverse agonism for the dominant, high functioning beta 1 adrenergic receptor in the human heart. Inverse agonism means the drug inactivates receptors that are in a constituently active state. That turns out to be important for the enhanced efficacy in that genotype.

The other unique property of the drug is that it s the only beta-blocker that lowers norepinephrine. No other beta-blocker will reduce systemic adrenergic activity. And that property in turn acts with another set of polymorphisms of the or the alpha 2 adrenergic receptor which basically regulates norepinephrine release. We ll talk about how that works on the next slide.

This is a cartoon of the neuroeffector junction in the heart. Adrenergic neuron shown here, cardiomyocyte here. Bucindolol blocks the beta-1 receptor, not only blocks it, but prevents norepinephrine from occupying the receptor. All beta-blockers do that. But it also inactivates these receptors which have a high propensity to be constituently activated if there of this genotype, the beta-1 ArgArg genotype. It is the only beta-blocker that actually does this. And this, we believe, is what causes the enhanced response in patients with that genotype.

The other version of this receptor is a glycine at the 389 position. And there is some efficacy of the drug in patients with that receptor or that genotype, but it s nowhere near the efficacy that you find with the beta-1 ArgArg. The norepinephrine lowering is due to beta-2 receptor blockade, but the regulation of norepinephrine release is greatly influenced by alpha 2 C receptors, which come in two types.

One is the wild type, shown here, and the other is a deletion polymorphism; a deletion variation of the alpha 2 C receptor — a four amino acid deletion. And that variant basically destroys the function of the receptor. And when this alpha-2 C receptor variant is present, the norepinephrine lowering property of bucindolol is greatly enhanced. And exaggerated norepinephrine lowering actually is not conducive to good outcomes in heart failure. A small amount of norepinephrine lowering associated with this receptor, the wild type receptor, on the other hand enhances efficacy.

So, the bottom line is, when you have this alpha-2 C deletion variant, coupled with this beta-1 389 glycine variant, you have a situation where patients are prone to getting into trouble and efficacy is essentially lost with this combination. And this combination basically is present in 10% to 13% of patients. Over here, patients with the beta-1 389 homozygous state responses are markedly enhanced.

So, here are just some outcomes across clinical trials. The three data columns on the left are data from US clinical trials, that is trials conducted in US patients. The data are exhibited as reduction in event rates. This is the Phase III trial done with bucindolol called BEST. These reductions in event rates across these major clinical endpoints all primary and secondary endpoints of this trial are statistically significant.

Most of them have very small P values, less than .01. The one that s not quite significant is the primary endpoint which had a P value of .053. The data across the entire cohort of these patients though, in this trial, as well as the Phase II data will be the basis for approval of bucindolol. The pharmacogenetic targeting will be how we select the patients to be actually treated.

So, in addition, we have two other data columns with US patients treated in Phase III heart failure trials. This is the sum total of all US patients enrolled in Phase III heart failure intention to treat trials. And just looking at the all cause mortality endpoint, you can see that in the MERIT trial, there actually was not a reduction in this endpoint, in fact a 5% increase. Here s the COPERNICUS trial where there s a small reduction, not significant.

And over here are the data with beta-blockers. In the COPERNICUS and MERIT trials, which include three-fourths of the patients coming from Europe. And when you enroll European patients, you essentially get a better response. And these are very impressive responses and very different in the US. And then you take the beta-1 ArgArg very favorable genotype here out of BEST and here are the reductions in clinical endpoints. And they exceed, numerically in every case of what is obtained, even under the [best] conditions with the most responsive patients in other clinical trials.

So, here are the three genotype groupings. The very favorable genotype that will be will literally have a circle drawn around it, in terms of who we want to treat with this drug shown here. Here are the reduction in endpoints. You ve already seen most of these data. Over here is this unfavorable genotype the beta-1 Gly and the alpha-2 C deletion in combination, 13% of BEST, 10% of the general population.

These event rates or these changes in event incidence basically cluster around zero. Some are actually worse than a placebo, with an arrow up here for cardiovascular mortality. For example, some show a slight reduction in event rate. But if you average across all major clinical endpoints, you end up with zero efficacy. And so, these patients, we believe, should not be treated.

So, again, here s a summary of the timelines for major events to expect in the coming year. The filing has occurred, as we ve said, notified by the FDA on September 19th. LabCorp s PMA going in in about a month or so; Cardio renal advisory meeting expected next April or so. PDUFA date late May; and then commercial launch in 2010.

So, we intend to commercialize this drug ourselves. Based on the fact that a specialty sales force is ideally suited for the heart-failure market, which is driven by heart-failure cardiologists. Dick Brewer is the President and CEO of ARCA biopharma who s a very experienced commercialization executive with experience from Genentech, as well as from SCIOS and a track record in the space of heart failure.

We think that pricing and reimbursement will not be an issue. I m not going to go into detail here on this. We re going to price at the upper range. Essentially on the same range as the current Coreg or carvedilol pricing. Based on discussions with Medicare, and based on our consultants, we believe that we ll be able to operate within Part D, in the second tier, and even up into the first tier, potentially based on our pharmacogenetic our pharmacoeconomic data. And then the test will be covered by Medicare Part B, and that does not appear to be an issue, at least according to LabCorp.

So, onto the long-term potential of the Company which is invested in NU172. This is a short acting anticoagulant. It s basically a 26 nucleotide DNA aptamer, thrombin inhibitor. And it will be focused, initially at least, on the coronary artery bypass market. And the idea here is to replace heparin.

And so, I m not going to go through this but there are a lot of criteria, in terms of what you would want at an ideal, short acting anticoagulant. They are shown here. Importantly, you want something that has rapid onset and rapid offset, so you get rapid reversal of anticoagulation and you don't have to use an antidote, and that s certainly the case here.

There are other idea characteristics, and NU172 basically has all of these. And so, I m going to show you data from the Phase IIb trial that was recently completed. This is in normal volunteers and it consisted of a 2 milligram per kilogram bolus, followed by an infusion of 6 milligrams per kilogram per hour. And the idea was to look at the consistency of the anticoagulation profile, and obviously in Phase I to look at safety.

There were no safety issues. And here s the anticoagulation on the Y axis excuse me, on the Y axis is the ACT. And you can see at the end of the bolus and the beginning of the infusion, there s a rapid achievement of profound anticoagulation at 400 in an ACT is easily what you need for bypass surgery or any other anticoagulation.

And during the infusion there s and absolute straight line in terms of the ACT. And as soon as you shutoff the infusion, there s basically rapid reversal of the anticoagulation, and we believe this is an ideal profile.

So, that s the story of this combined company. Thank you, and I d be happy to entertain any questions.

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### **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 transcript 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 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.