

*These are my personal notes/transcriptions from listening to the June 25 Advaxis Conference call/update. It is not meant to be a word for word transcription. Access is provided to other Advaxis investors as a convenience. Investors are responsible for doing their own due diligence and verification of facts.*

**Here, I'm adding my own impression & thoughts about today's conference:**

- 1) We are reminded that LmLLO is the only other agent besides Avastin that has met GOG's strict requirement of 20% or greater 12 months survival threshold in advanced cervical cancer. In fact, LmLLO reached 27%, but several patients are still alive. The update will occur in September at which time we'll potentially see a revised higher rate. We're reminded why GOG, the collaborative group that actually sets the treatment flowchart for gynecological diseases, has been so eager to drive the trials, especially pushing treatment to earlier stage disease.
- 2) It is highly encouraging to me to see that both GOG and ADXS management understand the ongoing significance and importance of aggressively pushing into the adjuvant space. This is highlighted when asked about a "Plan B" in case the FDA does not grant SPA. The AIM2CERV SPA being designed for adjuvant treatment (in combination with chemo/radiation) in curative intent settings may not be as easily approved by the FDA -- presumably because when you've cut out or irradiated all tumors (curative intent), subsequent determination of value-add of LmLLO is not as "easily seen" as compared to when you administered LmLLO to widely metastatic patients. In other words, without any tumors solely addressed by LmLLO left to follow, the treatment effect is not as easily evaluated. However, my thinking is that with the India monotherapy metastatic data, which has clearly satisfied GOG's strict requirements, coupled with the rapidly increasing familiarity with how immunotherapy works on the part of FDA reviewers, I have high hopes that the FDA will realize that adjuvant treatment is not only the SENSIBLE thing to do, but the ETHICAL approach. Why wait for these patients to develop widely metastatic disease, when you can quickly intercept and eliminate microscopic seeds in earlier stage? We'll soon know whether the FDA grants SPA in about a month+ from today. Mauro's extensive experience designing these trials should increase probability of acceptance / SPA.
- 3) We're reminded that LmLLO has shown early ZERO 2-year recurrence rate in anal cancer with negligible temporary (24 hour) toxicity. Similar to GOG in cervical, this spectacular early data explains why RTOG/NRG is now seeking to drive a pivotal trial! The competitive significance of these highly respected oncology groups (basically these groups determine the treatment flowchart) -- is that if LmLLO can eventually win approval for early stage disease, in combination with existing modalities, there may be much fewer cases of widely metastatic patients left for Adoptive T cell procedures and other more "intensive" procedures to fight over in the solid tumor space.
- 4) It should be noted that the above impressive efficacy is achieved using LmLLO **monotherapy**. While the preclinical synergy with various checkpoint and costimulatory antibodies remain to be verified in humans, the science is sound, and today, management clearly and unequivocally states this is a major direction that industry has moved towards (no surprises there) and a top priority for Advaxis. Management discussed how they have systematically gone after the main candidates - PD1, PDL1, IDO, and now with Sorrento, the "costims" (OX40, GITR, LAG3, TIM3). it is clear that they see this as a top priority, and rightly so. Significantly, a statement by Mayes matches my own personal view that success in this arena will **greatly increase** shareholder value.
- 5) In today's call, it is clear that a "new" *game-changing* area the company is positioning intently for the future is **targeting of cancer neo-antigens**. (note: I really like how management is always thinking ahead. They were one of the very first to jump into the combination PD1 space and now they are smartly thinking about how to address patient specific antigens). My own personal research in immunotherapy has told me neo-antigens are indeed an important concept. Investors new to neo antigens can easily read up on

pubmed. For example [this article](#). The idea is basically to leverage the ease and flexibility of LmLLO to rapidly engineer Listeria to express these neo-antigens that are specific to each patient (instead of expressing a common antigen such as HPV). My thinking: The implication here would be surgical/biopsy access to a tumor would be required. This would be similar to autologous CAR-T and TIL therapy, only that there would be no creation or manipulation of Tcells outside the body. Rather, the Listeria will be modified and once re-introduced, be able to effectively create in-vivo, a good number of patient specific Tcells. There may indeed be advantages to this approach versus allogeneic Tcell or Dendritic Cell approaches in that T/DC cells tend to require very specific culture environments for optimal survival and expansion. Leaving all of that to happen naturally in the body eliminates room for error from mishandling of immune cells. But being still autologous, I would imagine the final solution must necessarily offer significant cost and logistical advantage over autologous Tcells. For example, some sort of turnkey process, perhaps an “all in one” box that can be installed at clinics/hospitals, where pt biopsy/tumor samples can be immediately converted into appropriate neo-antigen expressing Listeria. No need for round trip shipping of cells or tumor samples. Possibly very quick turnaround time. In order to maintain the logistical advantage of being worldwide scalable, this would be desirable.

- 6) I'm pleased to see that the company clearly thinks that there is room for dose optimization via escalation. They state they are currently evaluating higher doses and fully intend to broadly incorporate higher doses if it turns out to be beneficial.
- 7) When asked about spreading too thin, Dan commented on how they've been getting a fair number of INBOUND inquiries (execs wanting to jump ship into ADXS). This is no surprise to me because of my firm belief that LmLLO will have a sustainable role to play in the I/O landscape. With the company market cap persisting at this ridiculously low value, it is of no surprise that industry execs see big upside in jumping ship.
- 8) On the canine front: it's nice to see the company expects a conditional canine-osteosarcoma license from the USDA in 2016.
- 9) On the global front, it's nice to see that ADXS expects Biocon to submit registration documents with the India FDA by 2nd half of this year. 75K deaths and 140K annual cases is an “epidemic” level problem indeed. I'm adding here a snippet from scottmiyadi that I find interesting:

*scottmiyadi: “Its my belief that Biocon in India may provide a wildcard THIS year to perhaps ameliorate the concern with cash burn and hence future dilutive cash needs. It was telling that there were several references and direct questions with regard to this initiative and although O'Conner and Mayes went out of their way to play it down it was clear that there is something afoot in this arena. Biocon has already applied for approval within the Indian marketplace. Approval means product for sale = licensing revenues, we are talking income folks. Given the dire need for a remedy/treatment for what is an epidemic in the subcontinent this means real \$, perhaps this calendar year. I think it's safe to say that is nowhere at this point discounted into the current share price.”*

Wrap up thoughts: All in all, it looks like everything is proceeding as planned, with the exception of the new, tantalizing foray into the neo-antigen space. When queried, management deflects on details of this foray. I will be eagerly watching to see what they come up with. If they can come up with something turnkey/point of care, and if the PD1/other checkpoint synergies materialize, they could really stand a strong chance to take a huge chunk of the market, especially if they keep up their aggressive push to early stage/adjuvant. In other words, there will be very few heavily metastatic patients left for the more “intensive” treatments like CAR-T/TCR (with the exception possibly being ZIOP point of care allogeneic/rapid turnaround/safety switch controlled). And maybe a final nail-in-the-coffin for adoptive TIL procedures (LBIO).

## NOTES / TRANSCRIPTION

In the first portion, Dan goes over the various milestones the company had set and evaluates how the company has fared in meeting them. I skip this portion as it is described in detail elsewhere including at:

<http://finance.yahoo.com/news/adxs-key-milestones-2h15-adxs-183500901.html>

### Business front

- in Jan said will conduct analyst & investor day. Done.
- said we'll continue to see clinical collaborations with other immunotherapies. Done.
- said wanted to set regional partnerships with ADXS HPV in latam. On track. Greg will update.

### OVERALL STATE OF BUSINESS

- exit 2014 with 1 candidate. Now have 3 proprietary.
- I expect at least one new candidate in 2016.
- we see convergence of interest on our Lm technology, not only in important cooperative groups, but also our internal team has been building momentum. Three important hires. Manufacturing, regulatory and clinical ops.
- ADXS now able to attract accomplished execs among the best industry has to offer.
- completed 2 financings. Raised \$140m since late 2013. Now approx \$100m in cash on BS.

### Cervical

- of a multitude of other agents evaluated by GOG in 17 trials, GOG determined that 20% or greater 12 month survival as a threshold for clinical relevance. Only one agent in history has successfully reached this threshold, namely Avastin.
- In early 2015, GOG informed ADXS that LmLLO had met their these strict requirements.
- 27% pts reached 12 mo survival. But several still alive.
- In May, we got more data about these last several pts. The update will occur in Sep, potentially ratcheting up the 12 month survival rate.

### Anal

- 12000 pts diagnosed, no improvements since 1970s
- Like GOG cervical, this is an investigator sponsored study. Open label. Non random. Early stage.
- In march, presented at scientific meeting. 10 of 10 complete responses.
- To date NO patients have recurred. Several pts gone over 2 years.
- Historical 2 year recurrence rate is around 45% (compared to ADXS 0%)
- Well tolerated. All toxicities resolved within 24 hrs. Chills. Rigors. Nausea.
- Caused NRG oncology to see if ADXS and Brown were willing to move to PIVOTAL setting.
- ADXS indicated we were interested. NRG is now seeking NCI support. Could start in 2016 if NCI support is forthcoming.

### Dan then talked about the new hires

- Maya Pujols - 20+ years manufacturing experience. Expertise will be essential as ADXS scales.
- Fred Frullo - formally global regulatory strategy at Bristol
- Tom Hare - VP of clinic ops. Built Incyte's clinical ops from something that looked very much like ADXS today into 50 programs at Incyte.

### Dave Mauro on clinical updates

## **CERVICAL**

- Talks about the recent SPA filing (45 days for FDA to get back)
- Expects FDA initial comments soon. Will engage with FDA on subsequent rounds to finalize. Hope to finalize Phase 3 trial before end of this year. However, will depend on length of SPA process.
- Will continue to evaluate women with end stage disease. ADXS HPV with higher doses. Expect to have this data available in 1H2016.

## **WINDOW OF OPPORTUNITY**

- H&N study
- immunologic impact on blood & tumor before and after surgery
- 9 enrolled. 10 target. Data available First half 2016.

## **ADXS-INCYTE**

- ADXS-HPV + IDO1. June 1 announced combination IND has been cleared by FDA.
- on track for 2nd half of 2015. Will evaluate safety and efficacy as mono & in combination in 20 pts with early stage cervical cancer. Prelim data second half of 2016.

## **ADXS-MedImmune**

- Safety/Efficacy in combo with anti PDL1
- IND accepted late 2014 for Phase1/2 with advanced recurrent/refractory and HPV associated H&N cancer.
- Pt enrollment this summer.
- Part A combination data in 1H2016.

## **ADXS-Merck**

- Keynote046 will establish max tolerated dose of ADXS-PSA alone and in combination with Keytruda
- Previously treated metastatic castrate resistant Prostate cancer.
- Previously seen antitumor response in preclinical. Suggesting that such a combination could be a promising alternative to current Standard of Care.
- April announced first patient dosed.
- Enrollment should be complete end of this year.

With respect to all of these combinations, disclosure of data will require agreement by partners.

## **CANINE**

Continue to collaborate with UPenn school of Vet Med to develop HER2 for dogs.

Prelim data presented at AACR - in approx 10 companion dogs, ADXS-HER2 in combination with palliative radiation delayed and prolonged survival, who are not candidates for surgery & chemo.

Importantly, this is the FIRST demonstration of Preclinical synergy between LmLLO and radiation.

May have important translational relevance for human pts for Osteosarcoma, as well as Breast, gastric, Esophageal, Lung.

Canine licensed to Aratana therapeutics.

Expect conditional license from USDA in 2016 based upon feedback from Aratana this spring.

## **Mayes on Business collaborations**

- He immediately starts talking about how it's becoming clear to the I/O community that combination strategies may produce superior benefits.
- Emphasizes how ADXS has demonstrated ability to **rapidly move into clinical programs and clear combination INDs within 30 days of filing.**
- Beyond Merck, MedImmune, Incyte, ADXS has most recently moved into non exclusive research with Sorrento in G1TR/OX40/LAG3/TIM3

- Looks forward to planning clinical trials with Sorrento to evaluate
- Primary goal is to determine if combination efficacy exists
- **SAYS THE COMPANY THINKS THAT COMBINATIONS WILL YIELD SIGNIFICANTLY HIGHER VALUATION FOR ADXS**

ADXS-HPV - Biocon plans to file for product registration THIS SUMMER

- HPV associated cancers remain at epidemic levels in this area (India)

### **Dan comes back on**

Talks about people asking him "what most excites him about ADXS"?

**Says the most exciting element is the UNIQUENESS and VERSATILITY and potential to be GAME CHANGING Specifically neo-antigens.**

Technological innovations have enabled pt specific tumors to be analyzed for neo-antigens

Recent research indicates these neo antigens may play a highly important role in immune responses

"A new era of personalized medicine remains around the corner"

Will focus specifically on leveraging LmLLO flexibility to address these

### **QUESTIONS**

#### **QUESTIONS BY RAM SELVARAJU of MLV**

Note: this is the Analyst with PhD in cellular immunology, MBA from Cornell that rvga128 pointed out

**- Analyst: very impressed by HOW QUICKLY you're moved forward on SO MANY FRONTS**

- Have 3 questions
- Cervical cancer study - how quickly you can proceed with enrollment. And how important is the SPA. For example, if FDA does not grant SPA, would you battle them or would you proceed anyway.
- Secondly, please comment on timeline for progress with SRNE for when you will initiate clinical study there. And how you envision it going forward with regard to SRNE's potential involvement in cell based immunotherapy.
- Finally, for canine osteo, can you comment on whether you plan to seek MUMS designation (similar to Orphan)

(1) Phase3 enrollment SPA question - Mauro: we expect first round of comments back within the next few weeks. Will have to see. SPA is certainly big. But we don't want to delay the study if we spend a lot of time going over small parts of the protocol. Clearly we want to get buy in on the indication as well as primary end points. In terms of enrollment - we are looking at feasibility. Our expectation around most phase 3 studies would be to have enrollment between 12-18.

(2) SRNE collaboration - Plan to prepare assets for combo collaboration over the balance of this year, with studies commencing one in first half 2016 and other in 2nd half.

(3) MUMS (like Orphan Designation but for animals). Aratana is handling. We expect Aratana is taking full advantage of all regulatory advantages.

#### **QUESTIONS BY DAVID MOSCOWITZ at EquitiesIQ**

Q: Mt Sinai H&N cancer trial - you expect enrollment by EOY. When can we see data?

Mauro: two part study. Stage 1 enrolls 10 pts on treatment arm. 10 pts on control arm. We're at 9 pts right now.

Expect 10th pt by EOY. Our hope is to have data from 10 treated pt in first half 2016. End points are looking at effects on blood and tumor. Biology. No efficacy endpoints. We hope to show nice mechanism of action.

Q: neo-antigen program. Strategic side, how you plan to approach that? And Lm differentiation vs other immunotherapy programs?

Mauro: This is a very good example where the science & feasibility is catching up as it relates to personalized medicine. We've been monitoring this over past several months. Come to the view that specifically our technology has unique ability to maximize potential by neo antigens.

Petit: we believe ADXS platform is **the most effective way to generate T-cell immunity**. Override Tregs/MDSCs in the tumor microenvironment. Also have the ability to engineer plasmids to present antigens of interest. Clear now that Neo-epitopes are the best handles for immune system to get a hold of. High throughput DNA sequencing technology will enable us to adapt the ADXS platform to grab hold of these neo antigens.

Q: back to the strategic progress - is this something you'll develop in house or are there companies out there you'd like to deal with?

A: we're evaluating all that now...

#### **QUESTIONS BY DAVID XXX from xxx capital**

Q: Top level question on the technology. A lot of people out there are doing combinations. can you go into mechanism of Lm technology itself and why it would be interesting?

A: LmLLO is a perfect complement to checkpoint inhibitor. 2 modes of failure.

- 1) insufficient quantity of Tcells generated
- 2) shutdown by PDL1 (tolerance) or run into MSDC/Tregs.

The Advaxis Vector itself has the effect of MULTIPLE adjuvants. LLO fusion reduces MSDC/Tregs in the microenvironment. We can solve 2 of the problems that hold back checkpoints. Beyond that, there are other mechanisms besides the checkpoints. There are mediators of immune tolerance. Tregs and MDSCs in the TME are the next frontier. By nature, LmLLO already addresses that problem. We see future synergy with those agents as well.

Q: the areas you're targeting - what other areas would you want to target besides HPV, HER2 etc.

A: we see targets in 2 categories. Targets in tumors in groups of patients. Like PSA, HPV-E7. Other known targets. Mutated RAS, ALK, RAF etc. Common targets.

Beyond that, there are other targets that are specific to individual tumors. We're evaluating both the common and the less common targets.

Greg: Just to complement Robert's background - we are undergoing a fairly complete and thorough review of antigens in house and outside, that may be appropriate to bring forward in an IND later this year or next year.

#### **QUESTIONS BY Swayampakula Ramakanth of HC Wainwright**

Q: could you please highlight the data from previous studies that could help us understand the high risk localized cervical cancer pt, especially those that are targeted in the AIM2CERV study and what should we expect from the outcome.

A: Mauro: typically we enrolled stage 1 all the way up to stage 4a. what we've tried to do in this study is target those patients that have the highest risk of recurrence. In other words, those that would have the greatest benefit. Data is mixed. In some, recurring within 12 months. Earlier stage disease recur somewhere before 24 months. In this study, we are trying to identify highest risk pts that recur within 12-18 mo. This study is unique in that there's never been a study specifically run in this pt population.

Q: in your Indian study or other studies with this pt population, do you have any data for this sub-population?

A: good question. Not really. All of our data to date has been in Nth line metastatic population. Historically, when people move into the adjuvant space, as we are doing with AIM2CERV, investigators really like to see very strong data in the metastatic space. **We and GOG believe we've established Proof of Concept in the metastatic space, and we want to move into into adjuvant where we believe we will provide highest patient benefit. We will pursue aggressively. AIM2CERV is in early line of therapy.**

Q: We know you're conducting the high dose study. How do you anticipate using that data, also do you need to see the high dose effects, before planning your late stage studies in the metastatic indication?

A: We think the value in perhaps using a higher dose of ADXS therapy will be primarily in the metastatic setting - where we're treating pts with very large bulky lesions. What we'd like to do is to really understand if higher doses are safe and tolerable as well as efficacious. If that's the case, we will broadly incorporate higher doses into other metastatic diseases. Just to note we're also evaluating higher doses in PSA and HER2 programs. **We believe there is certainly room to increase the dose and possibly increase efficacy.**

Q: Couple of strategic questions. At end of 2014, you had 1 product in clinical development. Now you have 3 products. It's a small number to say, but the number of studies undergoing are numerous. Is there a resource constraint going on at this point? Would you actually have risk of lower efficiency to increase number of clinical programs? What's the push and fold for that?

A: You've seen us adding leaders and doers in this industry. People with track record of success. **In fact, we get a fair number of inbound inquiries to work at this company. Which is tremendous.** To be critical of ourselves, we haven't added early enough some of these resources. Our approach - we wanna be sure that when we add, we definitely have the need, and not adding too quickly. I don't think we're doing that, maybe a little of the opposite. Now, with the studies underway, with the resources we have in house and the external CRO resources, we are adequately staffed to do what's on our plate today. As we look to enhance the levels of trials that we're doing, we'll make sure we have the right people both internally and externally.

Q: One more strategy question. Some of these combination studies getting started. And we're targeting to see data early half 2016. How should we think about the maturation of these relationships into 2016, because at this point, we have little else than sharing of xxx for the current trials. How do you envision your team working with these partners so you can get a good value out of these combinations?

A: Greg touched on this earlier. Our MO has been to first see if we work with leading emerging immunotherapies. PD1/PDL1 are covered. IDO is secure. Monoclonal library gives us access to the costims GITR/OX40/TIM3/LAGE. Without defining economics in those collaborations, but first understanding whether we see synergies. **The one advantage we have here - are there are 2 Lm immunotherapy companies. There are several checkpoint/costim companies. Gives us an advantage, not only for shareholders, but for collaboration.**

Q: What's the current status of the license programs with Biocon and global Pharma

A: GlobalBiopharma - expect them to initiate a trial in non smoking asian women with HPV associated lung 2nd half of this year. With Biocon, we expect them to submit registration documents with India FDA by 2nd half of this year.

#### **QUESTIONS BY David Sands at xxxx capital:**

Q: You've proven your ability to execute. The proof is in the pipeline, enrollment of pts, and worldwide alliances. My question is about SPA for cervical. What is your plan B in case you don't get it?

A: When we look at the SPA, the goal of what we're trying to do is to really get alignment on the protocol with the FDA. 2 things we can do. 1, take the advice and move forward into the study that we planned. Really trying to understand where we're aligned, and where we're not. If the FDA feels that the adjuvant approach is not the best approach, then we will continue to develop the drug in the metastatic space. Perhaps the original plan of Phase3 for the company or else 265 study. We think we have lots of options, many which are positive.

Q: Next events: biocon could provide good news? Can you provide some vision in terms of how many pts biocon expects to treat and where do you see the halo effect in the USA?

A: The goal of biocon was to take the India study and present that as an early opportunity to DCTI (India FDA). We've been working the past several months to prepare the dossier with Biocon (they're done the heavy lifting). **Those activities have gone well and near completion.** By 2nd half of this year (Greg commented more like this summer). We'd like to keep expectations on the low side. Again, it's one study. 110 pts. We and Biocon very much like the data. Since then, we've had emergence of data from 0265. That data will be included in the dossier to India FDA. Possible they will come back and ask for more work. As you probably know, cervical cancer in India is a major health problem. Over 75K annual deaths from cervical. 140K cases per year incidence rate. Unmet medical need is Extreme. We really appreciate Biocon has recognized this.