

Newsletter October 2016

Øystein Rekdal,
Chief Scientific Officer:

PRE-CLINICAL EVIDENCE SHOWS LTX-315 MAKES "COLD" TUMOURS "HOT"



Together with a highly recognized oncological research environment at Harvard University, Lytix Biopharma is investigating LTX-315's ability to make "cold" tumours "hot", and current evidence points to an increase in immune cells in tumours.

A "cold" tumour contains a low number of T cells and is not highly responsive to immunotherapy treatments. If LTX-315 does help increase the number of immune cells within the tumour, it will likely also increase the effect of other immunotherapy treatments and be a strong candidate for combination therapies.

Øystein Rekdal, Chief Scientific Officer of Lytix Biopharma, is currently working with several distinguished research teams to examine the effect of LTX-315 in gene-engineered tumour models and metastatic cancer models. Current evidence points to an increase in immune cells in both injected and non-injected tumours.

- The indications that our molecule is helping T cells infiltrate "cold" tumours is very exciting. "Cold" tumours do not typically respond well to immunotherapy treatment, but our treatment may be able to change that. It seems that LTX-315 does not only increase the number of T cells but also expands T cell clonality, meaning that different T cell clones recognize different tumour antigens. If LTX-315 increases the effect of other immunotherapies, it will be a very useful tool when used in combination with other drugs, Rekdal explains.

In addition to its collaboration with Harvard, Lytix Biopharma is engaged in ongoing research with Oslo University Hospital and the Gustave Roussy Institute of Oncology in Paris (IGR).

Together with IGR, Lytix Biopharma has published findings in five scientific journals regarding the mode of action and the use of LTX-315 in combination with other well-known immune stimulants. This research has generated the attention of the international immune oncology community. At the International Cancer Immunotherapy Conference in New York in September, Guido Kroemer (one of the Conference Co-chairpersons) presented LTX-315 as one of several promising candidates for cancer treatment in the future.

New findings lead to adjustments to the treatment protocol in the LTX-315 trials

The clinical trial protocol for LTX-315 underwent a significant amendment this summer, with changes made to improve the safety profile of the drug.

Four patients in the current study experienced significant allergy-like reactions immediately after receiving a LTX-315 injection. While all recovered quickly, appropriate treatment changes have been made to reduce or eliminate the risk of clinically significant allergic reactions. LTX-315 does not cause any other significant side-effects (e.g. bone marrow suppression, cardiac, renal or hepatic toxicity) unlike many chemotherapy and targeted agents.

Dr. Andrew Saunders, Chief Medical Officer in Lytix Biopharma, believes that the new treatment protocol will not only improve the drug's safety profile but may also increase the efficacy of LTX-315.

-These findings are important. The adjustments we have made are intended primarily to reduce the risk of clinically significant allergic reactions. However, they will also potentially maximize the tumour response due to the more intensive LTX-315 injection schedule, which will be six injection days in 3 weeks. In contrast to most patients treated to date, where most tumour lesions were injected once per injection day, larger tumour lesions will now receive up to 4 injections per injection day, Dr. Saunders says.

The reduction in the LTX-315 treatment duration will also decrease the risk of development of antibodies (IgE) against LTX-315, which are believed to be the most

likely cause of clinically significant allergic reactions. The risk of such reactions increases with increasing duration of treatment or exposure to the allergen - in this case potentially LTX-315.

-The upside to changing our protocol is that in addition to having a safer protocol, we also have a more practical and optimized treatment schedule that will be more acceptable to patients and treating physicians, Saunders says.

Patients will also be tested for the presence of antibodies against LTX-315 and receive three different allergy preventative treatments at the start of each injection day. Clear and standardized treatment guidelines have been issued to standardize treatment of all allergy-like reactions.



Dr. Andrew Saunders
Chief Medical Officer in
Lytix Biopharma

RECRUITMENT TO RESUME IN NOVEMBER

Thus far, 28 patients are enrolled in the trial, all treated with LTX-315 monotherapy.

The newly amended protocol will have three treatment arms, monotherapy (all tumour types), in combination with Ipilimumab (melanoma) and in combination with Pembrolizumab (Breast cancer). Ipilimumab and Pembrolizumab are anti-CTLA4 and anti-PD1 checkpoint inhibitors, respectively. Each arm consists of 9-12 patients. Patients enrolled in the first arm, monotherapy with LTX-315, will be assessed for evidence of an abscopal effect, meaning that the treatment has also affected non-injected tumors (shrinkage and infiltration of immune cells on biopsy).

The second and third arms of the study focus on using LTX-315 in combination with other immunotherapy drugs. Arm B includes patients with advanced stage, malignant melanoma type skin cancer. Patients are given a combination of LTX-315 and ipilimumab, produced by Bristol Meyers Squibb under the brand name Yervoy. Arm C includes patients with advanced stage breast cancer and a combination of LTX-315 and Merck's pembrolizumab.

Saunders believes that these treatments will have a strong synergistic effect with LTX-315 and expects that combination therapies hold the most potential for future product development.

Evidence of abscopal effect on non-injected tumours

In June 2016, Lytix Biopharma documented the first biopsy proven (histological) evidence that LTX-315 eradicated non-injected tumour lesions in a patient undergoing treatment with LTX-315 monotherapy.

A 38 year-old female patient with widespread, advanced adrenocortical adenocarcinoma was enrolled in the study at the Institute Curie in Paris. The patient had a long history of prior treatments including several surgeries. Chemotherapy, radiotherapy and most recently, prior to LTX-315 treatment, six-months of treatment with anti PDL1 immunotherapy drug was administered. Her best response to anti PDL1 was stable disease for 4 months and then progression of her disease during the last 2 months of treatment. The first injections with LTX-315 were administered 5 weeks after the anti PDL1 treatment was discontinued. After 7 LTX-315 injections in 5 weeks, the patient showed stabilization of her disease and shrinkage in several non-injected distant tumors (lung and liver tumours). A large abdominal flank lesion that was not injected and was biopsied at week 6 after 7 LTX-315 injec-

tions showed no tumour present - only dead (necrotic) cells. This compared to a biopsy at baseline prior to LTX-315 treatment of the same lesion that confirmed tumour present. This patient remains in stable disease and further follow up is awaited.

-This is a major milestone. We have confirmed no viable tumour left in a distant, non-injected tumour lesion. We suspect that this remarkable effect is possibly due to the use of two sequential immune therapies, anti-PDL1 followed by LTX-315. This indicates that the use of combination therapy is probably key and is grounds for our excitement in embarking now on the assessment of LTX-315 in combination in the coming months. The combination of LTX-315 with other immunotherapy drugs may produce dramatic results, says Dr. Andrew Saunders.



Håkan Wickholm
CEO in
Lytix Biopharma

Letter from the CEO

RECENT DEVELOPMENTS

Since our last newsletter Lytix Biopharma has seen decisive developments in several areas:

- The recruitment/inclusion of hospitals for our Phase I study with three arms (monotherapy, as well as in combinations with immune checkpoint inhibitors (ICIs) for melanoma and breast cancer treatment) has progressed well.
- Clinical (biopsy proven) confirmation of an abscopal effect (response in distant non-injected tumour).
- Important scientific progress has been made with regards to how LTX-315 potentially can improve outcome in adoptive T-cell therapies.
- Data indicating that LTX-315 can make "cold" tumours "hot"; facilitating many patients responding to checkpoint inhibitors as most do not currently respond.
- Cooperation with Harvard University and Professor Michael Pittet has been established for the study of LTX-315's ability to convert "cold" tumours to "hot" tumours.
- Cooperation with other renowned institutions like Institut Gustave Roussy, Paris and Weill Cornell Medicine in New York has been renewed and/or enhanced.
- On the 'negative' side, there has been a delay in the ongoing LTX-315 Phase I study due to necessary changes and improvements of the study protocol. These changes will however enhance the probability of the study's success in the longer run.
- Finally, Lytix Biopharma has established close cooperation with financial advisors to ensure that funding is adequate, both in the medium and long term.

Based on the developments over the past few months, I feel even more confident that Lytix Biopharma's studies and product development is approaching a level that will lead to even more interest for LTX-315.

NEW FINANCING

In this context, Lytix Biopharma's Board has decided to go ahead with a pre-IPO financing round in November/December, with the stated goal of raising a minimum of 60 mNOK to fund the rest of the Phase I study, which is expected to be concluded by the end of Q2 2017.

The pre-IPO will be followed by an IPO, presently scheduled for Q3/Q4 of 2017, i.e. after final read-outs are available from the Phase I study. Thereafter, Lytix Biopharma intends to raise around 300 mNOK in an IPO to fund Phase II studies for LTX-315 in combination with ICIs.

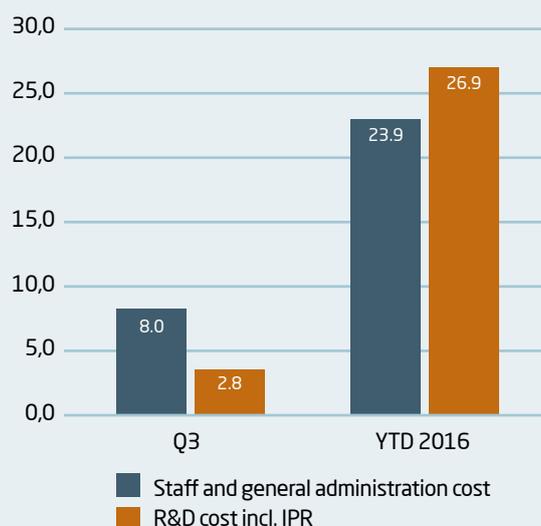
We will revert to our shareholders during November with an update on the schedule and terms for the pre-IPO.

PRELIMINARY FINANCIALS Q3 2016 (MNOK)

	Q3/2016	YTD 2016
Income - public grants, other revenue	0.4	4.2
Staff and general administration cost	-8.0	-26.9
R&D cost incl. IPR	-2.8	-23.9
Total Operational Cost	-10.8	-50.8
EBIT	-10.4	-46.6

Staff cost include all employed R&D personnel. Earned tax refund («Skattefunn») is not included and will be booked as a reduction in operational cost by year-end. All figures are for the parent company, preliminary and not audited.

COST DISTRIBUTION Q3 AND YTD 2016 (MNOK)



INCOME

Lytix has in 2016 on-going public grants from The Research Council of Norway and "Skattefunn" (Tax refund). The grants are booked at the time for received payment. In an industry characterized by long-lasting R&D programs with significant implied risk, the financial support from public sources has been very valuable. For our shareholders the grants are essential to relieve risk on the equity capital. The company's management work continually with opportunities for part financing of our comprehensive R&D program with public funding. Other income is minor and related to special consultancy to other companies.

COST AND INVESTMENT

The cost level in Q3 has been significantly lower than planned related to a halt in the current clinical study and later upstart of the planned combination studies within malignant melanoma and breast cancer. In other areas, the cost level has been around the expected level. The company's continued investment in R&D and IPR portfolio is fully expensed. The company financed the 100% owned subsidiary Amicoat AS with 5 mNOK in equity during Q3.

EQUITY AND CASH

The last equity issue took place in January this year with gross proceeds at 79 mNOK.

The board has prepared a strategy in order to finance the extensive R&D program for the forthcoming years. Cash by the end of Q3 was 27.9 mNOK and in combination with incoming public grants, the company has sufficient cash until early 2017.

The company has no interest-bearing debt.

Quality is the “mantra” in everything we do

As CMC Manager at Lytix Biopharma, Mette Husbyn is responsible for planning and coordinating the development of chemical processes, control procedures, documentation and supply for non-clinical and clinical studies of the company's drug candidates.

Mette Husbyn
CMC Manager in
Lytix Biopharma

Husbyn has an MSc in Organic Chemistry from NTNU 1987 and a PhD in Peptide chemistry from UiO 2003



CMC is short for chemistry, manufacturing, and control. Mette Husbyn is involved in the projects from early research phase and throughout all the phases of pharmaceutical development.

- These phases encompass working with the active pharmaceutical ingredient (API), the drug product and the investigational medicinal product (IMP), which is the finished, labeled and packed product ready for use in clinical studies, Husbyn explains.

According to Husbyn, quality is the “mantra” in every stage of pharmaceutical development. Her key tasks include development and optimization of the manufacturing processes and the control procedures throughout the various phases in order to enable a robust scale-up of the processes from e.g. milligrams to kilograms and at the same time ensure that quality is not compromised.

Close partnerships secure high quality standards

As Lytix Biopharma is a virtual company with no manufacturing or other lab capacity, close collaboration with the “right” partners is a key to success.

- Prior to selecting a supplier, we carefully evaluate criteria such as

technical knowledge and abilities, quality systems, reputation and financial situation in addition to cost.

She points out that planning ahead is one of the most important aspects of CMC management.

- In pharmaceutical development, we know for sure that project plans are “living documents” that will need to be adapted throughout the process, Husbyn says.

In general, CMC will make plans based on the clinical plans. Since it may take up to a year from when Lytix Biopharma places an order until the final IMP is ready to be used in clinical studies, looking ahead is essential.

Regulatory compliance across the markets

Husbyn reveals some of the more challenging sides of being CMC Manager.

- We are currently running studies in five different countries. This means that we have to comply with each of the countries' regulatory framework. Although guidelines for the US and most EU countries are similar, we may receive very different questions from the respective assessors, Husbyn explains.

Busy times for Lytix Biopharma

Lytix Biopharma's CMC Manager is currently working on the establishment of a manufacturing process for LTX-315 API that will enable commercial supply. In addition, Husbyn is looking for a new supplier for the company's drug product as the current manufacturer is unable to support late phase and commercial supply.

LATEST NEWS

FROM LYTIX BIOPHARMA

- > In May Lytix Biopharma presented the company in 'The Next Wave Company' session at BioEquity Europe - an annual meeting assembling members of the financial community and business development and licensing professionals in life science.
- > Lytix Biopharma published LTX-315 article in Cell Death and Differentiation. Title: The oncolytic peptide LTX-315 overcomes resistance of cancers to immunotherapy with CTLA4 checkpoint blockade.
- > At CIMT, in Mainz in May, Lytix Biopharma presented LTX-315's ability to make tumors more T-cell inflamed.
- > Lytix Biopharma was represented by Håkan Wickholm (CEO) at BIO International in San Francisco in June, and Lytix Biopharma presented a poster at the International Cancer Cluster Showcase.
- > LTX-315 was featured in two oral presentations at World Preclinical Congress in Boston in June.
- > Håkan Wickholm (CEO of Lytix Biopharma) was representing Lytix Biopharma at Nordic Life Science Days (NLSD) in Stockholm in September, the largest partnering conference for pharmaceutical and biotech companies in Scandinavia.
- > LTX-315 was presented at Basel Life Science week in September.
- > Håkan Wickholm, CEO, represented Lytix Biopharma at Sachs Annual Biotech in Europe Forum. The Forum is recognised as the leading international stage for those interested in investing and partnering in the biotech and life science industry and is highly transactional.
- > Lytix Biopharma has progress in its pipeline. The company is exploring novel second generation oncolytic molecules for treatment of deep seated tumors. LTX-401 is a novel oncolytic β -amino acid derivative with potential immunogenic properties. Two papers have recently been published in high-quality peer-reviewed journals as products of a collaboration with University of Tromsø, Norway, and Institute Gustav Roussy, France.
- > Lytix Biopharma's lead project LTX-315 was presented by Professor Guido Kroemer, Institute Gustave Roussy, as an interesting emerging treatment of solid tumors at the 2nd CRI-CIMT- EATI-AACR International Cancer Immunotherapy Conference, September 25-28, in New York.

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