

## **INVESTOR PRESENTATION**

November 2017





#### **COMPANY IN BRIEF**

Lytix Biopharma is a clinical-stage pharmaceutical company, developing novel immunotherapies to fight cancer.

The company's clinical stage product, LTX-315, reshapes the tumor microenvironment through an effective release of potent immune stimulants and tumor antigens "turning cold tumors hot". The 'release and reshape' effect of LTX-315 sensitize tumors to other types of therapies opening up for a variety of combination treatments.

#### SELECTED COLLABORATORS















#### TODAY'S PRESENTERS



#### **Edwin Klumper**

CEO, M.D., PhD, MBA

- Life science entrepreneur with a strong combination of scientific and business background
- 25 years of experience in in the international pharmaceutical and biotech industry with an expertise in clinical oncology drug development



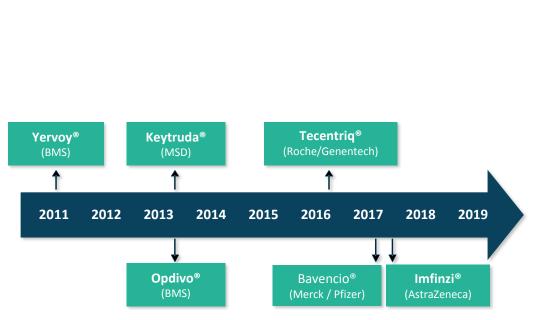
#### Torbjørn Furuseth

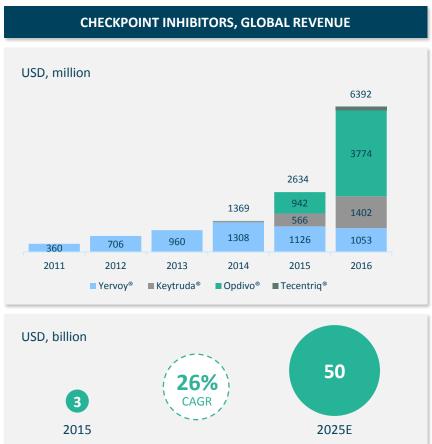
CFO, M.D.

- Entrepreneurial mindset with broad experience from most aspects within life sciences sector
- Management consultant at McKinsey & Co serving clients within the Pharma and Health Care practice
- Medical Doctor with three years of practice

## IMMUNO-ONCOLOGY HAS BECOME THE MOST ATTRACTIVE PHARMACEUTICAL SEGMENT

#### THE FIRST WAVE IN CANCER IMMUNOTHERAPY IS THE IMMUNE CHECKPOINT INHIBITORS

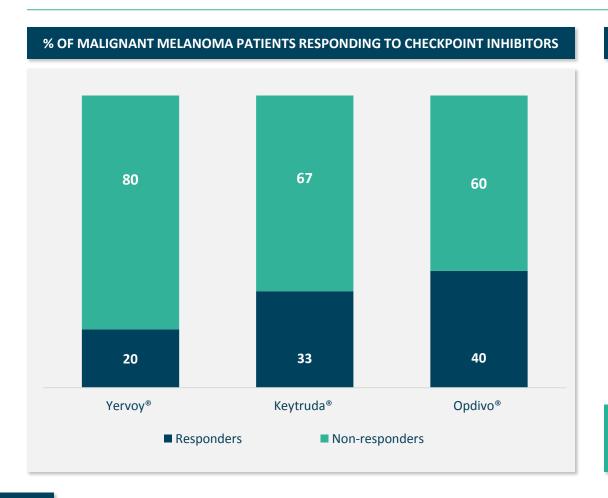






## THE MAIN CHALLENGE IN CANCER IMMUNOTHERAPY IS TO TURN COLD TUMORS HOT

#### ONLY A SUBSET OF PATIENTS RESPOND TO CHECKPOINT INHIBITORS – HIGH T CELL INFILTRATION AIDS RESPONSE



#### HOT TUMORS RESPOND BETTER TO IMMUNOTHERAPY

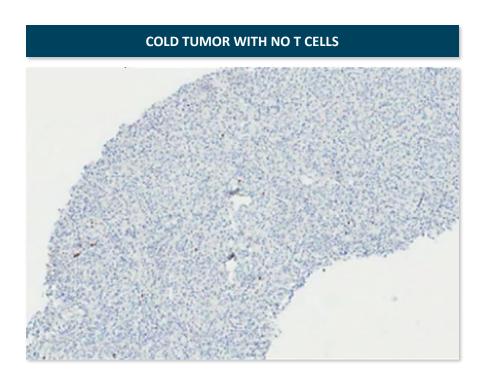
- Checkpoint inhibitors are proving to be effective in several cancer types
- Despite the clinical success of checkpoint inhibitors, only a subset of patients exhibit durable responses
- Immune checkpoint inhibitors seem to work only in "hot" T cell inflamed tumors – tumors exhibiting high levels of cancer specific T cells (killer cells specifically trained to detect and attack cancer cells)

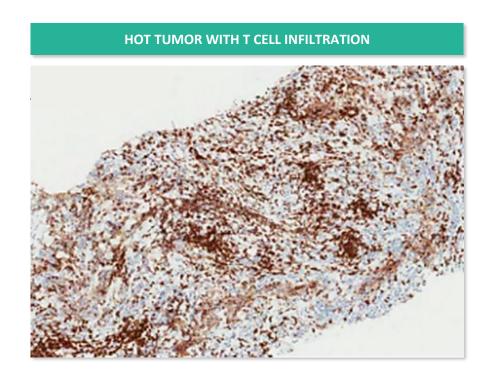
Strong need for compounds that can increase levels of cancer specific T cells in the tumor, i.e. bring the soldiers into the battlefield



# LYTIX' LEAD CANDIDATE, LTX-315, IS A FIRST-IN-CLASS ONCOLYTIC PEPTIDE THAT TURNS "COLD TUMORS HOT"

88% OF EVALUABLE PATIENTS SHOWED ENHANCED CANCER SPECIFIC T CELL INFILTRATION FOLLOWING INJECTION





BASELINE

LTX-315 TREATED



## MARKET OVERVIEW – CURRENT AND PLANNED INDICATIONS

#### **MALIGNANT MELANOMA**

#### METASTATIC PATIENTS

Incidence, USA: 30,000

5 year survival: 18%

Response rate to IO: 33-60%

(Including combinations)

#### TRIPLE NEGATIVE BREAST CANCER



#### METASTATIC PATIENTS

Incidence, USA: 39,000 Incidence, 8MM 115.000

5 year survival: 26%

Response rate to IO: 5-18%

#### **SOFT TISSUE SARCOMA**



#### METASTATIC PATIENTS

Incidence, USA: 1,900-3,700

5 year survival: 16%

Response rate to IO: 8-18%

#### **HEAD AND NECK**



Incidence, USA: 63,000

5 year survival: 20-30%

Response rate to IO: 13-18%

Phase I ongoing - Phase II planned

Phase I ongoing - Phase II planned

**Phase II planned** 

**Phase II planned** 

Robert et al. NEJM.org, April 19, 2015; Postow et al. NEJM.org, April 20, 2015; Robert et al. NEJM.org, November 16, 2014; http://www.cancer.net/cancer-types/breast-cancermetastatic/statistics, Nanda et al. J Clin Oncol 34:2460-2467; Global Data, 2016; Paoluzzi et al. Clin Sarcoma Res (2016) 6:24; Ferris et al. N Engl J Med 2016;375:1856-67. 2016; Pulte et al. The Oncologist 2010;15:994-1001, 2010; Seiwert et al. http://dx.doi.org/10.1016/S1470-2045(16)30066-3

## DRUG DEVELOPMENT PIPELINE

Ongoing

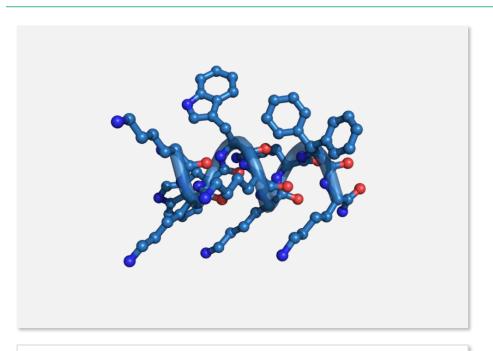
Indication	Program	Research	Preclinical	Phase I	Phase II	Phase III
All solid tumors	LTX-315					
Malignant melanoma	LTX-315 in combo with ipilimumab					
Triple Negative Breast Cancer (TNBC)	LTX-315 in combo with pembrolizumab					
TNBC or malignant melanoma	LTX-315 in combo with checkpoint inhibitor					
Sarcoma	LTX-315 in Adoptive T cell Therapy					
Head & neck cancer	LTX-315 in Neoadjuvant setting					
Deep-seated solid tumors (e.g. liver)	LTX-401					

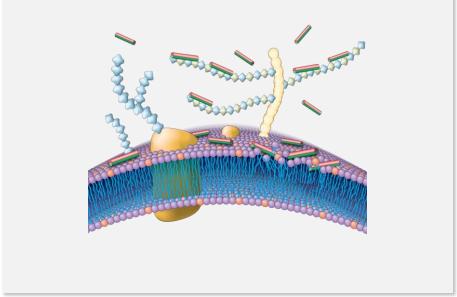
Planned



## LTX-315 IS AN OPTIMIZED MOLECULE DESIGNED FROM HOST DEFENSE PEPTIDE

#### HOST DEFENSE PEPTIDES HAVE A DUAL MODE OF ACTION: DIRECT KILLING AND IMMUNE MODULATION

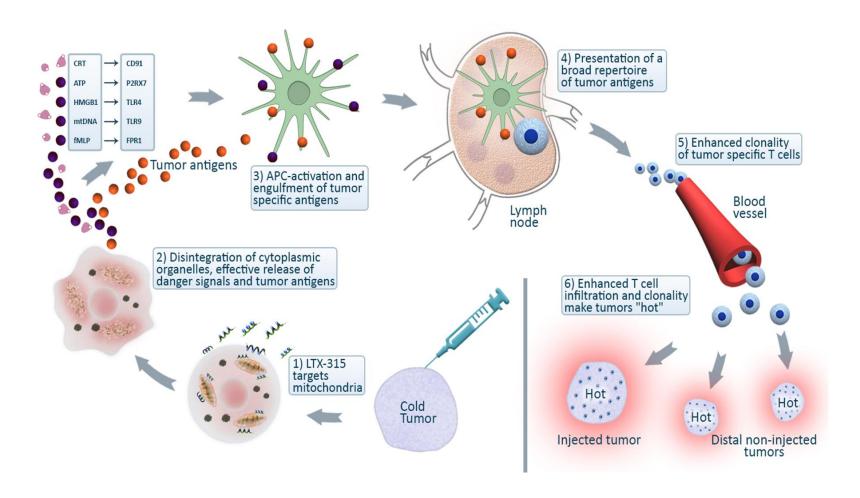




- LTX-315 is composed of five cationic residues and four lipophilic residues, including one synthetic
- It is able to form an amphipathic structure upon interaction with anionic membranes
- LTX-315 shows specificity for cancer cells overexpressing anionic molecules
- Followed by internalization and targeting of intracellular organelles



## LTX-315'S UNIQUE MODE OF ACTION RESULTS IN EFFECTIVE "RELEASE AND RESHAPE" IN THE TUMOR MICROENVIRONMENT





## LTX-315 INCREASES NUMBER AND DIVERSITY OF TUMOR INFILTRATING T CELLS

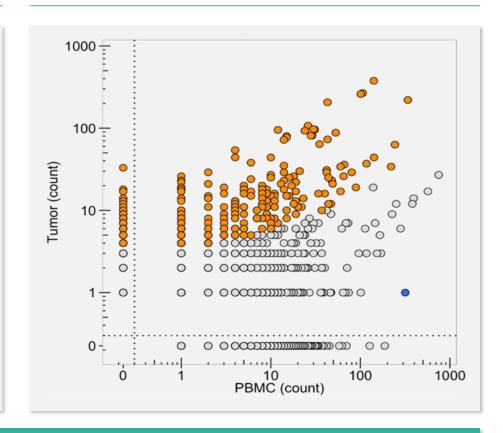
#### **UNTREATED B16 MELANOMA**

# Expanded Stable Contracted

PBMC (count)

100

#### TREATED B16 MELANOMA

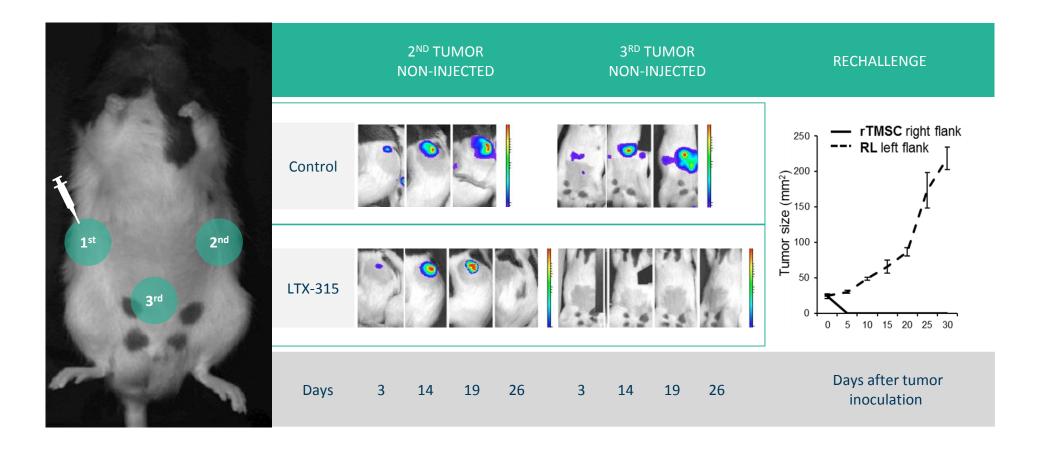


#### **EXPANSION OF T CELL CLONALITY IN TREATED TUMORS**

1000



# LTX-315 DEMONSTRATES SYSTEMIC IMMUNE RESPONSE – COMPLETE REGRESSION WITH TUMOR SPECIFIC MEMORY





## STRONG INTERNATIONAL COLLABORATIONS DEMONSTRATING LTX-315 ANTI-TUMOR EFFECTS



LTX-315's ability to reprogram tumors

Prof M. Pittet



LTX-315's ability to release neo-antigens

Prof R. Schreiber



LTX-315 and involvement of Toll-like receptors (TLR)

Dr. J. Oppenheim



LTX-315's ability to circumvent resistance to PD1- blockade using TLR agonists

Profs L. Zitvogel & G. Kroemer



LTX-315 in combination with immuno-chemotherapy

Prof G. Mælandsmo



LTX-315 in combination with irradiation

Prof S. Demaria



LTX-315 and chemotherapy in translational sarcoma models

Prof B. Brodin



## **OVERVIEW OF LTX-315 CLINICAL PROGRAM**

	2010-2012	2013-2016	2016-2017
Туре	Phase I	Phase I	Phase I/II - Ongoing
Indication	All solid tumors	All solid tumors	Monotherapy arm All solid tumors Combo with pembrolizumab Breast cancer (TN) Combo with ipilimumab Malignant melanoma
Treatment regime	Monotherapy Single lesion	Monotherapy Multiple lesions Sequential Concurrent	One Monotherapy arm Two Combination arms Multiple lesions
<i>&gt;</i>	6 weeks	6 weeks + maintenance until PD	3 weeks
Sites	1	8 🛟 🕽	12
No patients	14	28	3 dose cohorts of 3 patients per cohort <sup>1</sup>



# LTX-315 TURNS TUMORS HOT AND ENSURES INFILTRATION OF CD8+ T CELLS NEEDED TO KILL THE CANCER

COMBINATION WITH PEMBROLIZUMAB: 4 OUT OF 5 EVALUABLE MONOTHERAPY: 15 OUT OF 17 EVALUABLE PATIENTS (88%) **PATIENTS MYO-EPITHELIOMA BREAST CARCINOMA BREAST CARCINOMA BREAST CARCINOMA** 

LTX-315'S ABILITY TO TURN COLD TO HOT CONFIRMED IN PATIENTS



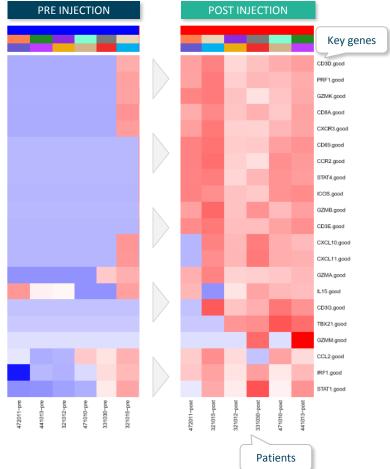
# LTX-315 TURNS TUMORS HOT COMPREHENSIVELY BY UPREGULATING KEY GENES INVOLVED IN TUMOR REGRESSION

#### **COMMENTS**

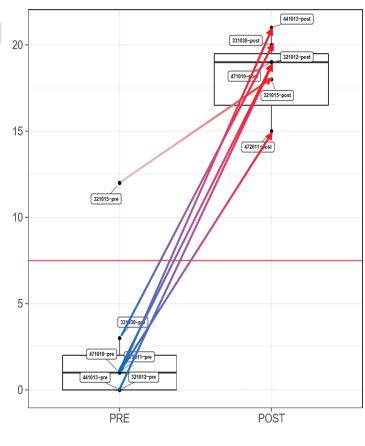
- Of the 15 patients in monotherapy where tumors turned from cold to hot, six had injected tumors with adequate biopsy material for nanostring analysis
  - 5 pairs change from cold (genes expression in blue) to hot (in red)
  - 1 pair with increased infiltration
- Immunosign® 21 analysis show clear effect on key genes involved in immune-mediated tumor regression and ability to convert cold tumors hot
- LTX-315 upregulates key genes involved in the immune mediated tumor regression in patients

#### INCREASED KEY GENE EXPRESSION POST INJECTION



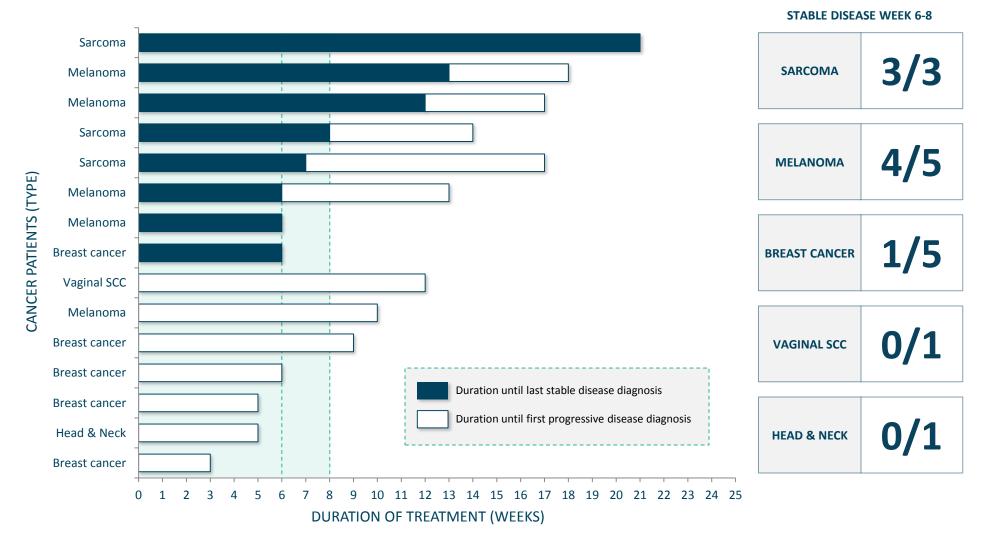


#### **IMMUNOSIGN® 21 SCORE**





# STABLE DISEASE ACHIEVED IN 8 OF 15 EVALUABLE PATIENTS WITH LARGE TUMOR BURDEN AND EXTENSIVE PRETREATMENT





## ANTI-TUMOR EFFECTS DOCUMENTED IN NON-INJECTED TUMOR

#### PATIENT BACKGROUND

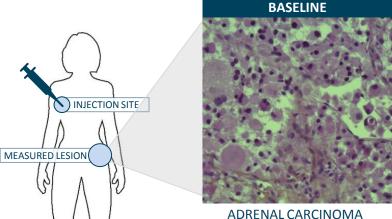
- 38 year female, adrenocortical cancer, diagnosed in year 2000. Metastasis to lung, liver, peritoneum, bone.
- Multiple prior treatments: surgery, chemotherapy, radiotherapy
- Progressive disease on anti PD-L1 as last prior treatment before starting LTX-315
- Clinically stable disease for approximately 16 weeks

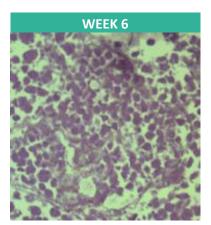
#### **TUMOR SIZE DEVELOPMENT**



TIME OF TREATMENT

#### LARGE NON-INJECTED LESION PRE/POST INJECTIONS

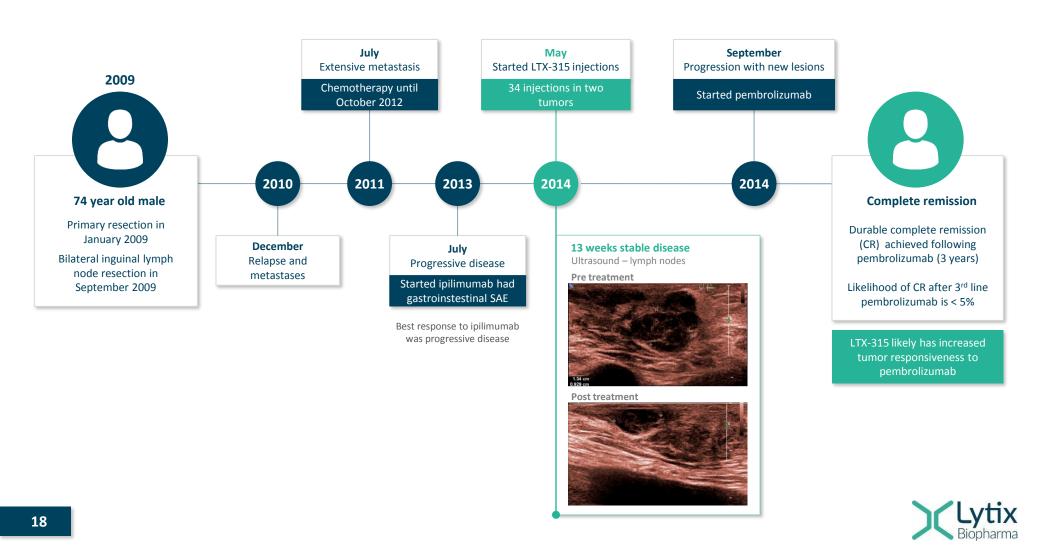




NO VIABLE CANCER CELLS



## DURABLE COMPLETE RESPONSE IN STAGE IV MELANOMA PATIENT WITH PEMBROLIZUMAB POST LTX-315 TREATMENT



# MELANOMA PATIENT IN LTX-315 + IPILIMUMAB COMBINATION IN DURABLE STABLE DISEASE FOR 38 WEEKS (ONGOING)

#### PATIENT BACKGROUND



#### 52 year old female

Stage IIIC BRAF/NRAS – ive vulvular nodular melanoma (very poor prognosis)





#### NON-INJECTED TUMOR VOLUME DEVELOPMENT



Baseline measures (mm²): Tumor 1: 462, Tumor 2: 459, Tumor 3: 1824, Tumor 4: 304



## SUMMARY OF CLINICAL TRIAL RESULTS TO DATE

MONOTHERAPY

#### PHASE I

#### SAFETY

- LTX-315 dose related hypotension (drop in blood pressure) at doses > 8mg per injection
- Low grade (mild/moderate) transient allergy side-effects (flushing, rash, itch, hypotension)

#### EFFICACY

"Cold to hot" documented with CD8+ T cell infiltration in injected tumors

#### **PHASE I**

#### SAFETY

- Low grade (mild/moderate) transient allergy side-effects (flushing, rash, itch, hypotension)
- Anaphylaxis AEs (4 patients) after prolonged (> 10 weeks) treatment in 3 pts and at 6 mg per injection in 1 pt

#### EFFICACY

- Stable Disease (SD) observed in 8 of 15 patients (CT scan) for mean of 11 weeks
- Regression in 9 of 38 injected lesions (24%)
- "Cold to hot" i.e. increased CD8 + T cell infiltration in 15 of 17 patients (88%)

#### MONOTHERAPY/COMBINATIONS

#### PHASE I/II - ONGOING

#### SAFETY

- Low grade (mild/moderate) transient allergy side-effects (flushing, rash, itch, hypotension)
- No significant LTX-315 related allergic reaction adverse events
- No increase in frequency or severity of checkpoint inhibitor-related adverse events

#### EFFICACY

- Monotherapy (2 evaluable patients by week 8)
  - Stable Disease in 2 of 2 sarcoma patients at week 8
- LTX-315 + ipilimumab (1 evaluable patient by week 8 or more)
  - Stable disease ongoing 38+ weeks in 1 of 1 patient
- LTX-315 + pembrolizumab (7 evaluable patients by week 8 or more)
  - Partial remission (PR) in 1 patient at week 6 after only two pembro infusions
  - Stable disease in 3 patients after 8 weeks and 1 continuing at week 16 (ongoing)
  - "Cold to hot" i.e. increased CD8+ T cell infiltration observed in 3 of 3 patients

#### Completed

#### Complete

#### Final results expected H1 2018



## LTX-315 IS THE ULTIMATE PERSONALIZED CANCER THERAPY



#### **EFFICACY**

- Comprehensive and rapid
   disintegration of mitochondria and
   intracellular organelles
- ✓ Induces all hallmarks of immunogenic cell death and additional immune stimulants
- ✓ Access all cancer cells through electrostatic interaction



#### **SAFETY**

- ✓ Transient side effect profile
- ✓ Low risk of neutralizing antibodies
- ✓ No risk of T cell mediated responses towards agent
- ✓ No risk of integration into host genome
- ✓ No risk of virus mutations



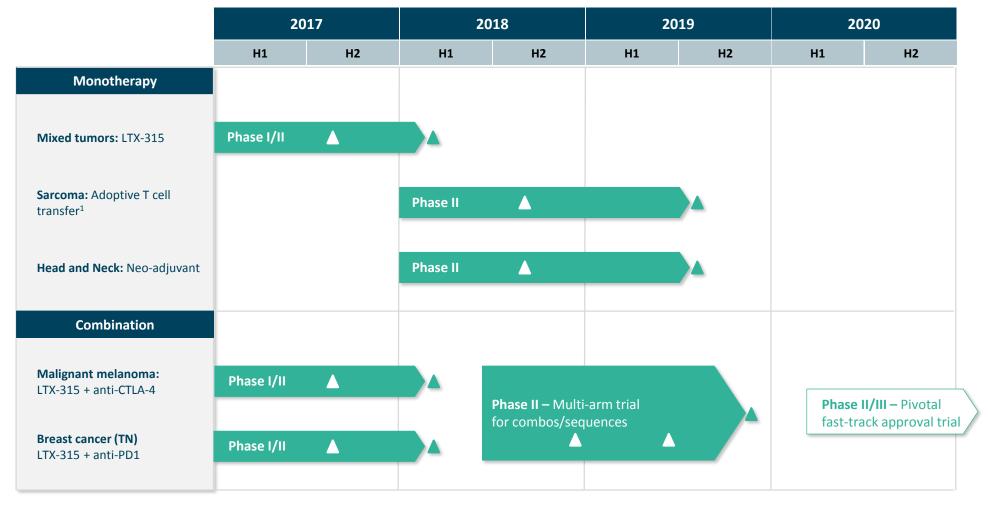
#### **DRUG PRODUCT**

- ✓ Short half-life of ~20min
- ✓ Low manufacturing cost
- ✓ No potency assay testing
- ✓ Easy handling and logistics, storage at 2 to 8°C
- ✓ No potential GMO issues

Oncolytic peptide LTX-315 shows promise to be efficacious and a simple way to activate tumors locally



# CLINICAL DEVELOPMENT PROGRAM WITH MULTIPLE READOUTS PRODUCING STRONG NEWSFLOW







## PHASE II COMBINATION TRIAL WITH LTX-315 AND IMMUNE CHECKPOINT BLOCKERS IS IN ITS DESIGN STAGE

#### TRIAL DESIGN IS BEING DISCUSSED WITH OUR EXPERT PANEL ADDRESSING THE LATEST INSIGHTS

#### **ASSUMPTIONS**

- Anti-CTLA-4 and anti-PD/PDL-1 are the only approved checkpoint inhibitors today
- Combination therapy is required to improve outcomes
- Combination of anti-CTLA-4 concomitant with anti-PD/PDL-1 is too toxic
- Combination of local and systemic treatment is gaining more and more acceptance
- Preclinical data show synergy between LTX-315 and anti-CTLA-4 and/or anti-PD/PDL-1
- Fundamental research provides arguments to sequence immune targeted treatments

#### TRIAL DESIGN

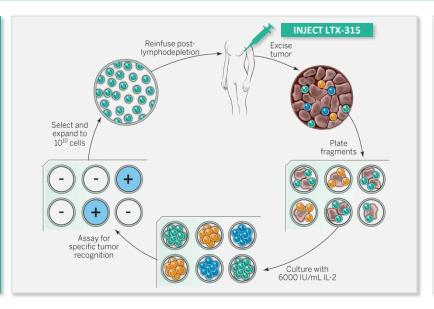
- Indications are metastatic melanoma and triple negative breast cancer
- Address subpopulations of patients with different immune signatures, for example
  - PD/PDL-1 positive or negative tumors
  - Inflamed versus non-inflamed tumors
- Multi-arm trial with cohorts of 10 15 patients
- Arms to combine LTX-315 with anti-CTLA-4 or anti-PD/PDL-1, and sequencing the immune checkpoint inhibitors
- Expand the cohorts with the strongest efficacy signals
- "Pick the winner strategy" for the next phase going into a randomized phase II/III regulatory trial



# EXPLORATORY PHASE II TRIALS IN SARCOMA AND HEAD&NECK CANCERS ARE UNIQUE OPPORTUNITIES

#### TRIAL DESIGN IS BEING DISCUSSED WITH OUR EXPERT PANEL ADDRESSING THE LATEST INSIGHTS

SARCOMA



- Sarcoma is a known 'cold tumor' also known as an 'immune desert'
- High unmet medical need as effective therapies are lacking
- Test LTX-315's ability to improve adoptive T cell therapy
- LTX-315 to prime tumor specific infiltrating lymphocytes, and to collect, cultivate and replenish them to treat the patient
- Immune signatures and kinetics through multiple tumor biopsies
- Response rates of tumor regression

HEAD & NECK CANCER



- Neo-adjuvant study is a unique opportunity to better understand tumor immune signature after surgical removal of tumor
- Follow patient up for time to recurrence



## **USE OF PROCEEDS**



S E K

**85**<sub>m</sub>

#### Phase II combination trial with immune checkpoint inhibitors

- Malignant melanoma
- Breast cancer
- Adaptive, multi-arm trial with cohorts of 10 15 patients. Expand cohorts with strongest efficacy signals
- Arms to combine LTX-315 with anti-CTLA-4 or anti-PD/PDL-1, and sequencing the therapy



S E K

35<sub>m</sub>

#### Phase II adoptive T cell therapy trial in Sarcoma

- Explore LTX-315's ability to stimulate high amount of T cells in tumor prior to excision
- Position LTX-315 as an important compound to improve T cell therapies

#### Phase II neoadjuvant therapy trial in Head & Neck Squamous Cell Carcinoma

- Explore LTX-315's ability to induce immune response and a long term immunity prior to surgery
- Develop detailed translational understanding of LTX-315's properties



S E K

**80**<sub>m</sub>

#### Pipeline development

- Conduct CMC and regulatory development for LTX-315 and follow-on candidates
- Develop second generation of oncolytic peptide LTX-401
- Strengthen Business Development and partnering activity



SEK

**70**<sub>m</sub>

#### **Science and Intellectual Property**

- Continue and further develop the strong scientific understanding of LTX-315 and the pipeline compounds
- Generate translational data to better understand clinical effects and support trial design
- Develop rationale and support positioning of the products in the fast evolving immuno-oncology landscape



## LYTIX BIOPHARMA INVESTMENT HIGHLIGHTS



#### UNIQUE PRODUCT

- Turning "cold tumors hot" with a broad and deep immunogenic activation
- Promising clinical data in patients refractory to other available treatment
- Ideal combination drug for checkpoint inhibitors and other modalities
- Strong patent portfolio with protection until 2032, and being further expanded

#### MULTIPLE VALUE TRIGGERS

- Differentiated company in the fast growing immuno-oncology segment
- Potential as a local cornerstone treatment in multiple tumor types
- Multiple shots on goal with clinical trials in different settings
- Pipeline with 2nd generation oncolytic peptide entering preclinical development

#### STRONG TEAM

- Management team and Board of Directors with international pharmaceutical drug development and commercial experience
- Strong international network and collaborations

