Alissa Mission Statement

- Alissa Pharma is a new biotechnology company focusing on radioimmunotherapy with novel targeted antibodies for hematology and solid tumors.
- Alissa Pharma has a patented platform technology for the development of bispecific monoclonal antibodies combined with radioisotopes to address unmet medical needs in hematology and oncology.
Executive Summary

- Lead platform: $^{90}$Y antiferritin polyclonal antibody
- First product: Ferritarg ready to enter Phase III trial
  - Originally developed for Hodgkin lymphoma at two preeminent US institutions: Johns Hopkins and MD Anderson
  - Safety and efficacy already demonstrated in Phase I and II trials in >300 patients
- Initial indication: refractory/relapsed Hodgkin lymphoma
  - Market potential in excess of $100 million in US alone
- Orphan protection secured in US and Europe
- Second product: A well-patented monoclonal antiferritin antibody (AMB8LK) for pancreatic cancer, hepatic cancer and neuroblastoma
Alissa has secured worldwide rights in all radiopharmaceutical indications for the antiferritin technology

Alissa will commercialize/partner Ferritarg

Alissa will develop the monoclonal antiferritin AMB8LK antibody for solid tumor indications

Ready to initiate clinical program for AMB8LK in pancreatic cancer

Second platform technology with radiolabeled bispecific antibodies for targeted oncology/hematology uses
# Well Balanced & Diversified Portfolio

<table>
<thead>
<tr>
<th></th>
<th>Candidate Selection</th>
<th>Preclinical Development</th>
<th>Phase I–II</th>
<th>Phase III</th>
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<tbody>
<tr>
<td>Ferritarg</td>
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<tr>
<td>Refractory &amp; Relapsed Hodgkin Lymphoma</td>
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<tr>
<td>AMB8LK</td>
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<tr>
<td>Pancreatic cancer</td>
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<tr>
<td>Liver cancer</td>
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<tr>
<td>Neuroblastoma</td>
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<tr>
<td>Bispecific anti–PSMA</td>
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<tr>
<td>Prostate cancer</td>
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<tr>
<td>Bispecific anti–CD 138</td>
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<tr>
<td>Multiple Myeloma</td>
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<tr>
<td>Triple Negative Breast cancer</td>
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Management Team

- Jack Talley, President & CEO
  - 35 years of pharmaceutical industry experience
  - President of Penwest Pharmaceuticals, EpiCept and Actinium Pharmaceuticals
  - Successfully took three companies public

- Stephane Allard, Co-Founder & Chief Medical Officer
  - 30 years of pharmaceutical industry experience
  - President of Biovest and Synthelabo Research and VP of Medical Affairs at Sanofi
  - Chief Medical Officer of EpiCept /Immune Pharmaceuticals
  - Led the development efforts for Ambien and Eloxatin
  - Responsible for the approval of Ceplene in Europe, an immunomodulator for remission maintenance of acute myeloid leukemia
Management Team, cont.

- Jean Kadouche, Co-Founder & Chief Scientific Officer
  - PhD (Pasteur Institute, Paris) in Immunology, Master in Pharmacy
  - Head of the Immunology Department at Saint-Louis and HEGP (Hopital Européen Georges Pompidou) Hospitals, Paris
  - >25 years developing 100+ monoclonal antibodies
  - Consultant with Roche, Ortho-Diagnostic, Merck
  - Biotech entrepreneur (founder or co-founder of Clonatec, Novagali, MAT BioPharma, Immune Pharmaceuticals)
  - Licensing & Strategy Director at Sangstat (acquired by Genzyme)

- Mark Gladstone, Chief Financial Officer
  - 30 years of financial services experience at E. F. Hutton, Drexel
  - Partner at Strategic Wealth Management Group
  - Former partner at Bradley Hummel & Company; provided seed capital to Watson Pharmaceuticals and Caraco Pharmaceuticals
Ferritin is an iron storage protein of 440 kDa overexpressed on the cell surface in various tumors.

Selective ferritin overexpression allows development of highly potent anti-tumor agents.

Ferritin is selectively overexpressed in cancers that represent unmet medical needs, notably:

- Hodgkin lymphoma
- Hepatocellular carcinoma
- Pancreatic cancer
- Neuroblastoma
Antiferritin Preclinical Data

- Ferritarg
  - Antiferritin polyclonal antibody DOTA–immunoconjugate labeled with radioisotope
  - Loaded with $^{90}$Yttrium for therapeutic use
  - Preclinical studies confirmed specificity of antiferritin polyclonal antibody for ferritin–expressing tumors in cell culture
  - Strong isotope linkage to antibody due to DOTA chelate
Ferritarg Mode of Action

Cell

Ferritin antigen

90Y Ferritarg

Polyclonal antibody

DOTA Chelate

90Y
Ferritarg Mode of Action

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<tr>
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<tbody>
<tr>
<td>Yttrium –[90]</td>
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</tr>
<tr>
<td>Half-life</td>
<td>64 hours</td>
</tr>
<tr>
<td>Energy emitter</td>
<td>Beta (2.3 MeV)</td>
</tr>
<tr>
<td>Path length</td>
<td>$\chi_{90}$ 5 mm</td>
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<tr>
<td>Administration</td>
<td>Outpatient</td>
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</table>

Yttrium

Half-life: 64 hours
Energy emitter: Beta (2.3 MeV)
Path length: $\chi_{90}$ 5 mm
Administration: Outpatient
Incidence of Hodgkin Lymphoma

- US: 9,060 new cases/year (NCI, 2012)
- Europe: 9,000 new cases/year
- Japan: 5,000 new cases/year
- Refractory (20%) or relapsed (30%) Hodgkin lymphoma
  - Potential population for this indication: 7,000 patients
  - Patients have received up to three courses of therapy
Ferritarg Market Potential

- The treatment is a single administration of Ferritarg

- Projected minimum price/treatment is $60,000/patient at the time of launch
  - Alternative treatments can cost in excess of $100,000 per patient

- Three years following launch, Alissa is expected to achieve approximately $75M in sales

- Patients could receive 2 or 3 courses of therapy
# Ferritarg Projected Market Penetration

<table>
<thead>
<tr>
<th>Year</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
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<tbody>
<tr>
<td>Total sites</td>
<td>60</td>
<td>70</td>
<td>75</td>
</tr>
<tr>
<td>New patients per site</td>
<td>14</td>
<td>15</td>
<td>16</td>
</tr>
<tr>
<td>Recurrent patients per site</td>
<td>6</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Total patients per site</td>
<td>20</td>
<td>23</td>
<td>24</td>
</tr>
<tr>
<td>Total patients treated</td>
<td>1,200</td>
<td>1,610</td>
<td>1,800</td>
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</tbody>
</table>
Overview of Current Therapies for Hodgkin Lymphoma

- Initial treatment
  - Stage I & II: Combination of chemotherapy (CT) and external beam radiation (EBR)
  - Stage III & IV: multi-agent CT
- Refractory and recurrent Hodgkin lymphoma
  - 20% fail all curative attempts
  - Autologous stem cell transplantation (ASCT) better than conventional rescue CT
  - 50% relapsing after high dose CT with ASCT treated with EBR if recurrence in lymph nodes
  - Second-line high dose CT used in 50% of patients with nodal or extranodal recurrences
  - Third-line usually single agent CT
- Typical 30% response rate of six months duration
Treatment of Hodgkin Lymphoma

First-line therapy

One line of induction chemotherapy (ABVD, BEACOPP …) with (or without radiotherapy)

CR

Primary refractory, PR

No relapse (long-term CR)

Relapse

Second-line therapy

Salvage chemotherapy (DHAP, MINE, Dexa-BEAM) + high dose chemotherapy + ASCT

CR

PR

Progressive disease

Radiotherapy Contraindicated

Antiferritin RIT (1,2,3)

No relapse (Long-term CR)

Radiotherapy

Third-line therapy

Relapse

Antiferritin RIT (4)

Antiferritin RIT (5)
Outcomes with Current Therapy for Refractory/Resistant Hodgkin Lymphoma

- **Adcetris® (Seattle Genetics, $4 B valuation)**
  - Indicated for Hodgkin patients who have failed chemotherapy or relapsed post BMT
  - Complete response in 32% of patients
  - Up to nine cycles of therapy
  - Unfavorable safety profile, common severe neuropathy
  - Black box warning due to progressive multifocal leukoencephalopathy
  - Approved based on single arm trial with durable response rate as primary endpoint

- No current competitive clinical activity
## Clinical Outcomes with Ferritarg

Over 300 patients treated in the US at Johns Hopkins and MD Anderson

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Response Rate</th>
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</thead>
<tbody>
<tr>
<td>Vriesendorp (1991)</td>
<td>29</td>
<td>62% (31% CR)</td>
</tr>
<tr>
<td>Herpst (1995)</td>
<td>39</td>
<td>51%</td>
</tr>
<tr>
<td>Vriesendorp (1995)</td>
<td>134</td>
<td>60% (50% CR)</td>
</tr>
<tr>
<td>Vriesendorp (1997)</td>
<td>87</td>
<td>67–90% (with CT)</td>
</tr>
<tr>
<td>Vriesendorp (1999)</td>
<td>90</td>
<td>60–90% (30–42% CR) with 0.4 or 0.5 mCi/kg</td>
</tr>
<tr>
<td>Decaudin (2006)</td>
<td>9</td>
<td>78% (11% CR)</td>
</tr>
</tbody>
</table>

- Phase II data confirmed optimal dose of 0.4 mCi/kg
- Hematologic toxicity reversible and controllable
Ferritarg Dose Ranging Response Rates from Vriesendorp

Tumor response rates

- % RR
- % CR

90Yttrium mCi/kg

0.3, 0.4, 0.5, 0.25X2
# Improvement of Radiolabeling for Ferritarg

<table>
<thead>
<tr>
<th></th>
<th>Vriesendorp</th>
<th>Alissa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chelator</td>
<td>In–house (&gt;15 steps) (Quadri et al, 1992)</td>
<td>GMP Manufacturing</td>
</tr>
<tr>
<td>Radiolabeling in</td>
<td>5 steps</td>
<td>Ready-to-use protocol</td>
</tr>
<tr>
<td>Nuclear Medicine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Department</td>
<td></td>
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<tr>
<td>Human Serum Stability</td>
<td>66.5% after 2 hours</td>
<td>&gt;93% after 48 hours</td>
</tr>
</tbody>
</table>
Patient G, 37 Years Old, in 2\textsuperscript{nd} Relapse

Before Ferritarg treatment  After Ferritarg treatment (S +10)

⇒ Global decrease of fixation (in red) estimated at 50%
Clinical Development Plan

- Single arm multi-center Phase III study to be performed in Adcetris failures in US and Europe
- Design finalized and size agreed after consultation with the respective regulatory agencies (FDA & EMA)
- Ferritarg injected with $^{90}$Yttrium (dose of 0.4mCi/kg)
- Efficacy criteria:
  - Primary Endpoint – Response rate, time to relapse
  - Secondary – Time to relapse, overall survival
- Estimated 100 patients in 20 sites (10 in US; 10 in Europe)
- Study start within twelve months of funding
- Study duration: approximately 24 months
Ferritarg: Regulatory Strategy

Regulatory Path to approval

US/European Phase I/II
- >300 patients
- MTD established
- Optimal dose 0.4mCi/Kg

European Pivotal Phase III
- Under PA EMA
- ~100 patients

EMA approval
European market

FDA approval
US market
Ferritarg Regulatory Status

- Orphan Drug Application
  US: Designation 06–2286 (09/12/2006)
  Europe: 02/10/2003 C (2003) 3563
- Fast track review by FDA and EMA
- IND submission six months post funding
- End of Phase II meeting planned with FDA within nine months of funding
Ferritarg Manufacturing and Administration

- Manufacturing site:
  - Preparation of rabbit antiferritin polyclonal antibody
  - Antibody isolated from the sera of rabbits hyperimmunized with ferritin isolated from human liver (Sanofi/Genzyme)
  - Synthesis of the DOTA-immunoconjugate
- Nuclear medicine department of the hospital receives product
- Product contains a solution of antibody linked to chelating agent and other components (buffers) and isotope
- Out-patient therapy with a single dose administration

Ferritarg is a sterile, pyrogen-free, clear, colorless, preservative-free solution
AMB8LK in Pancreatic Cancer

- Pancreatic cancer has a very poor prognosis with less than 5% survival rate at 5 years
- Ferritin overexpression in pancreatic cancer is a target for delivery of radioactivity at the tumor site
- AMB8LK, IgG1, a chimeric monoclonal antibody, has a very high affinity and specificity for human ferritin
- AMB8LK is conjugated to bifunctional chelating ligands to be radiolabelled
- Preclinical studies have been performed in mice bearing Capan-1 xenografts as a model of human pancreatic adenocarcinoma
- Preclinical IND enabling studies are completed, protocol prepared, ready to initiate clinical program
Specificity of AMB8LK

- AMB8LK has a high specificity for Capan-1, Hep G2 and Hep G2 ATCC using flow cytometry

<table>
<thead>
<tr>
<th>Cell Line</th>
<th>Label</th>
<th>MFI</th>
<th>Ratio VS control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capan-1</td>
<td>Isotype</td>
<td>4.13</td>
<td>6.40</td>
</tr>
<tr>
<td></td>
<td>AMB8LK</td>
<td>26.43</td>
<td></td>
</tr>
<tr>
<td>Hep G2</td>
<td>Isotype</td>
<td>3.18</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AMB8LK</td>
<td>56.65</td>
<td>17.81</td>
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<tr>
<td>Hep G2 ATCC</td>
<td>Isotype</td>
<td>3.61</td>
<td>4.47</td>
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<tr>
<td></td>
<td>AMB8LK</td>
<td>16.13</td>
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MFI = Mean fluorescence intensity
Biodistribution of DTPA–AMB8LK

- Biodistribution in Capan-1 tumor-bearing nude mice at 120 hours after injection of $^{90}$Y–labelled Ab
AMB8LK Preclinical Data in Pancreatic Cancer

- Preclinical study performed at the Nuclear Medicine Research Laboratory at St Bartholomews Hospital, London (Pr. Mather)
- The immunoconjugate with $^{90}$Y showed greater than 98% stability over 7 days
- DTPA–AMB8LK has a high reactivity with ferritin

“We believe that, in the case of solid tumors, targeted radionuclide therapy is likely to be most effective when used in combination with other treatment modalities. The high expression of ferritin in pancreatic cancer suggests that this is a promising target and we plan to pursue preclinical studies of yttrium–labelled DTPA–AMB8LK in combination with gemcitabine.” *

AMB8LK Patents

  Jean Kadouche, Rafael Levy
  Use of antiferritin monoclonal antibodies in the treatment of some cancers

  Jean Kadouche, Emmanuelle Sabbah–Petrover, Olivier Chose
  Nucleotide and protein sequences of an antibody directed against an epitope common to human acidic and basic ferritin monoclonal antibodies or antibody–like molecules comprising these sequences and uses thereof

- Option for monoclonal antiferritin antibody secured
Bispecific Antibody (BiAb) Platform

- BiAb consists of 2 different heavy chains and 2 different light chains → has 2 different antigen binding sites which can respectively bind 2 different antigens

- BiAb could provide a new mode of action to therapeutic antibodies
**Advantages of BiAbs**

- **Double targeting can:**
  - Attack multiple targets
  - Block various pathway signals
  - Target tumor heterogeneity
  - Increase specificity and/or synergistic therapeutic effects

- **Retargeting can:**
  - Attract and activate killer cells (T and NK cells, macrophages)

- **Can conjugate with:**
  - Toxins via a linker (ADC)
  - Vectors (nanoparticles, emulsions, liposomes)
BiAb by Alissa Pharma

Alissa Technology

- Targeted therapy (RIT, Imaging) using BiAb construction with one arm linked to the tumor antigen and the second arm linked to a hapten attached to a radioisotope with a chelate

- Alissa owns the technology for the construction of BiAb (WIPO/PCT Submission number 46558, July 6, 2012, PCT/IB2012/053482)

- Alissa has the worldwide license for the hapten and the chelate to attach the radioisotope
Alissa BiAb Technology and Construct

Bivalent Hapten

Diagnostic or Toxic Agent

Cancer Cell

Cell Surface Marker (CSM)

Nucleus

Fab anti-EpCAM, anti-PSMA, anti-CD138

Fab anti-peptide HSG

Alissa Pharma
Alissa will develop its own BiAbs

- **PSMA**
  - PSMA combined with an radioisotope
  - Treatment of patients with prostate cancer

- **Anti – CD138**
  - Anti – CD138 with an radioisotope
  - Treatment of residual disease in multiple myeloma
  - Treatment of breast cancer with triple-negative (ER–negative, progesterone receptor (PR)–negative, HER2/neu not overexpressed) (approximately 15%)
Alissa BiAb Partnership with Industry

- Alissa will partner with pharmaceutical companies in constructing a bispecific antibody for the company target.
- Alissa will develop with the client the hapten and chelate appropriate for the radioisotope chosen by the pharmaceutical partner.
- Alissa will receive research support, milestones and royalties.
Collaboration in Radioimmunotherapy (RIT)

- Collaboration between Alissa – Chelatec, Jean-François Gestin and Pierre Cherel

  Jean-François Gestin, Directeur de Recherche INSERM, UMR 892/CRCNA
  Institut de Recherche Thérapeutique de l'Université de Nantes
  http://www.isotopforlife.com
  GIP ARRONAX 1, rue Aronnax CS 10112, 44817 SAINT HERBLAIN Cedex

- Access to the Nantes cyclotron
Scientific Advisory Board

- Dr. Andrew Zelenetz, MD, PhD
  Former Chief of Memorial Sloan Kettering Cancer Center’s Lymphoma Service
- Dr. Jean–Francois Gestin, PhD
  French Institute of Health and Medical Research (INSERM, Unite 892)
Financial Highlights

- No debt
- All capital contributed by management team
- $10 million provides runway into Q3 2016
Proposed Deal Structure

- $25 million pre-money valuation
- Target raise $10–15 million
- Seeking lead institutional investor
Use of Proceeds

- Ferritarg Phase III development
- Monoclonal antiferritin development
- Bispecific antibody platform development
- General and administrative
Key Milestones

- Initiate Ferritarg Phase III development for Hodgkin lymphoma
- Develop antiferritin monoclonal for pancreatic cancer
- Initiate preclinical development for bispecific antibody platform
- Secure pharma partnership
Conclusions

- Alissa Pharma offers an attractive opportunity to capitalize on the growing market of targeted antibodies for hematology/oncology indications

- Alissa Pharma is developing a niche product for Hodgkin lymphoma with proven efficacy

- Potential to expand into other oncology indications including pancreatic cancer

- Bispecific antibody platform for future product line expansion
Contact Information

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jtalley@alissapharma.com