



**The Galectin-3 Inhibitor GR-MD-02 for
Combination Cancer Immunotherapy**
Supplemental Information to Corporate Presentation
February 6, 2018

NASDAQ: GALT
www.galectintherapeutics.com

Forward Looking Statements

This presentation contains, in addition to historical information, forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements relate to future events or future financial performance, and use words such as “may,” “estimate,” “could,” “expect” and others. They are based on our current expectations and are subject to factors and uncertainties which could cause actual results to differ materially from those described in the statements.

These statements include those regarding potential therapeutic benefits of our drugs, expectations, plans and timelines related to our clinical trials, potential partnering opportunities and estimated spending for 2018 and beyond. Factors that could cause our actual performance to differ materially from those discussed in the forward-looking statements include, among others, our trials may not lead to positive outcomes or regulatory approval.

We may experience delays in our trials, which could include enrollment delays. Future phases or future clinical studies may not begin or produce positive results in a timely fashion, if at all, and could prove time consuming and costly. Plans regarding development, approval and marketing of any of our drugs are subject to change at any time based on the changing needs of our company as determined by management and regulatory agencies. Strategies and spending projections may change. We may be unsuccessful in developing partnerships with other companies or obtaining capital that would allow us to complete our clinical trials or further develop and/or fund any future studies or trials.

To date, we have incurred operating losses since our inception, and our future success may be impacted by our ability to manage costs and finance our continuing operations. For a discussion of additional factors impacting our business, see our Annual Report on Form 10-K for the year ended December 31, 2016, and our subsequent filings with the SEC. You should not place undue reliance on forward-looking statements. Although subsequent events may cause our views to change, we disclaim any obligation to update forward-looking statements.

Developing Treatments Where Galectin-3 Protein is Implicated in Disease

Clinical Phase Studies With Galectin-3 Inhibitor (GR-MD-02)

- **Combination Cancer Immunotherapy (topic of this presentation; supplemental information to January 7, 2018 Corporate Presentation)**
 - Investigator-initiated phase 1b clinical trial of GR-MD-02 in combination with KEYTRUDA in advanced melanoma and other malignancies
 - Encouraging early data with 5 of 8 responders (2 CR and 3 PR) in advanced melanoma
- **Primary Program is in NASH Cirrhosis**
 - First randomized clinical trial of any drug to demonstrate a clinically meaningful improvement in portal hypertension or important aspects of liver biopsy in patients with compensated NASH cirrhosis
- **Psoriasis and atopic dermatitis**
 - Small open label studies show clinically significant effect demonstrating activity of drug in human disease

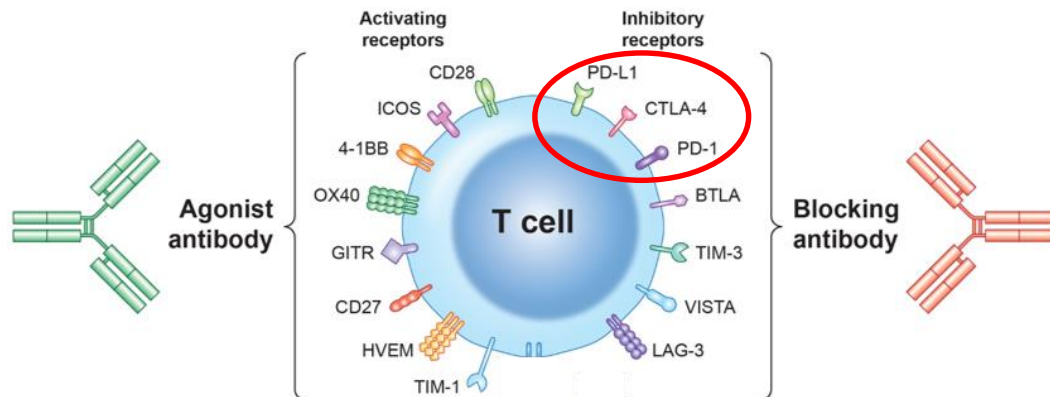
Combination Cancer Immunotherapy Development Program Summary

- The vast majority of human (& experimental animal) cancers have a large increase of galectin-3 protein
- Galectin-3 inhibits the immune system from killing cancer cells and has other effects that allows cancers to thrive and spread to other areas of the body
- GR-MD-02 is a glycopolymer (polysaccharide), considered a Nonbiological Complex Drug (NBCD) that binds to galectin-3 protein, has strong patent protection, and is administered intravenously
- GR-MD-02 has robust efficacy in pre-clinical cancer models when used with immunotherapy agents
- GR-MD-02 is well tolerated and safe in preclinical toxicology and clinical trials (2 P1, P2a and P2b), including when used in combination with the immunotherapy pembrolizumab (KEYTRUDA)
- Investigator-initiated phase 1b clinical trials of GR-MD-02 in combination with KEYTRUDA (and Yervoy) in advanced melanoma and other malignancies
- **Encouraging early data in KEYTRUDA trial with 5 of 8 responders (2 Complete responders (CR) and 3 Partial responders (PR) in advanced melanoma**

Critical Collaboration with Providence Cancer Center

- **The Earle A. Chiles Research Institute at Providence Portland Medical Center**
 - **Established 1993 by Dr. Walter Urba, MD, PhD**
 - **Internationally recognized team of scientists and clinicians with focus on cancer immunotherapy**
- **William L. Redmond, PhD**
 - **Associate Member and Director of Immune Monitoring Laboratory**
 - **Research focused on mechanisms regulating the efficacy of combination immunotherapy and reversing tumor-induced immune suppression**
 - **Conducted pre-clinical work with GR-MD-02**
- **Brendan D. Curti, MD**
 - **Director of Biotherapy Clinical Program**
 - **Principal Investigator of GR-MD-02 immunotherapy clinical trials**

T Cell-Modulating Antibodies For Cancer Immunotherapy



Multiple therapies have been developed, or are in development, that stimulate the immune system to treat cancer

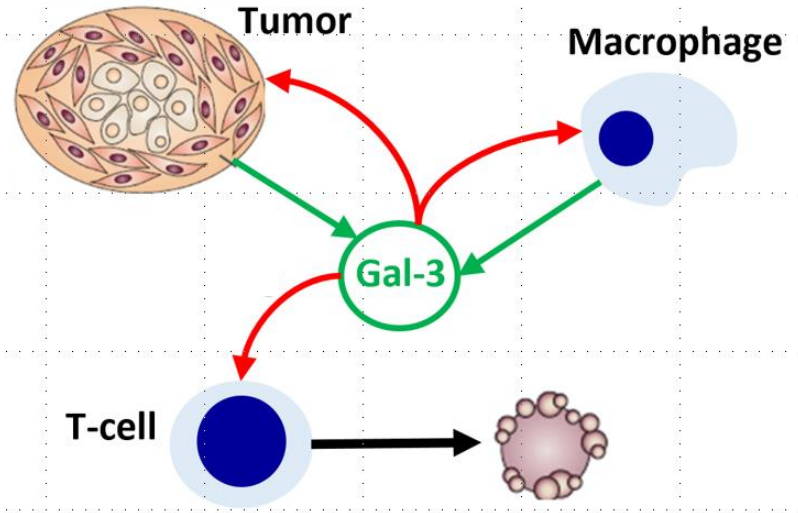
Recent effective classes of immunotherapies are those that stimulate T cells by blocking inhibitory inputs (blocking antibodies or checkpoint inhibitors) or stimulate T cells (agonist antibodies)

Marketed drugs (red circle)

- Anti-CTLA-4 (ipilimumab; Yervoy)
- Anti-PD1 (pembrolizumab; KEYTRUDA)
- Anti-PD-L1 (nivolumab; Opdivo)

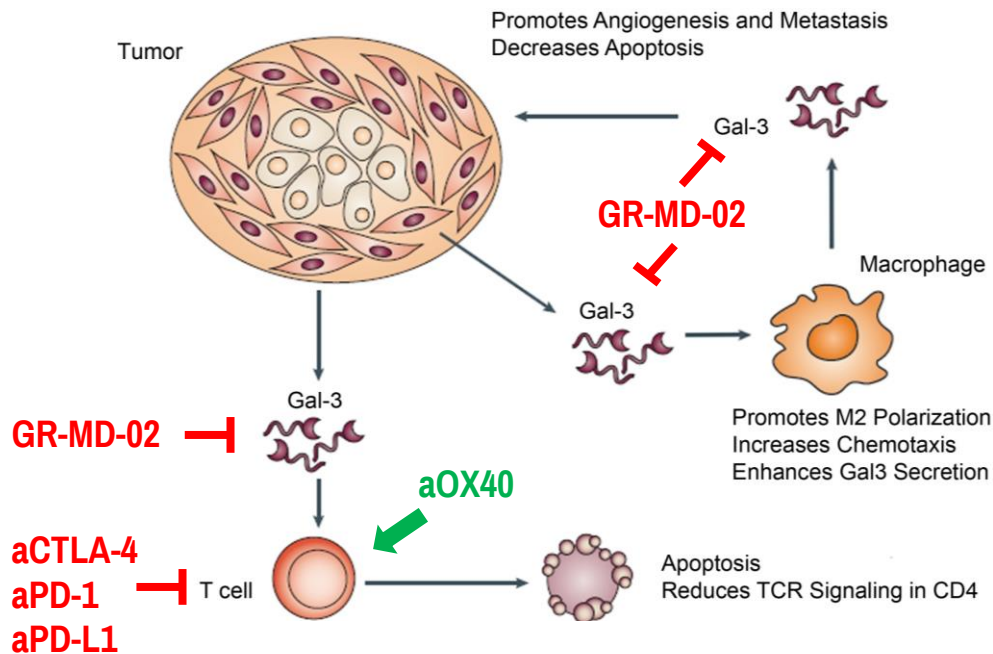
Gal-3 effects on cancer cells, macrophages and T-cells in the tumor microenvironment

- Gal-3 is produced by both tumor cells and macrophages and has multiple effects, including
 - Reducing T cell receptor signaling thereby blocking immune effects on tumor cells
 - Promoting T-cell apoptosis (cell death)
 - Promoting angiogenesis and metastasis of cancer cells
 - Promoting macrophage M2 polarization, increasing chemotaxis to recruit more macrophages, and enhancing gal-3 secretion



Rabinovich G, *Nat Rev Immunol*, 2009

The Galectin-3 Inhibitor GR-MD-02 Appears to Augment Anti-Tumor Activity of Cancer Immunotherapies



A galectin-3 inhibitor such as GR-MD-02 theoretically would have synergistic effects with other immunotherapies

Pre-clinical studies have shown positive effects on multiple tumors when GR-MD-02 was combined with:

Checkpoint inhibitors:

- **Anti-CTLA-4 (ipilimumab; Yervoy)**
- **Anti-PD1 (pembrolizumab; KEYTRUDA)**
- **Anti-PD-L1 (nivolumab; Opdivo)**

T-cell agonists

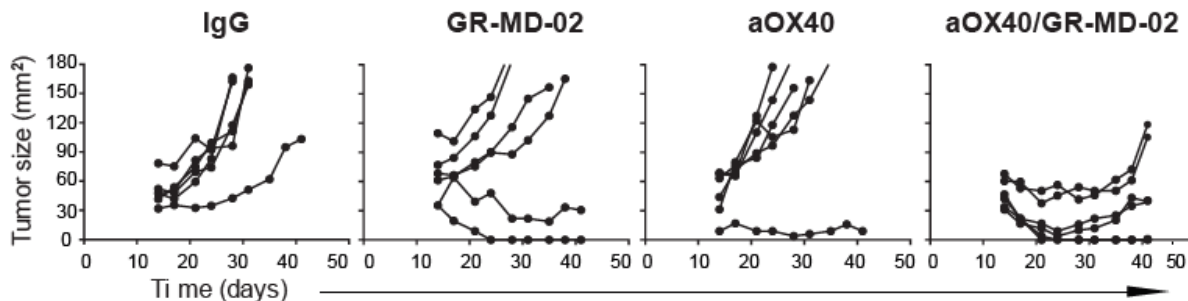
- **Anti-OX40 (in development)**

Pre-Clinical Summary: GR-MD-02 in combination with other immunotherapies, vaccines, and radiation therapy enhances efficacy in multiple tumor models

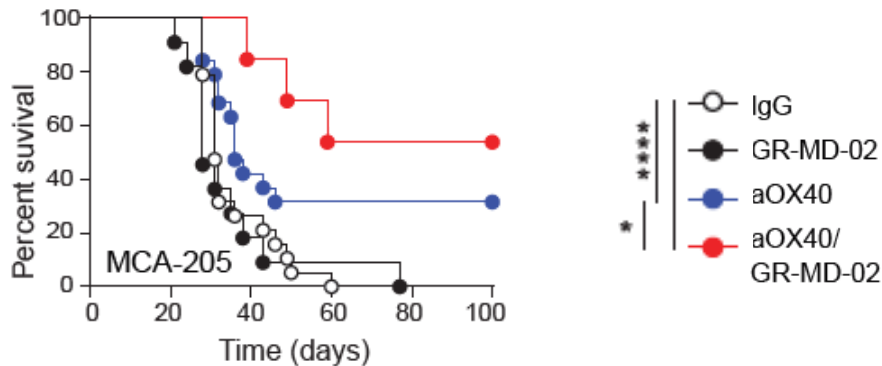
- **GR-MD-02 boosts frequency and persistence of antigen-specific T cells in non-tumor bearing mice alone and in combination with anti-CTLA-4**
- **GR-MD-02 in combination with anti-CTLA-4, anti-PD-L1, or anti-PD-1 reduces tumor size and enhances survival in multiple tumor models (melanoma, prostate, breast, sarcoma)**
- **GR-MD-02 in combination with the anti-OX40 immunotherapy agonist**
 - Improves survival and reduces lung metastases (4T1 breast cancer model)
 - Improves survival in the MCA-205 sarcoma model in a CD8 T cell-dependent manner
 - Reduces the frequency of suppressive cells (MDSC) in the tumor microenvironment
 - Reduces vascular endothelial frequency within the tumor
- **GR-MD-02 plus Lm-Her2 tumor vaccine augments expansion of tumor-specific CD8 T cells, increases tumor regression, and boosts tumor-free survival**
- **GR-MD-02 in combination with radiation therapy increases tumor regression and boosts tumor-free survival**

Preclinical Data Example: GR-MD-02 plus anti-OX40 antibody reduces tumor growth and prolongs survival in MCA-205 sarcoma in mice

The combination of GR-MD-02 with anti-OX40 markedly enhances effect on tumor growth of either agent alone



The combination of GR-MD-02 with anti-OX40 statistically significantly enhances survival over either agent alone



Phase 1b Clinical Trials Conducted by Providence Cancer Center

- **Galectin Inhibitor (GR-MD-02) plus Ipilimumab (Yervoy) in Patients With Metastatic Melanoma**

Trial initiated in 2015, enrolled 7 subjects with GR-MD-02 doses of 1 and 2 mg/kg

There were no adverse events identified due to GR-MD-02

No notable changes in the peripheral immune signature

Trial stopped due to changes in the standard of care for melanoma (Keytruda was approved and replaced the use of Yervoy in many patients)

- **GR-MD-02 Plus Pembrolizumab (KEYTRUDA) in Patients with Metastatic Melanoma and Other Cancers (oral head & neck, non small cell lung cancer)--ONGOING**

GR-MD-02 Plus Pembrolizumab (KEYTRUDA)

GR-MD-02 used in combination with a flat dose (200 mg) of pembrolizumab in the following patients:

Metastatic melanoma with progression after other treatment including pembrolizumab alone

Recurrent or metastatic HNSCC with progression after other treatment

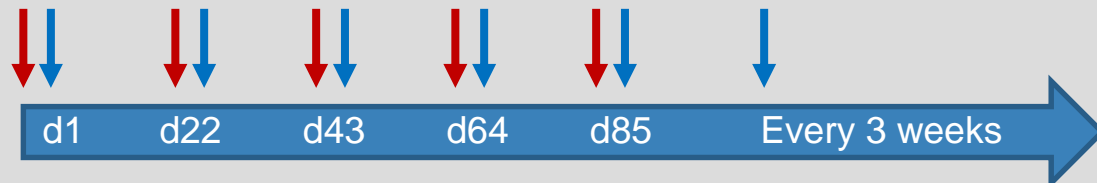
GR-MD-02

2 mg/kg (5 patients; completed)

4 mg/kg (3 patients; completed)

8 mg/kg (10 patients; underway)

Pembrolizumab



Imaging (CT/MRI/PET)
Immune cells and markers

<https://clinicaltrials.gov/ct2/show/NCT02575404?term=gr-md-02&rank=2>

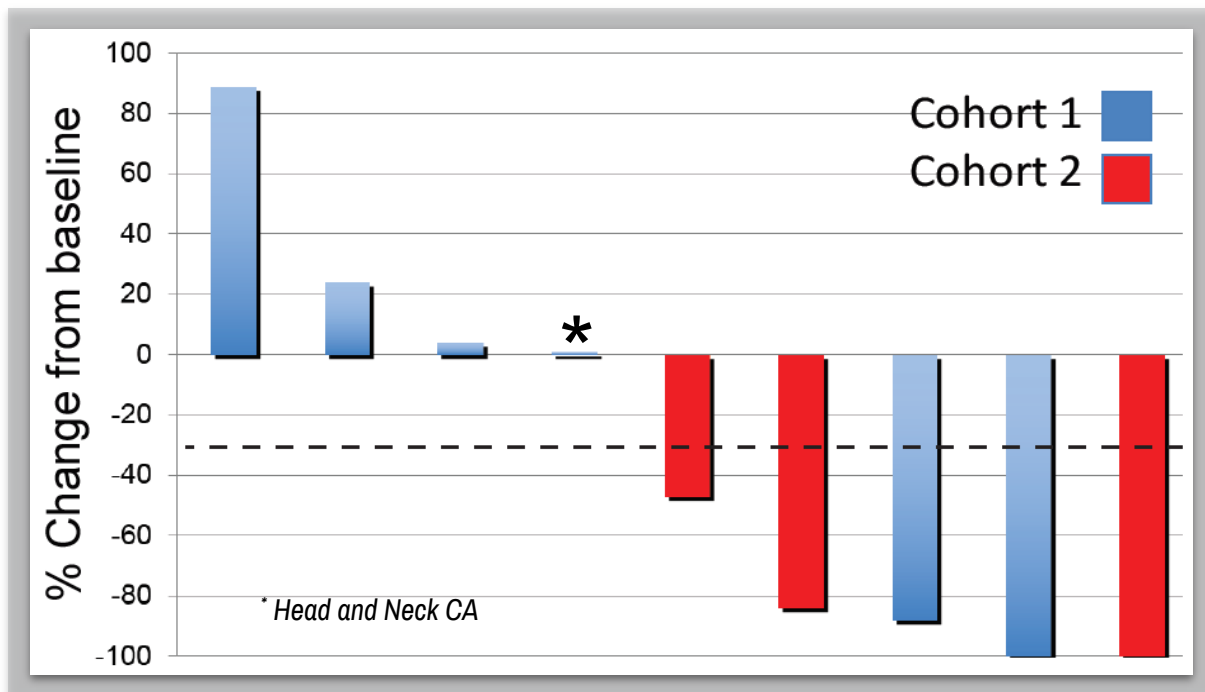
Pembrolizumab plus GR-MD-02 Patients: Cohorts 1 and 2

Cohort	Diagnosis	Gender	Age	Disease Sites	Prior Treatments	Response
1	Melanoma	Male	76	Subcutaneous (SQ), lung	Surgery/IL-2/RT/oncolytic virus/Yervoy	PR
1	Melanoma	Female	63	SQ, muscle, lymph node (LN)	Interferon/Yervoy	SD→PD
1	Melanoma	Female	82	SQ, bone, LN	Surgery, Radiation	PD
1	Melanoma	Male	62	Brain/bone/lung/SQ/LN/liver	IL-2, Yervoy, Opdivo	SD→PD
1	Melanoma	Male	65	SQ, LN, lung	Vemurafenib, Dabrafenib + Trametinib	CR
1	H & N Cancer	Male	55	LN	Surgery	SD→PD
2	Melanoma	Female	70	LN, lung	Surgery, IL-2, Radiation	PR
2	Melanoma	Male	83	Lung, pleura	Surgery	CR
2	Melanoma	Male	37	LN	Surgery	PR

SD=stable disease; PD=progressive disease; PR=partial response; CR=complete response

Clinical Results of GR-MD-02 plus Pembrolizumab (KEYTRUDA)

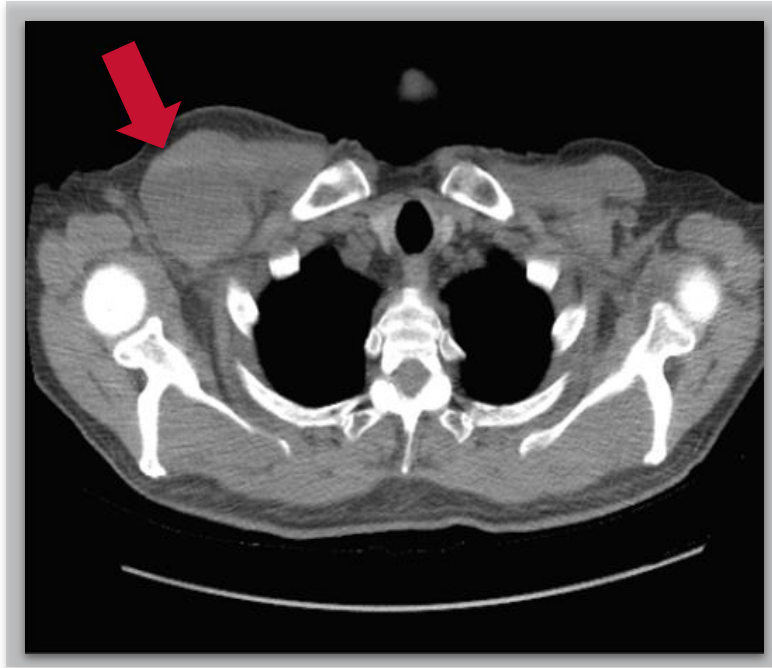
Waterfall plot of best objective clinical response post treatment (RECIST 1.1)



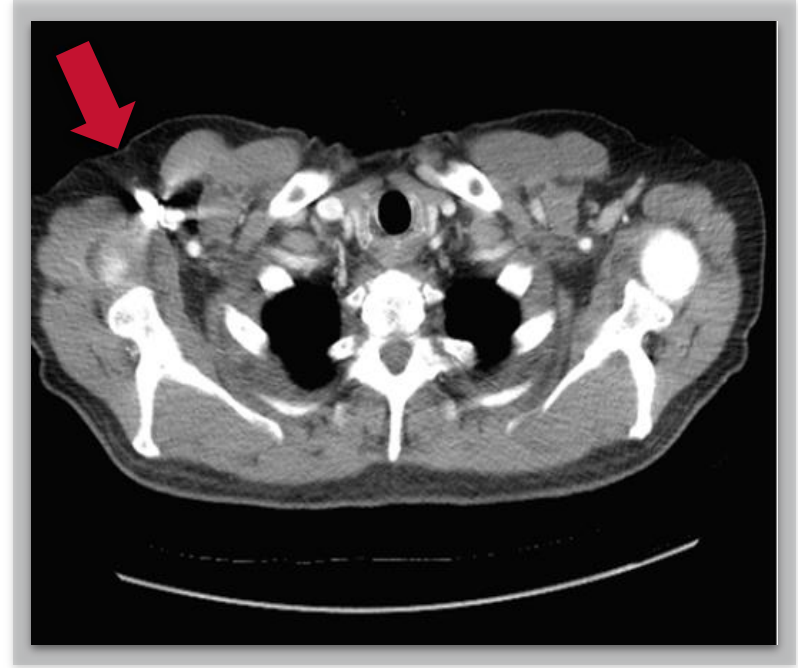
Response rate of 62.5% in melanoma compares favorably to best response of KEYTRUDA alone of 33%

CT Scan Showing Resolution of a Large Intramuscular Melanoma Deposit

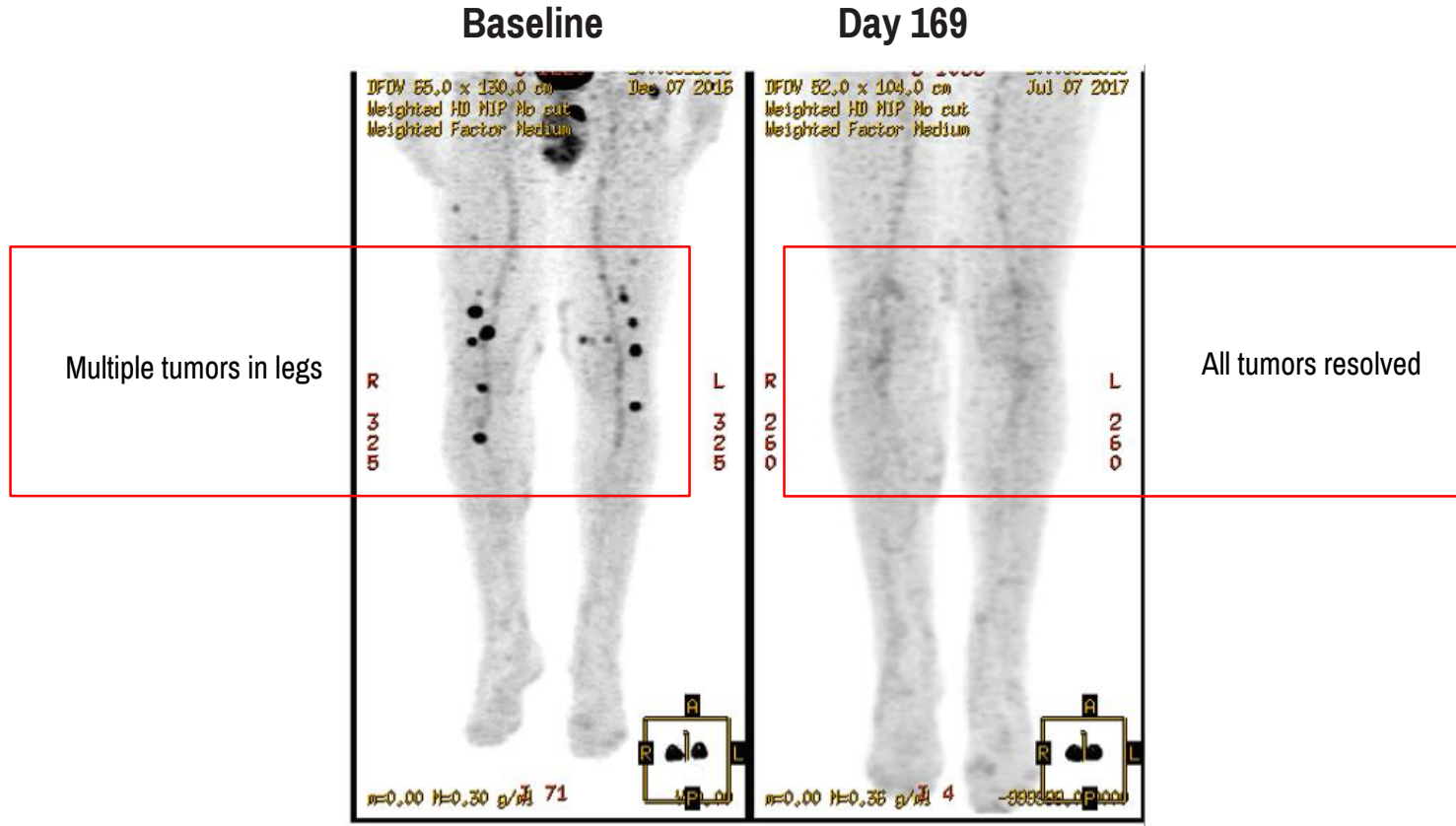
Baseline



Day 85



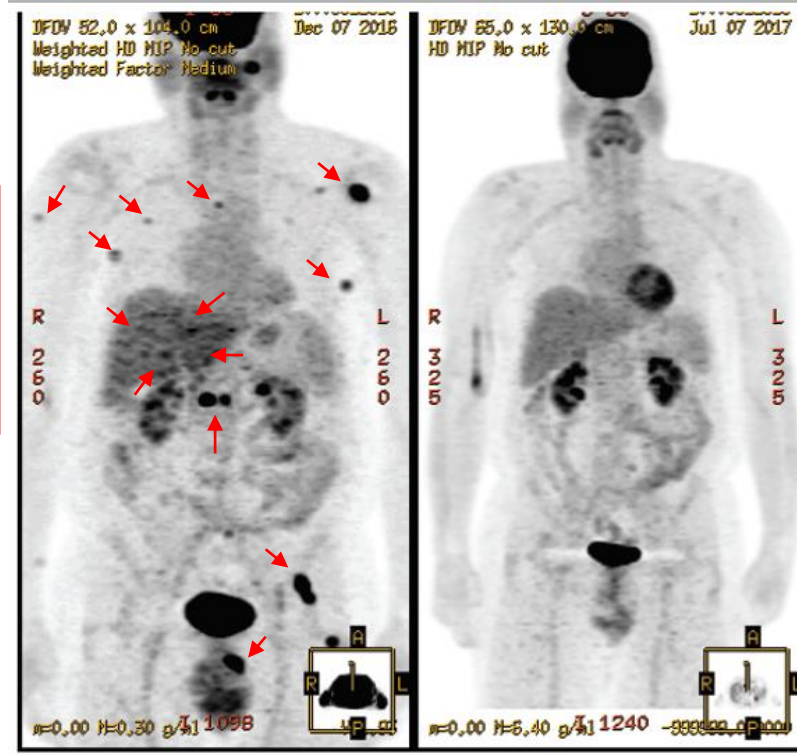
Multiple PET Scan-Detected Melanoma Deposits Resolved



Multiple PET Scan-Detected Melanoma Deposits Resolved

Baseline

Day 169

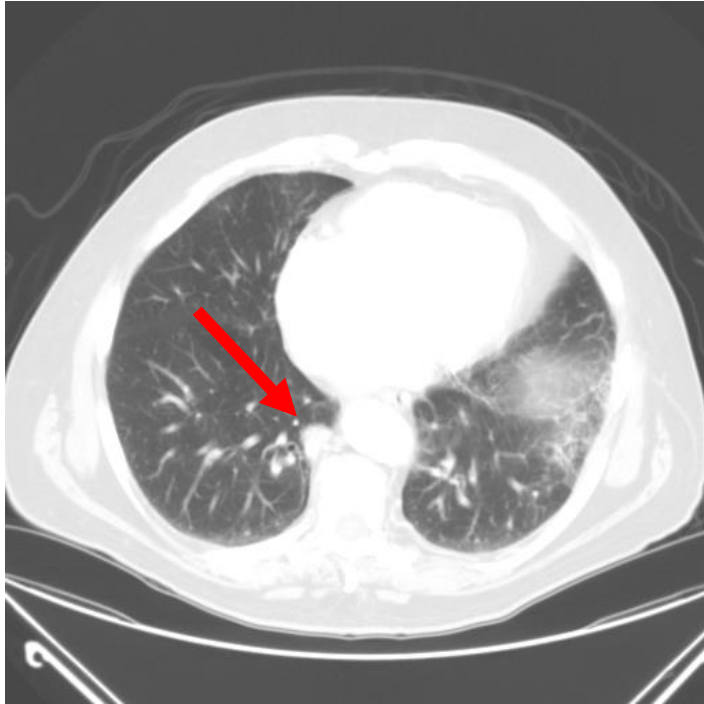


Multiple tumors throughout body (red arrows)

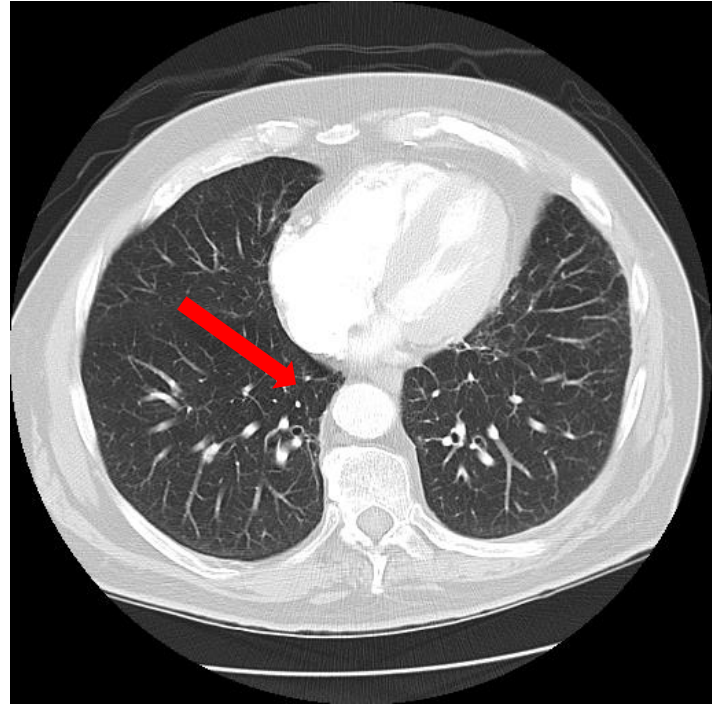
All tumors resolved: normal contrast seen in heart, kidneys and bladder

CT Scan Showing Resolution of a Lung Melanoma Deposit

Baseline



Day 85



Extensive Laboratory Analysis of Immune Cells and Immune Molecules

- **The immune monitoring laboratory at EACRI (Earle A. Chiles Research Institute) performs analysis of multiple type of immune cells and immune molecules in the blood and tumors of patients before, during, and after therapy**
- **This analysis suggests that responders to therapy appear to have higher baseline levels of activated T lymphocytes which may provide better targeting of patients likely to respond**
- **Measurement of Monocyte Derived Suppressor Cells (MDSC) suggests that these are decreased by combination therapy in patients who respond to therapy. This is an important and novel observation since MDSC cells impair the response of the immune system to tumors.**
- **The extensive immune monitoring of patients in this trial will help elucidate the mechanism of action of GR-MD-02 in combination with pembrolizumab and help to identify the patients who will most benefit from combination therapy**

Addition of GR-MD-02 to Pembrolizumab Appears Safe and Well Tolerated

- **Pembrolizumab has significant toxicities and adverse effects on patients**
- **In the patients treated thus far with the combination of GR-MD-02 and pembrolizumab, the Principal Investigator has documented that there have been no additional adverse events or toxicities attributed to GR-MD-02 over those that would be anticipated with pembrolizumab**
- **If this observation holds up in further patients, this would be a potential advantage of GR-MD-02 as a combination agent because most combination therapies with pembrolizumab that are currently used or being studied add significantly to the toxicity of the therapy**

Summary: GR-MD-02 for Combination Cancer Immunotherapy

- **Many combination approaches are under investigation using marketed and experimental cancer immunotherapy drugs**
- **As a galectin-3 inhibitor, GR-MD-02 represents a novel mechanism of action, differentiated from the many other drugs that are currently being tested**
- **As a combination agent, GR-MD-02 has a number of potential advantages**
 - Broad enhancement of anti tumor activity in pre-clinical studies with checkpoint inhibitors (e.g. anti PD-1/PD-L1), immuno-stimulatory agonists (e.g. aOX40), cancer vaccines, and radiation therapy
 - Potential novel and unique markers of anti-cancer activity
 - GR-MD-02 is safe and well tolerated and does not appear to increase adverse events when used in combination immunotherapy with pembrolizumab
 - Cost of manufacture is relatively inexpensive when compared to biologics
- **The third patient cohort treated with GR-MD-02 8 mg/kg, which will enroll at least 10 additional patients, is well underway with results anticipated in mid-2018**