August 18, 2014

OUTPERFORM

Reason for report:

INITIATION

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IMMUNE DESIGN CORP.

A Creditable Immuno-Oncology Play; Initiate at OP

• **Bottom Line:** We are initiating coverage of IMDZ with an Outperform (OP) rating and a $25 12-month price target. IMDZ is a clinical-stage biotechnology company focused on immunotherapies for cancer, and has two proprietary platforms, ZVex and GLAAS, for activating essential cells of the immune system to enable recognition and elimination of cancer cells.

• **Immune activation and cytotoxic T cell generation likely will have a role in future immunotherapy for cancer.** Immuno-oncology (IO) is emerging as a new pillar of cancer treatment due to the potential for durable response and functional cure. Despite the remarkable success of checkpoint inhibitors such as PD-1/PDL1 antibodies, currently only a minority of unselected patients with a few types of tumors achieve an objective response. Both the proportion of patients (about half) without tumor-infiltrating lymphocytes (TILs) as well as the adaptive tumor immune escape mechanism of PDL1 expression in response to TILs argue for the need for immune activation to generate tumor-specific cytotoxic T cells. Based on pre-clinical data, MEDACorp key opinion leaders (KOLs) believe vaccines are among the most important combination partners to pursue for checkpoint inhibitors.

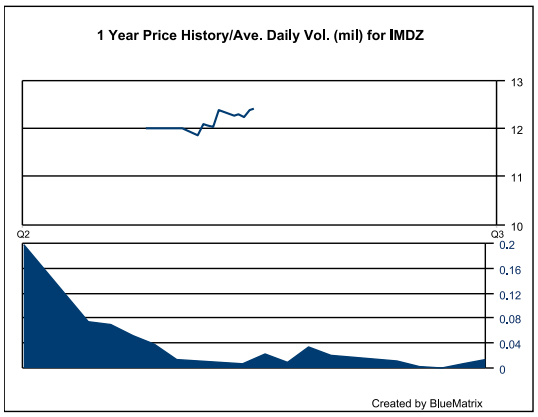
• **IMDZ has developed a novel approach for activating immune cells against specific and endogenous tumor antigens.** Issues of historical cancer vaccines included limited CD8+ T cell engagement and T cell sequestration associated with *ex vivo* peptide loading and mineral oil carriers. IMDZ's novel technology of *in vivo* targeting of antigens specifically to dendritic cells may overcome these limitations. In addition, the second platform, GLAAS, can further strengthen the response via the activation of CD4+ T cells and provide an opportunity for a unique combination.

• **KOLs see IMDZ as one of the strongest early-stage immuno-oncology companies.** We received excellent feedback from KOLs on the ZVex platform and pre-clinical data, GLAAS as an outstanding adjuvant, as well as the credibility and credentials of management. There were some questions about NY-ESO-1 as a target, but KOLs overall were enthusiastic about the story.

• **In light of the potential upside in the platforms being applied broadly to other cancer antigens, as well as established partnerships with AZN (MP) and SNY (MP) for infectious diseases and a food allergy, we see the valuation of IMDZ as inexpensive in comparison to other IO stories.** Clinical data starting in 1Q:15 and continuing throughout 2015 could provide near-term catalysts.

Key Stats:	**(NASDAQ:IMDZ)**
S&P 600 Health Care Index:	**1,300.41**
Price:	**$12.41**
Price Target:	$25.00
Methodology:	DCF analysis and probability-weighted sales
52 Week High:	$12.81
52 Week Low:	$11.51
Shares Outstanding (mil):	15.5
Market Capitalization (mil):	$192.6
Book Value/Share:	$0.00
Cash Per Share:	$5.40
Dividend (ann):	$0.00
Dividend Yield:	0.0%

Cash Per Share: Calculated on a pro-forma basis



Dec Yr	1Q	2Q	3Q	4Q	FY Rev	1Q	2Q	3Q	4Q	FY EPS	P/E
2013A	--	--	--	--	$1.6	--	--	--	--	($2.28)	NM
2014E	0.0A	0.0	0.0	0.0	0.0	($0.81)A	($0.54)	($0.36)	($0.36)	($1.42)	NM
2015E	--	--	--	--	0.0	--	--	--	--	($1.41)	NM
2016E	--	--	--	--	0.0	--	--	--	--	($1.11)	NM

Source: Company Information and Leerink Partners LLC Research
Revenues in millions. 2014E quarterly EPS don't total to annual figure due to change in shares outstanding.

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IMMUNE DESIGN: INITIATING WITH OUTPERFORM

AUGUST 18, 2014

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INVESTMENT THESIS

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VALUATION

- Our valuation for IMDZ is $25 a share based on DCF analysis and probability-weighted sales for G100 in Merkel cell carcinoma and low-grade non-Hodgkin's lymphoma (NHL) (10-30% probability), and for CMB305 in synovial sarcoma, melanoma, non-small cell lung cancer (NSCLC), and ovarian cancer (10-20% probability) with a 10% discount rate. We believe this discount rate is appropriate as we use probability-weighted sales for the products. We also assigned $50M to partnered programs but no value for potential products beyond NY-ESO-1.

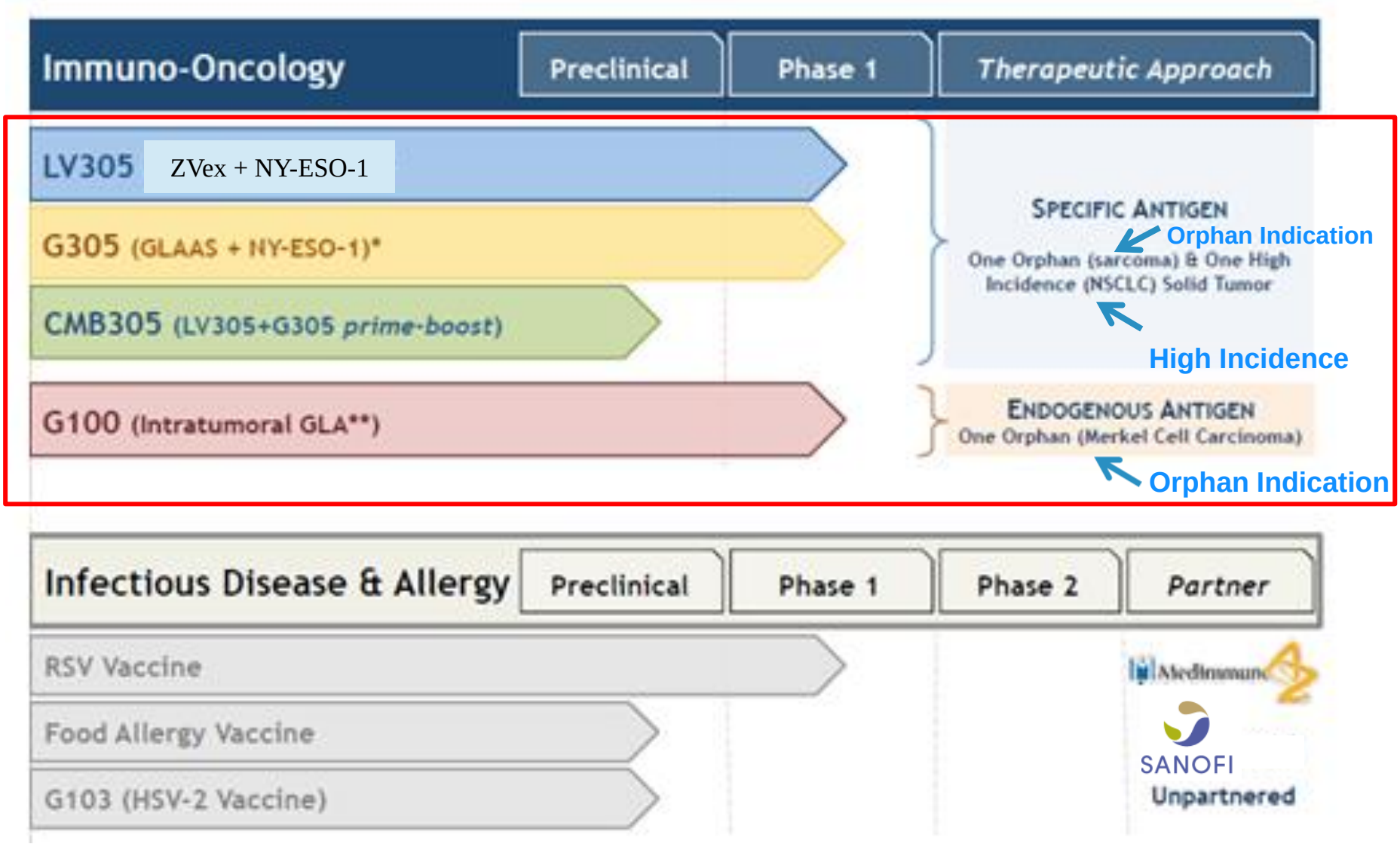
RISKS TO VALUATION

- Early stage of development with uncertainties in efficacy and safety
- Unknown future landscape in immunotherapy for cancer
- Initial target (NY-ESO-1) remains to be validated
- Ability to scale up and manufacture lentivirus as a product
- Lack of manufacturing capability and reliance on third-party manufacturers
- Competition from immunotherapeutic approaches.

IMMUNE DESIGN OVERVIEW

- Clinical-stage immuno-oncology story with two technology platforms and three candidates in the clinic (all Phase I, two intended as a combination)
- Employs synergistic immunological approaches to treating cancer by generating tumor specific cytotoxic T cells (CTLs)
- Two technology platforms:
  - IMDZVex™ (ZVex, also known as DCVex) is a lentivirus system that allows *in vivo* delivery of tumor antigens into dendritic cells
  - GLAAS™ is proprietary adjuvant for stimulating helper T cell response that can also create multiple candidates for treating different tumor types
- The three lead candidates being evaluated by IMDZ are LV305 (NY-ESO-1 delivered on ZVex), G305 (TLR4 agonist + full-length NY-ESO-1 protein, to be combined with LV305 as CMB305) and G100 (TLR4 agonist), Phase I started in 4Q:13 to 1Q:14, data expected in 1Q:15
- Initial activity seen in one complete response on G100 in loco-regional Merkel cell carcinoma (MCC), one ovarian cancer patient with large reduction in biochemical marker CA125 (from 600 to 220) in first cohort of three patients on G305
- Collaborative programs in infectious diseases and allergies, with MedImmune/AstraZeneca in three infectious disease indications and Sanofi for a select food allergy
- Seasoned management team with significant pharma & biotech experience. Distinguished academics such as the Nobel laureate David Baltimore as scientific founders. In addition, the leaders in the field of immunotherapy are on the scientific and clinical advisory board.

PIPELINE



- Currently NY-ESO-1 and endogenous antigens are the primary targets.

Source: Company Reports

2015 COULD BE A CATALYST-RICH YEAR FOR IMDZ

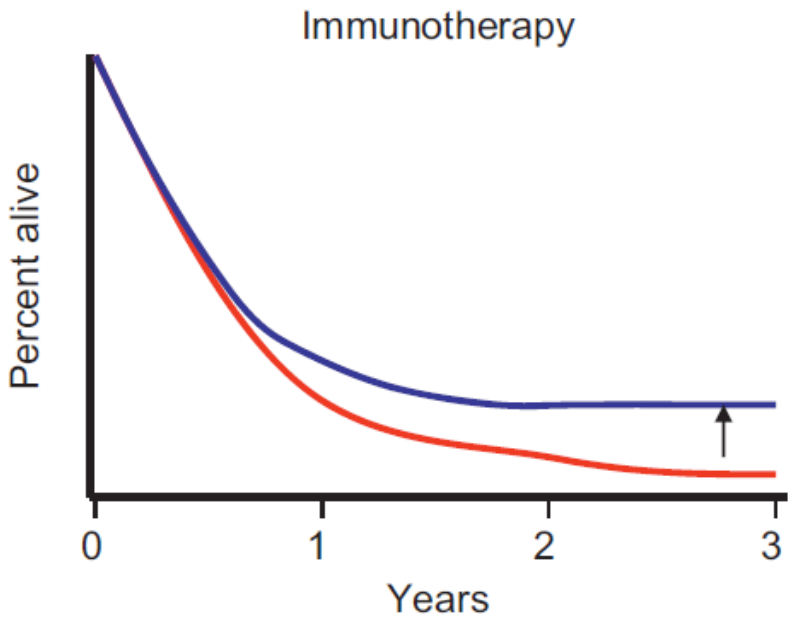
Drug	Timing	Description
G100	1Q:15	Phase I data from trial in MCC
	1Q:15	Initiate Phase I trial in follicular lymphoma
LV305	1Q:15	Phase I data
G305	1Q:15	Phase I data
CM305	1Q:15	Initiate Phase I in NY-ESO-1 positive solid tumors
	2H:15	Phase I data
	2H:15	Initiate Phase II

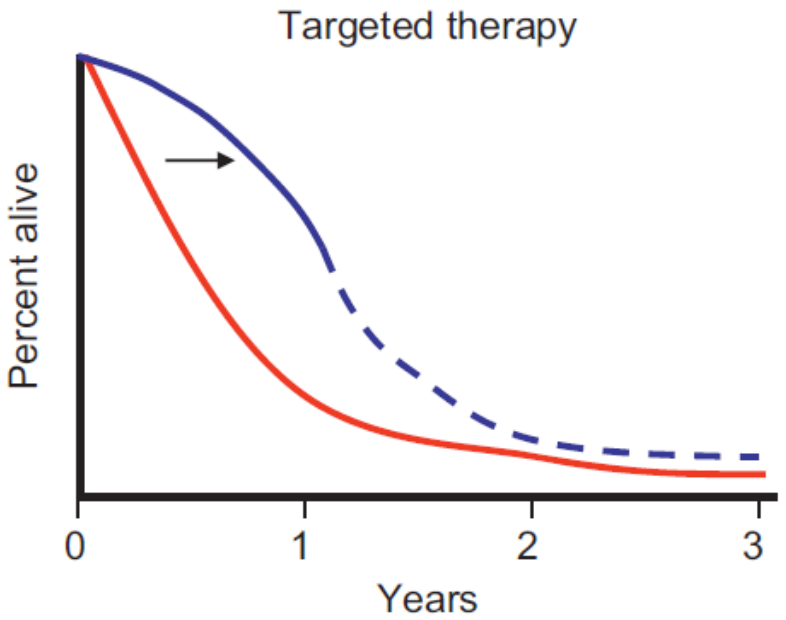
. Source: Company reports and Leerink Partners Research

Immuno-Oncology Is an Emerging New Pillar for Cancer Therapy

IMMUNOTHERAPY – LIFTING THE SURVIVAL CURVE

- For years, cancers have been referred to as a disease of the genome, where genetic alterations (including activation of oncogenes, inactivation of tumor suppressor genes, overexpression of growth factors and protein kinases) result in tumor formation and expansion
- While targeted therapies block driver oncogenes and induce rapid tumor response, resistance usually builds up quickly, resulting in an early improvement of survival curve but unclear beneficial effects in the long term
- Immunotherapy, on the other hand, has the ability to induce infrequent (until recently) but highly durable tumor responses, resulting in long-lasting survival benefit. This approach has improved treatment outcomes consistently with a single agent across a wide range of cancers. Combination data, while limited, have also been encouraging.





Source: Ribas et al, Clin Cancer Res 2012, 18:336

Source: Zinkernagel et al, Frontiers in fimmu 2014

YERVOY'S 10-YEAR OVERALL SURVIVAL DATA SUGGEST "FUNCTIONAL CURES" IN METASTATIC MELANOMA PATIENTS

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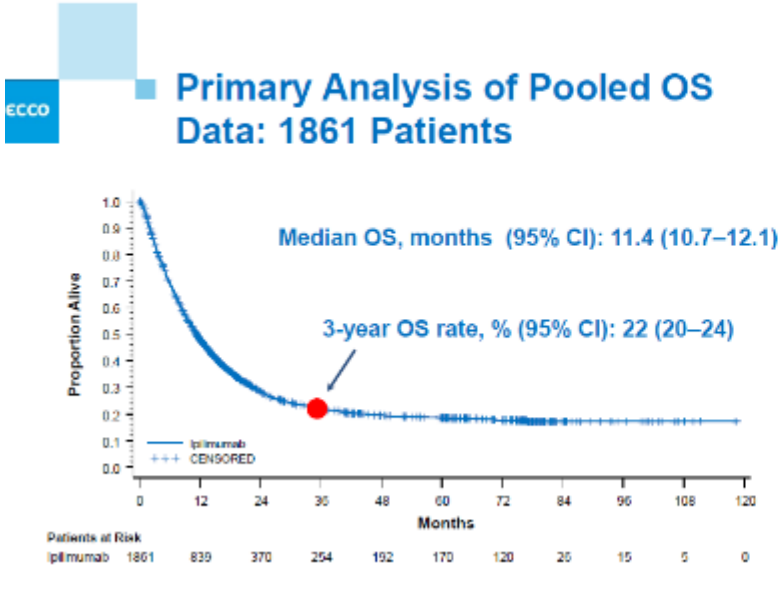
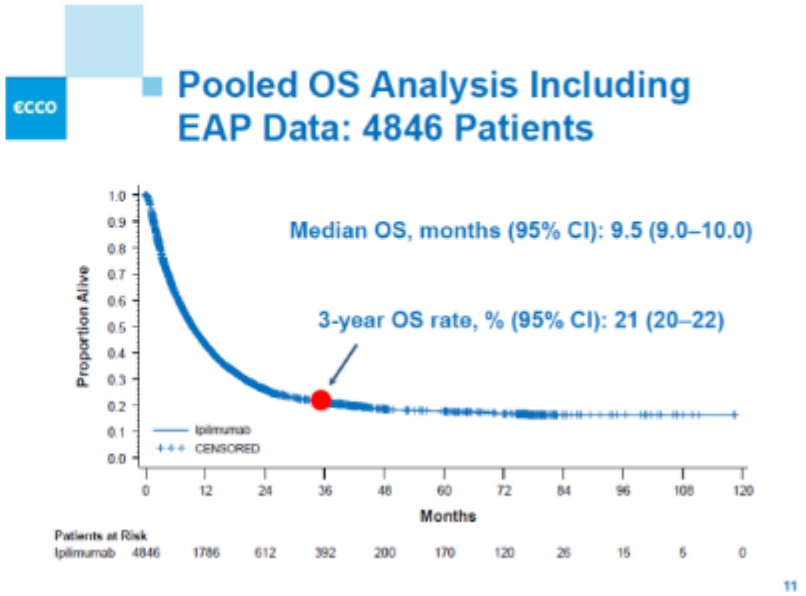
Trial data



Trial data + data from early access program (EAP)



- Approximately 20% of treated patients live for up to 10 years
- These data exhibit the consistent survival benefit of Yervoy in melanoma patients both in the clinic and practice.

Source: Schadendorf et al., ESMO 2013

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DESPITE THE SUCCESS TO DATE WITH CHECKPOINT INHIBITORS, COMBINATION THERAPY IS LIKELY THE FUTURE FOR IMMUNOTHERAPY

- A leading KOL in IO states that the impressive data on PD-1 agents, arguably the best ever single-agent activity seen in cancer, may be only the tip of the iceberg for immunotherapy in cancer. KOLs and industry leaders foresee improvement of tumor response rate from 20-30% currently with single-agent PD-1/PDL1 antibodies to over 50% through combinations

- Approaches to improving immunotherapy for cancer are generally thought to fall broadly in three areas: removal of immune checkpoint ("take the brake off"), stimulation of T cells ("rev up the engine"), and improving the access to tumor by T cells and release of tumor-specific antigens

- While it is too early to conclude on the best combination due to lack of head-to head comparisons, there is high interest in the combination of immuno-modulatory antibodies, either involving two inhibitors of immune checkpoint (like anti-PD-1 and anti-CTLA4 antibodies) or one checkpoint inhibitor plus a co-stimulatory agonist or another immunotherapeutic agent that generates T cell response. Some KOLs stated that their intuition would be that the latter approaches would be preferable as there is less likely an overlap between the effect of the two types of compounds

- With the clinical success of checkpoint inhibitors, it should now be possible to evaluate vaccine approaches in combination with a PD-1/PD-L1 inhibitor, where prime boost coupled with disabling the immune inhibition in the tumor microenvironment should lead to enhanced anti-tumor activity.

CHECKPOINT INHIBITORS RESULT IN OBJECTIVE RESPONSE IN GENERALLY LESS THAN HALF OF UNSELECTED PATIENTS

Efficacy Comparisons as of October 2013

	Anti-PD1						Anti-PDL1								
	Nivolumab			MK-3475			MPDL3280a			BMS-936559			MEDI4736		
Melanoma		*n*	*RR*		*n*	*RR*		*n*	*RR*		*n*	*RR*		*n*	*RR*
All Doses		**107**	**31%**		**117**	**38%**	Q3W	**34**	**32%**		**52**	**17%**		--	--
All Active Doses		52	35%		97	46%		--	--		38	21%		--	--
*	3 mpk	17	41%	10 mpk Q2W	52	52%	--	--	--	3 mpk	17	29%	--	--	--
	1 mpk	35	31%	10 mpk Q3W	45	38%	--	--	--	10 mpk	16	19%	--	--	--

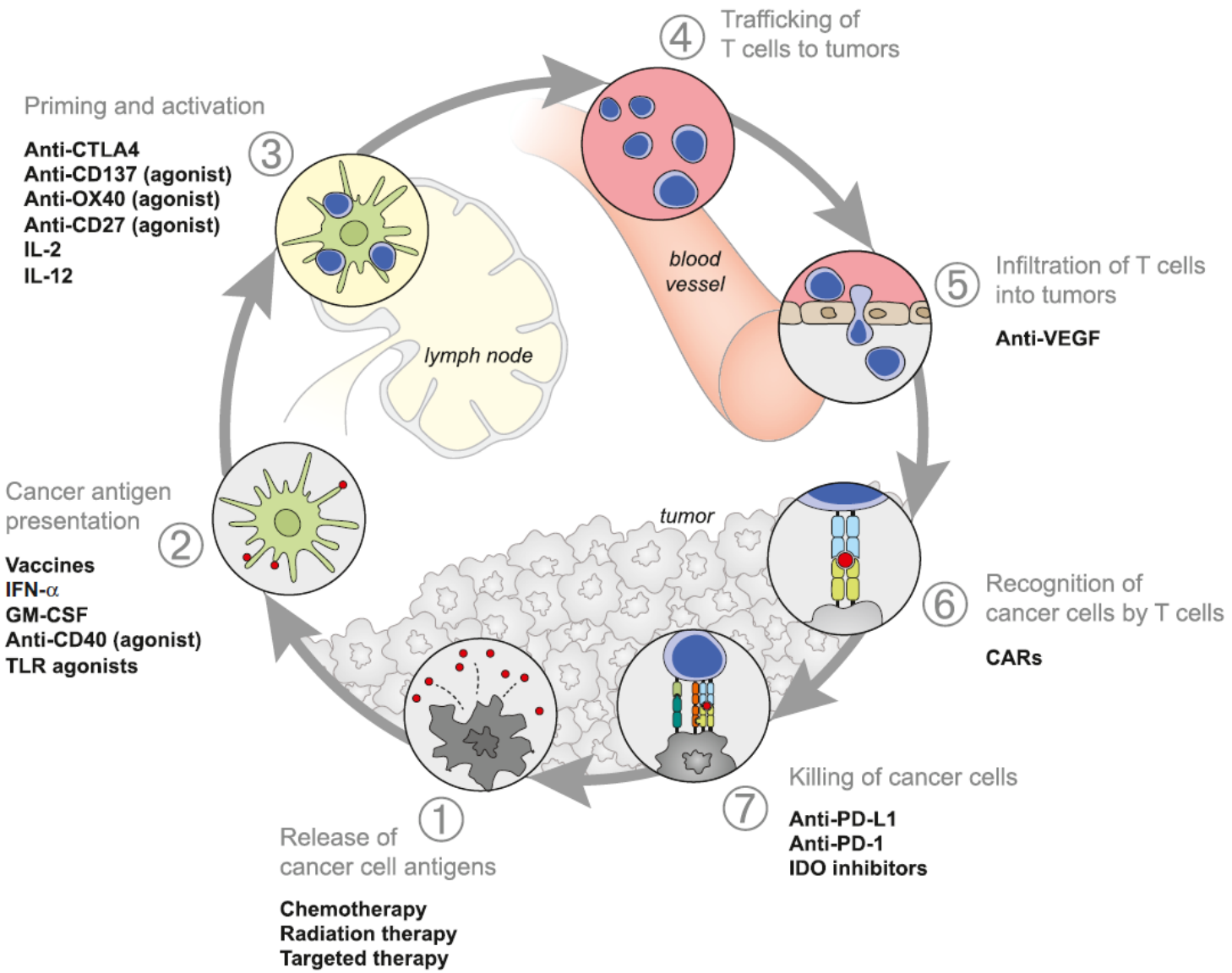
Efficacy Comparisons as of October 2013

	Anti-PD1						Anti-PDL1								
	Nivolumab			MK-3475			MPDL3280a			BMS-936559			MEDI4736		
NSCLC		*n*	*RR*		*n*	*RR*		*n*	*RR*		*n*	*RR*		*n*	*RR*
All Doses		**129**	**17%**		**33**	**21%**	Q3W	**53**	**23%**		**49**	**10%**		**6**	**50%**
All Active Doses		96	22%		33	21%		--	--		38	13%		5	60%
*	3 mpk	37	24%	10 mpk Q3W	33	21%	--	--	--	10 mpk	25	16%	0.3 mpk	3	67%
	10 mpk	59	20%	--	--	--	--	--	--	3 mpk	13	8%	1 mpk	2	50%
NSCLC - Non-Squamous															
All Doses		**74**	**18%**		**26**	**15%**	Q3W	**42**	**21%**		**36**	**11%**		--	--
All Active Doses		56	21%		26	15%		--	--		26	15%		--	--
*	3 mpk	19	26%	10 mpk Q3W	26	15%	--	--	--	10 mpk	17	18%	--	--	--
	10 mpk	37	19%	--	--	--	--	--	--	3 mpk	9	11%	--	--	--
NSCLC - Squamous															
All Doses		**54**	**17%**		**6**	**33%**	Q3W	**11**	**27%**		**13**	**8%**		--	--
All Active Doses		39	23%		6	33%		--	--		12	8%		--	--
*	10 mpk	21	24%	10 mpk Q3W	6	33%	--	--	--	10 mpk	8	13%	--	--	--
	3 mpk	18	22%	--	--	--	--	--	--	3 mpk	4	0%	--	--	--

Source: Leerink Immuno-Oncology Whitepaper, 2013

Immune Activation Likely Will Be Part of Future Immunotherapy

CANCER IMMUNITY CYCLE – NUMEROUS THERAPEUTIC TARGETS



- The generation of immunity to cancer is a cyclic process divided into 7 steps
- In cancer patients, the cancer immunity cycle does not perform optimally
- Each step can be targeted for cancer immunotherapy to reinitiate a self-sustaining cycle of cancer immunity without generating autoimmune inflammatory responses.

Source: Chen et al., Immunity 2013, 39:1; Note: CARs – chimeric antigen receptors; GM-CSF – granulocyte macrophage colony-stimulating factor

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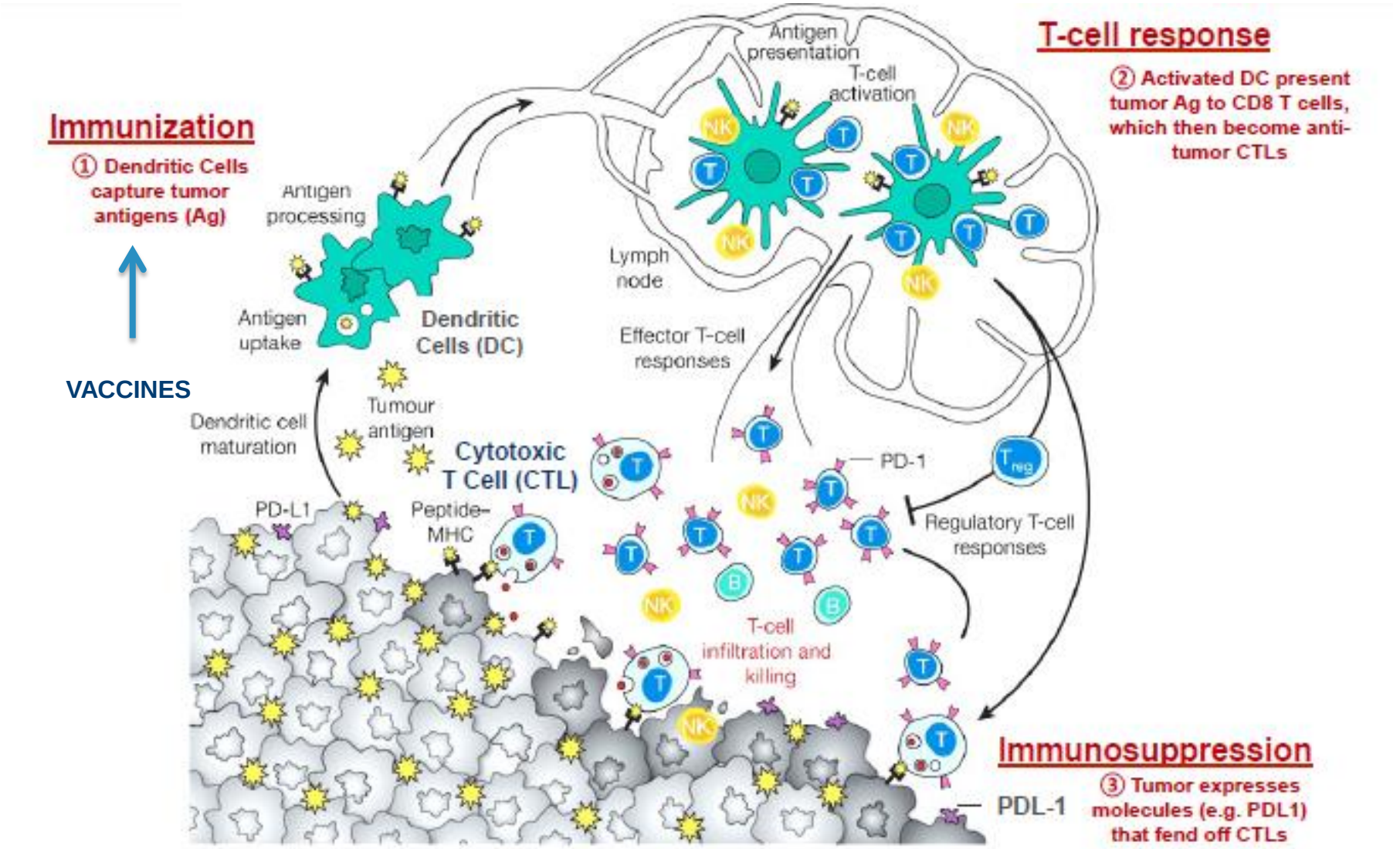
MULTIPLE WAYS TO UTILIZE THE IMMUNE SYSTEM TO TARGET TUMOREGENIC CELLS



The Dendritic Cell is at the core of making a tumor antigen/s being recognized as "foreign"
The Cytotoxic T Cell (CTL) is a major effector of "cancer immunotherapy"

Source: Mellman, Ira et al., Nature 2011 and Company Reports

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CANCER IMMUNITY CYCLE – POSITIVE AND NEGATIVE REGULATORS AT EACH STEP

- At each step of cancer immunity cycle, it requires the coordination of both stimulatory (promote immunity) and inhibitory (reduce immune activity/prevent autoimmunity) factors.

Steps	(+) Stimulators	(–) Inhibitors	Other Considerations	Example References
1. Release of cancer antigens	Immunogenic or necrotic cell death	Tolergenic or apoptotic cell death	Tumor-associated neoantigens and cancer testis antigens	Ferguson et al., 2011
2. Cancer antigen presentation	● Proinflammatory cytokines (e.g., TNF-α, IL1, IFN-α) ● Immune cell factors: CD40L/CD40 ● Endogenous adjuvants released from dying tumors: CDN (STING ligand), ATP, HMGB1 ● Gut microbiome products: TLR ligands	IL-10, IL-4, IL-13	Dendritic cell maturity	Lippitz, 2013; Mellman et al., 2011
3. Priming and activation	CD28:B7.1, CD137 (4-1BB)/ CD137L, OX40:OX40L, CD27:CD70, HVEM, GITR, IL-2, IL-12	CTLA4:B7.1, PD-L1:PD-1, PD-L1:B7.1, prostaglandins	Central tolerance, T cell repertoire, T regulatory cells	Franciszkiewicz et al., 2012; Lippitz, 2013; Riella et al., 2012; So et al., 2006
4. Trafficking of T cells to tumors	CX3CL1, CXCL9, CXCL10, CCL5			Franciszkiewicz et al., 2012; Peng et al., 2012
5. Infiltration of T cells into tumors	LFA1:ICAM1, selectins	VEGF, endothelin B receptor		Franciszkiewicz et al., 2013
6. Recognition of cancer cells by T cells	T cell receptor	Reduced peptide-MHC expression on cancer cells		Mellman et al., 2011
7. Killing of cancer cells	IFN-γ, T cell granule content	PD-L1:PD-1, PD-L1:B7.1, TIM-3:phospholipids, BTLA, VISTA, LAG-3, IDO, Arginase, MICA:MICB, B7-H4, TGFβ	T regulatory cells, myeloid-derived suppressor cells, M2 macrophages, hypoxia	Chen et al., 2012; Greaves and Gribben, 2013; Mellman et al., 2011; Topalian et al., 2012a

Source: Chen et al., Immunity 2013, 39:1

IN NEARLY HALF OF METASTATIC MELANOMA CASES, TILs ARE ABSENT, SUGGESTING A NEED TO ACTIVATE THE IMMUNE RESPONSE

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Presence of tumor-infiltrating lymphocytes (TILs) and PDL1 (B7-H1) in 150 melanocytic lesions

		TIL +		TIL -	
	Total	PDL1+	PDL1-	PDL1+	PDL1-
Benign nevi	40	14	4	0	22
Primary melanomas	54	19	15	0	20
Metastases	56	23	7	1	25
All	150	56	26	1	67
Benign nevi		35%	10%	0%	55%
Primary melanomas		35%	28%	0%	37%
Metastases		41%	13%	2%	45%
All		37%	17%	1%	45%

Source: Taube et al 2012 Sci Transl Med, Leerink Partners analysis

- Tumor-infiltrating lymphocytes are needed to mount an immune response and kill tumors. In the absence of tumor-infiltrating lymphocytes, checkpoint inhibitors such as PD1 and PDL1 antibodies would be unlikely to have an effect.

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PD-L1 EXPRESSION IS LIKELY IN RESPONSE TO THE PRESENCE OF TUMOR-INFILTRATING LYMPHOCYTES (TILs)

- In the same study analyzing 150 human tissues, a strong correlation was found between melanocyte expression of PD-L1 (B7-H1) and the presence of tumor-infiltrating lymphocytes (TILs) in human melanocytic lesions
- Approximately 98% of PD-L1 positive tumors had adjacent TILs, while in PD-L1 negative tumors only 28% had adjacent TILs, suggesting TILs led to PD-L1 over-expression in tumors
- The high correlation of PD-L1/TILs was also observed in benign nevi. IFN-gamma, a primary inducer of PD-L1, was also detected at the inter-face of PD-L1 tumors and TILs, but none in PD-L1 negative tumors. These findings suggested that TILs could produce factors driving PD-L1 expression as a negative feedback mechanism, an adaptive immune resistance exerted by the tumor.

Histology	Total	Number of cases/total cases (%)				P^*
		B7-H1$^{+/\pm}$		B7-H1$^-$		
		TIL$^{+/\pm}$	TIL$^-$	TIL$^+$	TIL$^-$	
Benign nevi	40	14/14 (100)	0/14 (0)	4/26 (15)	22/26 (85)	<0.0001
Primary melanomas (in situ or invasive)	54	19/19 (100)	0/19 (0)	15/35 (43)	20/35 (57)	<0.0001
Metastases	56	23/24 (96)	1/24 (4)	7/32 (22)	25/32 (78)	<0.0001
All	150	56/57 (98)	1/57 (2)	26/93 (28)	67/93 (72)	<0.0001

Source: Taube et al., Sci Transl Med 2012, 4:127

PD-L1 UP-REGULATION IS AN INDICATION OF ACTIVE IMMUNE RESPONSE

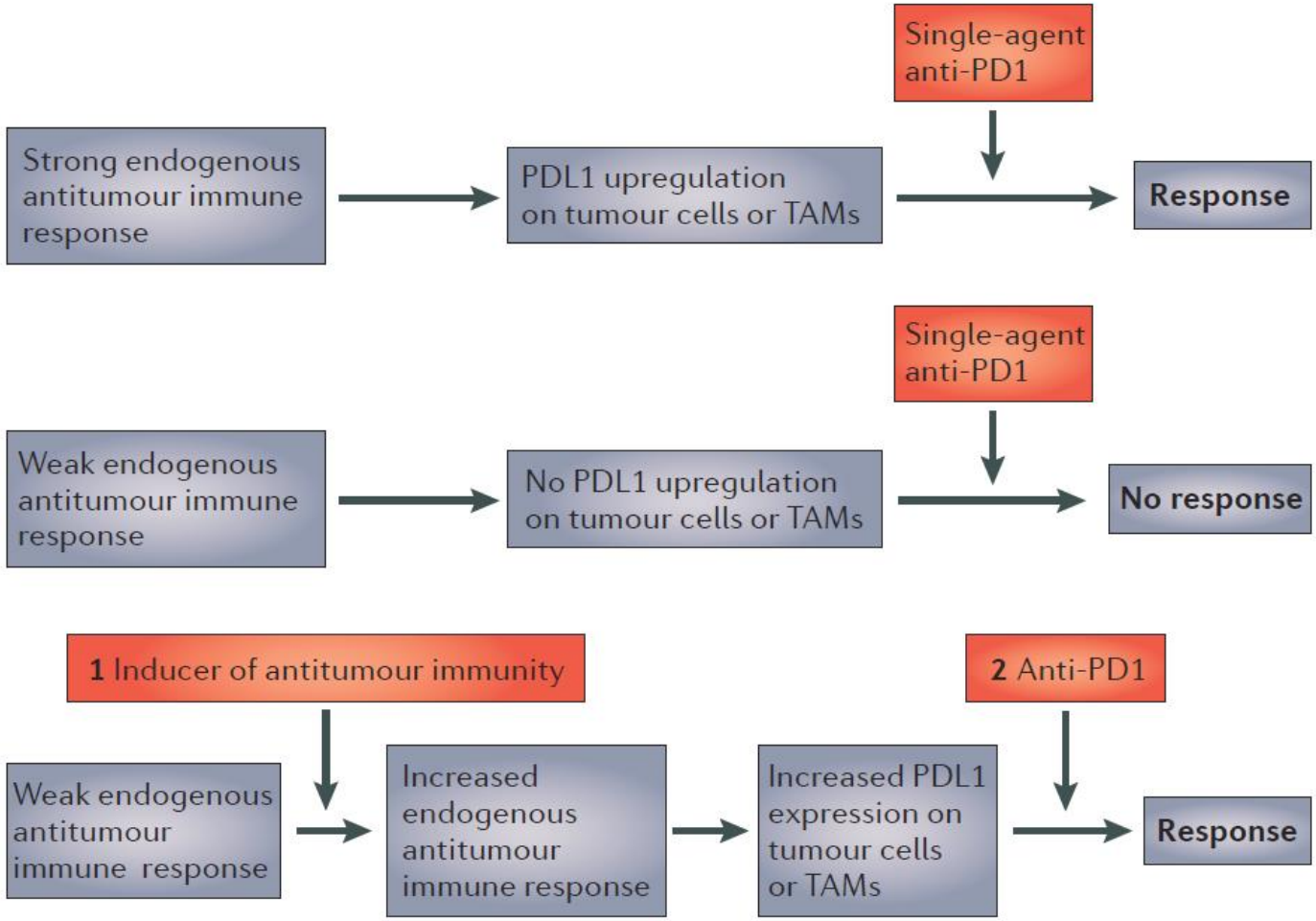
- Other studies also supported the hypothesis that PD-L1 up-regulation in multiple types of tumor cells is a reflection of tumor cells' adaptation to endogenous immune responses directed at tumor antigens – a process termed adaptive resistance

- Distinctive from the conventional view where immune resistance occurs either by immune escape (mutations) or up-regulation of immune-inhibitory ligands (driven by oncogene), up-regulation of PD-L1 in the cancer microenvironment is also associated with endogenous inflammatory immune responses. This seemingly paradoxical observation where expression of an immunosuppressive molecule correlates with improved survival outcome may only be resolved when PD-L1 expression level is viewed as a reflection of the existence of endogenous antitumor immunity

- To support this hypothesis, PD-1 and PD-L1 knockout mice do not develop spontaneous auto-immune responses but have exacerbated tissue responses to infection during the first year after birth.

Source: Taube et al., Sci Transl Med 2012, 4:127; Taube et al., Clin Cancer Res 2014, doi: 10.1158/1078-0432.CCR-13-3271; Topalian et al., Curr Opin Immunol 2012, 24:207

IMPLICATIONS OF ADAPTIVE IMMUNE RESISTANCE MECHANISM FOR COMBINATORIAL IMMUNOTHERAPY OF CANCER

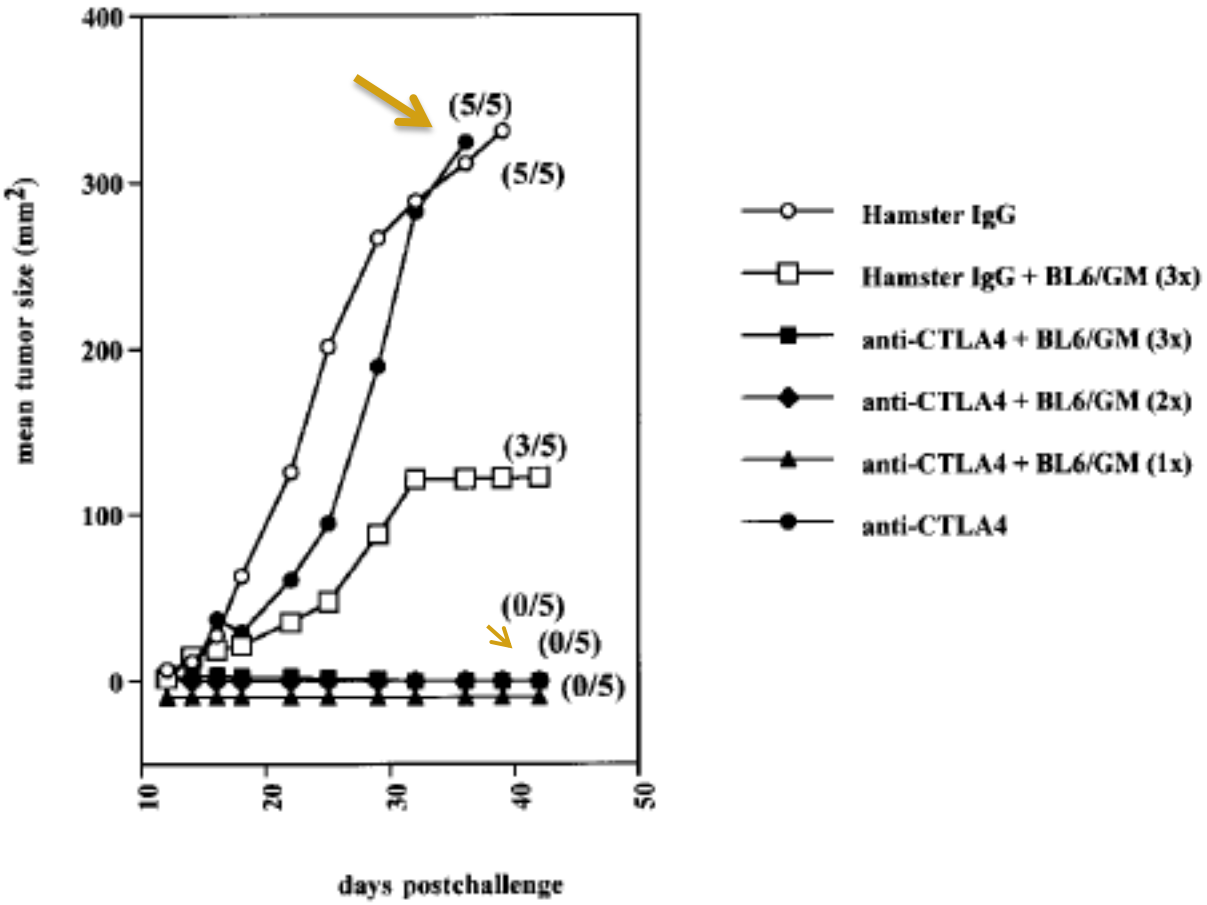


TAM: tumor associated macrophages

- The adaptive resistance mechanism implies that any treatment that induces anti-tumor immunity, such as vaccination, should provide therapeutic synergy with PD-1 pathway blockade.

Source: Pardoll, Nature Reviews Cancer, 2012

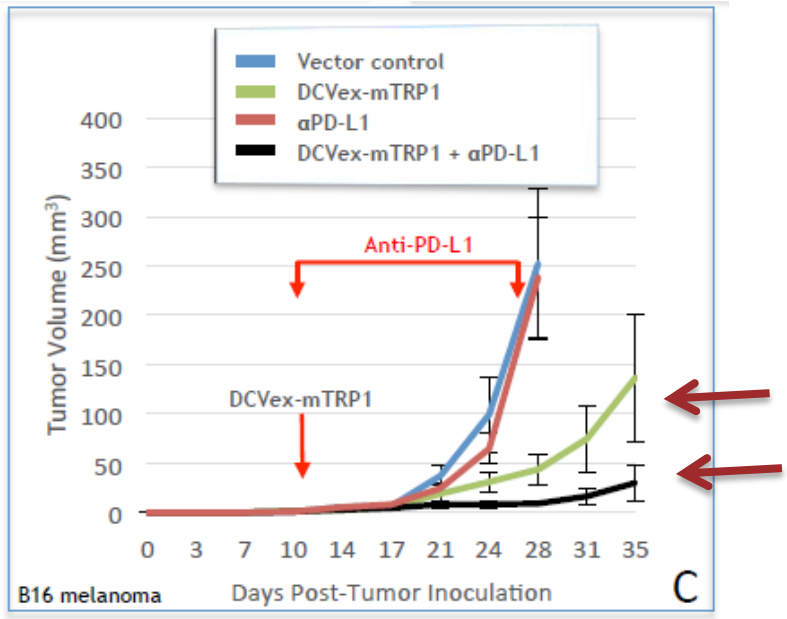
COMBINATION OF A VACCINE WITH A CHECKPOINT INHIBITOR PRODUCES "CURES" IN AN AGGRESSIVE TUMOR MODEL



- Combination of CTLA4 checkpoint inhibitor together with a vaccine containing BL6 cells + GM-CSF leads to the eradication of tumor cells in the melanoma mice model
- These data suggest that inhibiting checkpoints may not be sufficient to induce T cells to engage in a robust anti-tumor activity in tumors that are not immunogenic
- MEDACorp key opinion leaders stated that the combination of a checkpoint inhibitor and a vaccine has produced the best data in preclinical models

Source: van Elsas et al., J. Exp. Med 190(3), 1999

COMBINING ZVex WITH CHECKPOINT INHIBITOR RESULTS IN IMPROVED EFFICACY IN PRE-CLINICAL MODELS

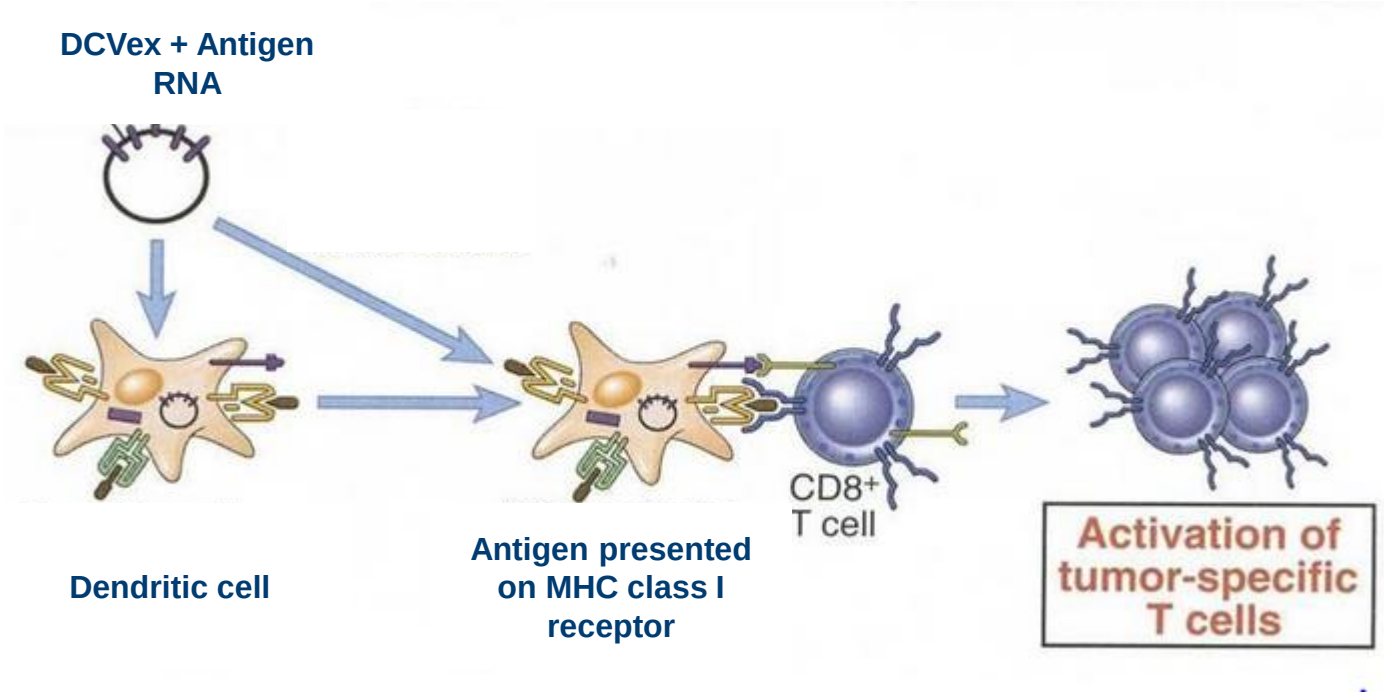


- Pre-clinical data from IMDZ shows that anti-tumor activity of ZVex™ expressing a self melanocyte antigen (TRP1) combined with anti-PD-L-1 (checkpoint inhibitors) was superior to either therapy alone
- Combination of a CTL-generating approach with a checkpoint inhibitor could provide added therapeutic benefit.

Source: Company Reports and Leerink Partners

IMDZ Has Developed a Novel Way of Delivering Antigens to Dendritic Cells and Generating Immune Response

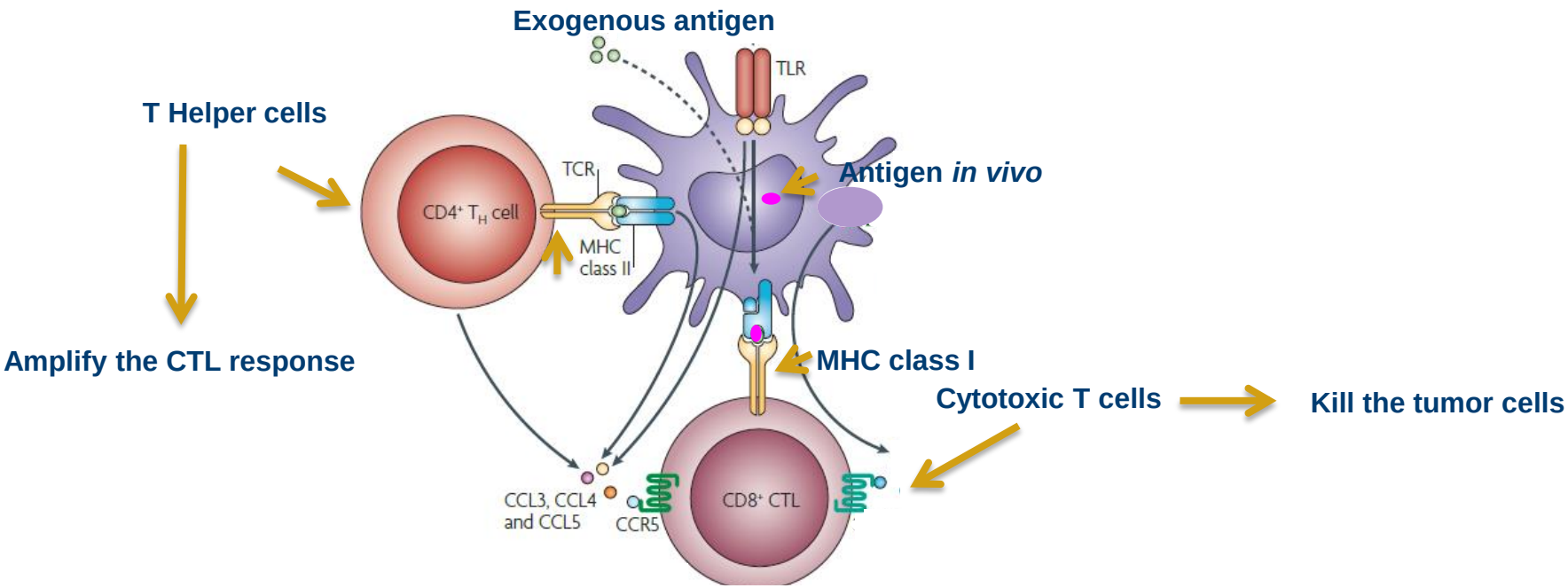
DENDRITIC CELL-SPECIFIC TARGETING



- IMDZ uses ***in vivo*** targeting to generate the immune response against a specific cancer antigen**,** enabling it to create antigen-specific **cytotoxic T cells (CTLs),** also known as killer T cells
- CTLs are an essential component of the immune system, and their activation is key to targeting and eliminating tumor cells
- The IMDZ approach is particularly novel as it traffics antigens to the right receptors (MHC class I) ensuring the activation of CTLs, and it has the capability to boost the CTL activation extracellularly.

Source: Company Reports and Leerink Partners

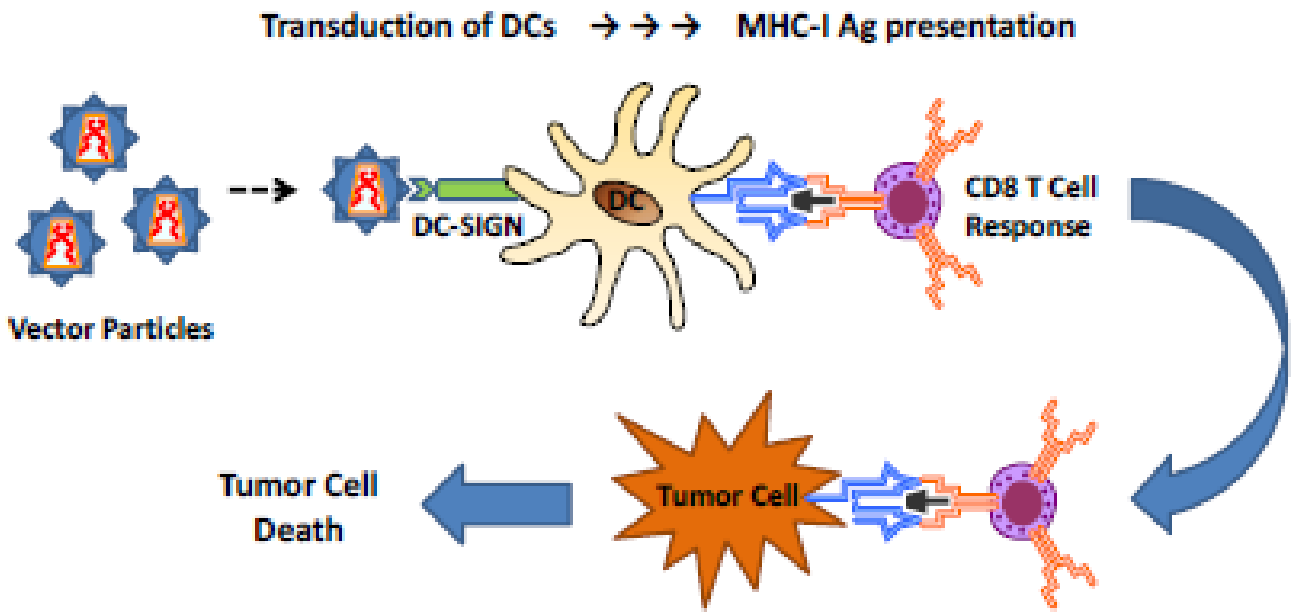
SPECIFIC *In Vivo* TARGETING OF DENDRITIC CELLS LEADS TO OPTIMAL ANTIGEN PRESENTATION AND PRODUCTION OF CTLS



- The IMDZ approach could potentially overcome problems with efficient uptake of antigen and CTL production by the *in vivo* targeting of dendritic cells
- Dendritic cells (DCs) are highly specialized antigen presenting cells (APCs) and play a central role in initiating and regulating an immune response
- DCs “introduce” T cells to antigens and provide the right context for the T cells to respond
- Specifically targeting DC’s *in vivo* leads to maximum CTL generation
- They are also essential for the activation of CD4 T helper cells that are required for the amplification of the CTL response.

Source: Dhodpkar et al, Sci Transl Med 2014

IMDZVex™ (ZVex™) IS DESIGNED TO GENERATE CTLs TARGETING SPECIFIC ANTIGENS



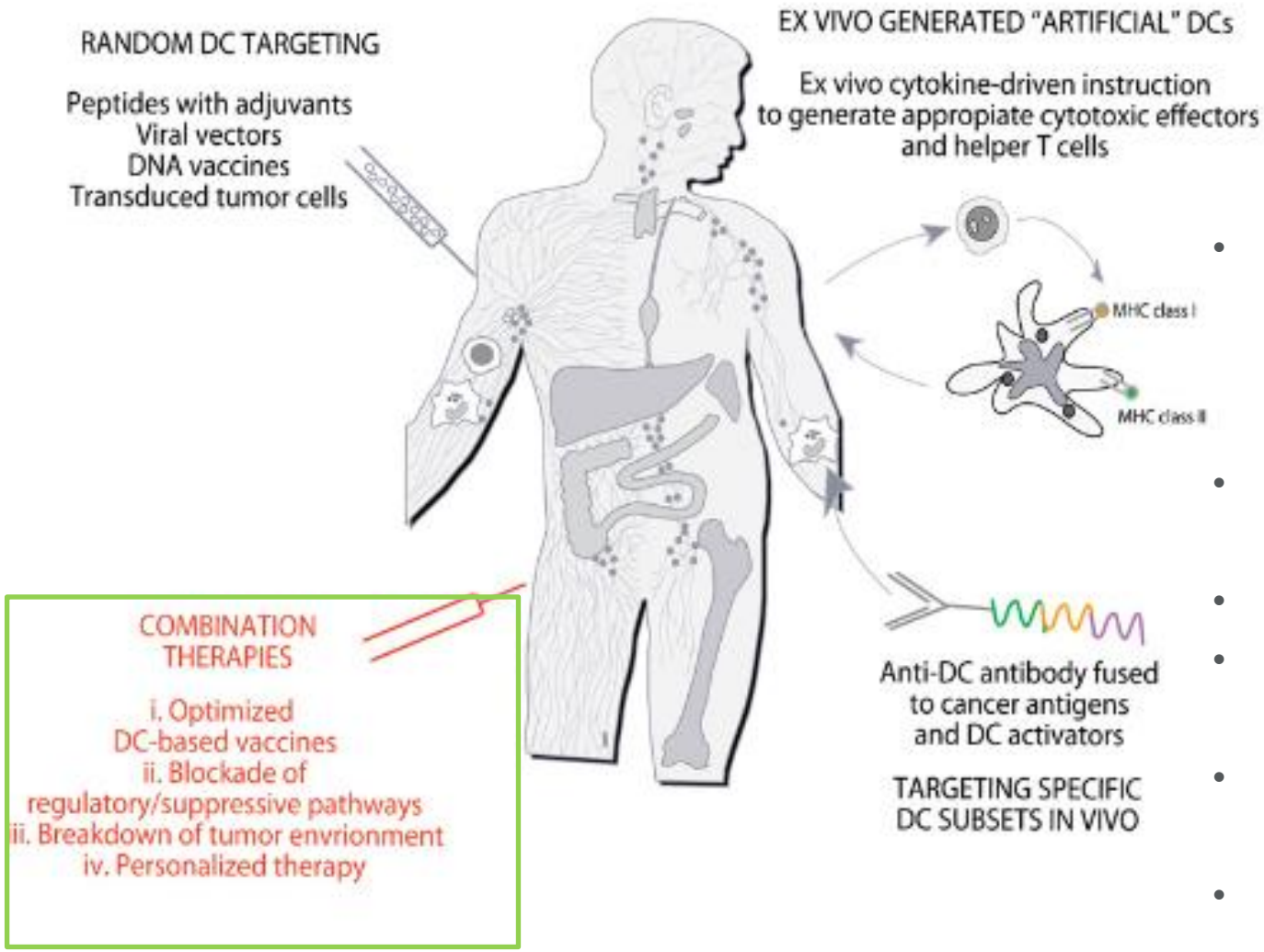
DCVex™ is designed to generate Ag-specific killer T cells to attack tumors

- ZVex™ (also known as DCVex) is a re-engineered lentiviral vector that selectively delivers tumor antigen in RNA form to DCs *in vivo* via envelope DC-SIGN interaction, ultimately leading to the generation and proliferation of antigen specific CTLs
- Specific targeting of DCs is shown to result in more potent CTL responses
- The platform can be used to generate numerous products that can target different antigens expressed on different tumor cells
- The vectors lack the ability to integrate, making them safer for patients
- This approach may have a potential therapeutic benefit as a single agent or in combination with other agents, including checkpoint inhibitors.

Source: Company Reports

IMDZ' Strategies Differ from Historical Cancer Vaccine Approaches

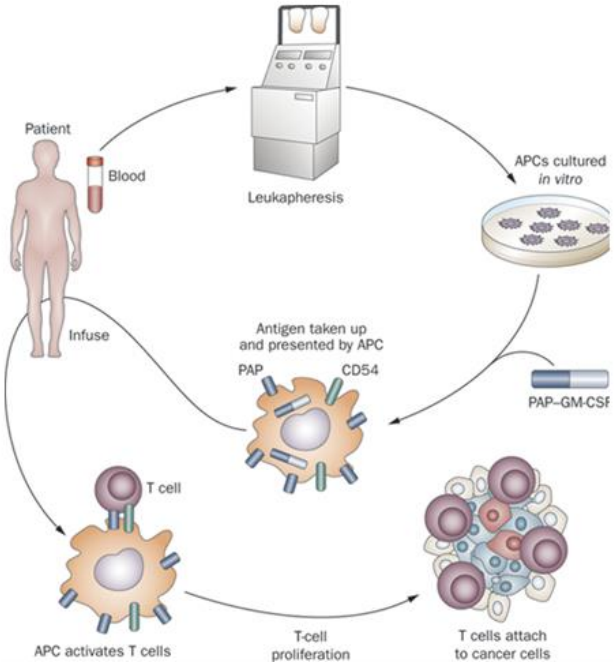
MULTIPLE WAYS TO TARGET DENDRITIC CELLS

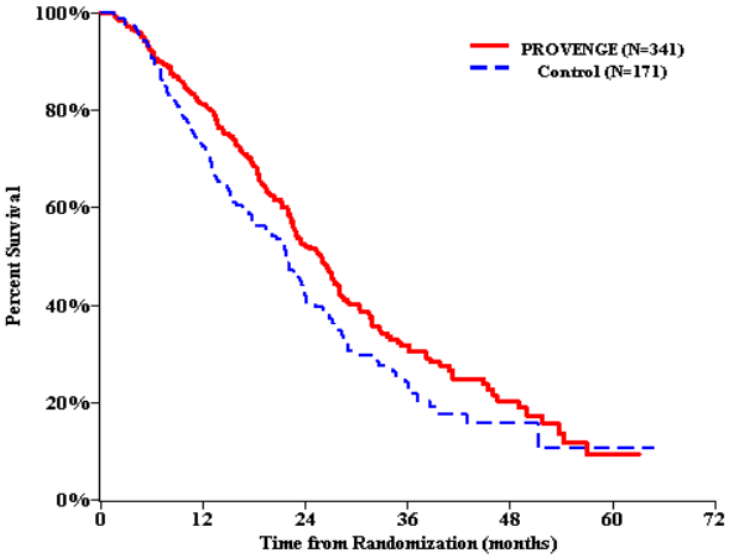


- Dendritic cells (DCs) are the most efficient antigen presenting cells (APCs) of the immune system
- Many different strategies are used to target and prime DCs:
- (a)- peptides- HLA binding
- (b)- lipids, viral vectors and transduced tumor cells
- (c)- *ex vivo* stimulation of immune cells
- (d)- antibodies fused to antigens.

Source: Palucka et al., 2013 Immunity 39

Ex Vivo DC ACTIVATION APPROACH: SIPULEUCEL-T (PROVENGE) PROVIDES A MODEST IMPROVEMENT IN OVERALL SURVIVAL





- *Ex vivo* approaches of stimulating DCs only showed ~4-month OS benefit
- This improvement was not accompanied by delayed disease progression
- In addition, treatment with Provenge is cumbersome and expensive.

	Study 1		Study 2	
	PROVENGE (N=341)	Control (N=171)	PROVENGE (N=82)	Control (N=45)
Overall Survival				
Median, months (95% CI)	25.8 (22.8, 27.7)	21.7 (17.7, 23.8)	25.9 (20.0, 32.4)	21.4 (12.3, 25.8)
Hazard Ratio (95% CI)	0.775[a] (0.614, 0.979)		0.586[b] (0.388, 0.884)	
p-value	0.032[a]		0.010[c]	

[a] Hazard ratio and p-value based on the Cox Model adjusted for PSA (ln) and LDH (ln) and stratified by bisphosphonate use, number of bone metastases, and primary Gleason grade.
[b] Hazard ratio based on the unadjusted Cox Model (not pre-specified).
[c] p-value based on a log-rank test (not pre-specified).
Abbreviations: CI = confidence interval.

Source: Provenge label

DATA FROM PHASE I AND II TRIALS OF *Ex Vivo* DC ACTIVATION BY SIPULEUCEL-T (PROVENGE) DOES NOT DIFFERENTIATE BETWEEN CD8 AND CD4 T CELLS

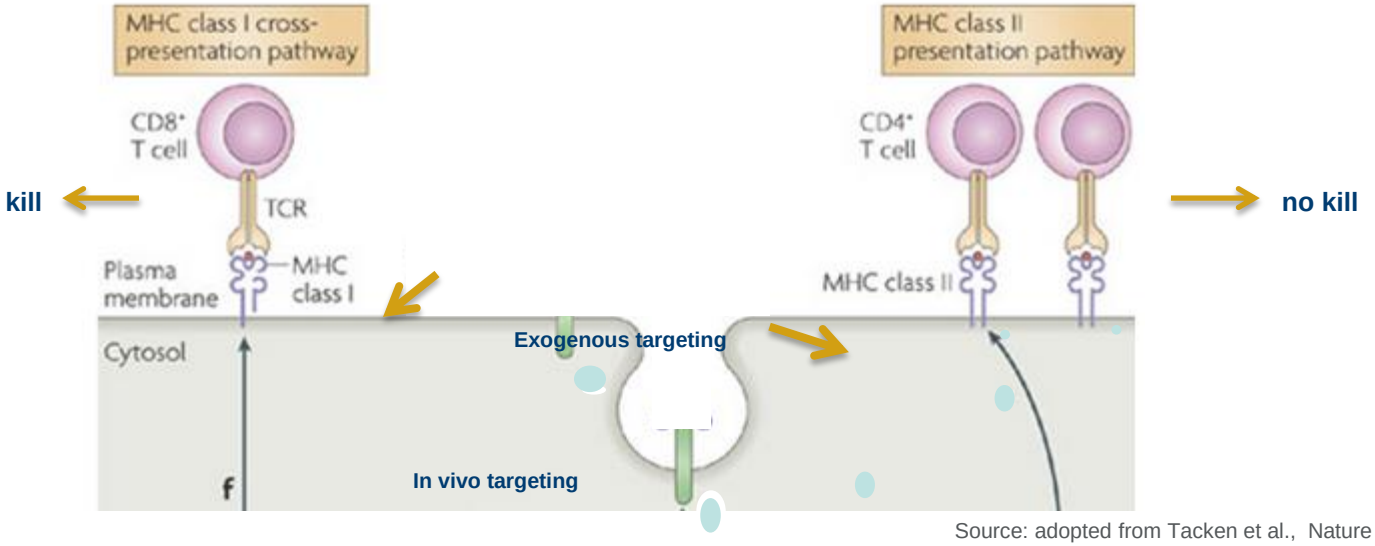
Table 2. Phenotype and Function of Provenge

	Phase I	Phase II	Total
No. of products	36	66	102
No. of nucleated cells, $\times 10^6$			
Median	1,308	2,376	2,172
Range	230-2,784	216-3,108	216-3,108
No. of CD54(+) cells, presumed dendritic cells, $\times 10^6$			
Median	30	278	123
Range	1.4-488	18.6-1,276	1.4-1,276
Phenotype markers, % of cells positive, mean ± SD			
CD54, dendritic cells	4.6 ± 5.8	14.8 ± 12.3	11.2 ± 11.5
CD3, T cells	69.3 ± 15.8	58.5 ± 15.5	62.3 ± 16.4
CD19, B cells	8.1 ± 5.9	6.7 ± 2.8	7.2 ± 4.2
CD14, monocytic cells	5.9 ± 6.3	14.8 ± 11.1	11.7 ± 10.5
CD56, natural killer cells	14.1 ± 7.8	14.6 ± 6.7	14.4 ± 7.1
AlloMLR EC50, $\times 10^4$ cells,* mean ± SD	13.1 ± 17.5	14.4 ± 37.9	13.8 ± 30.3

- The small clinical benefit seen with Provenge may have been a result of generation of low numbers of T cells
- These data use the CD3 biomarker, which is ubiquitously expressed in all T cells, and as a result it is difficult to conclude on the % of CTLs generated.

Source: Provenge label

EXOGENOUS PEPTIDE LOADING DOES NOT RESULT IN OPTIMAL ANTIGEN PRESENTATION AND GENERATION OF CTLs



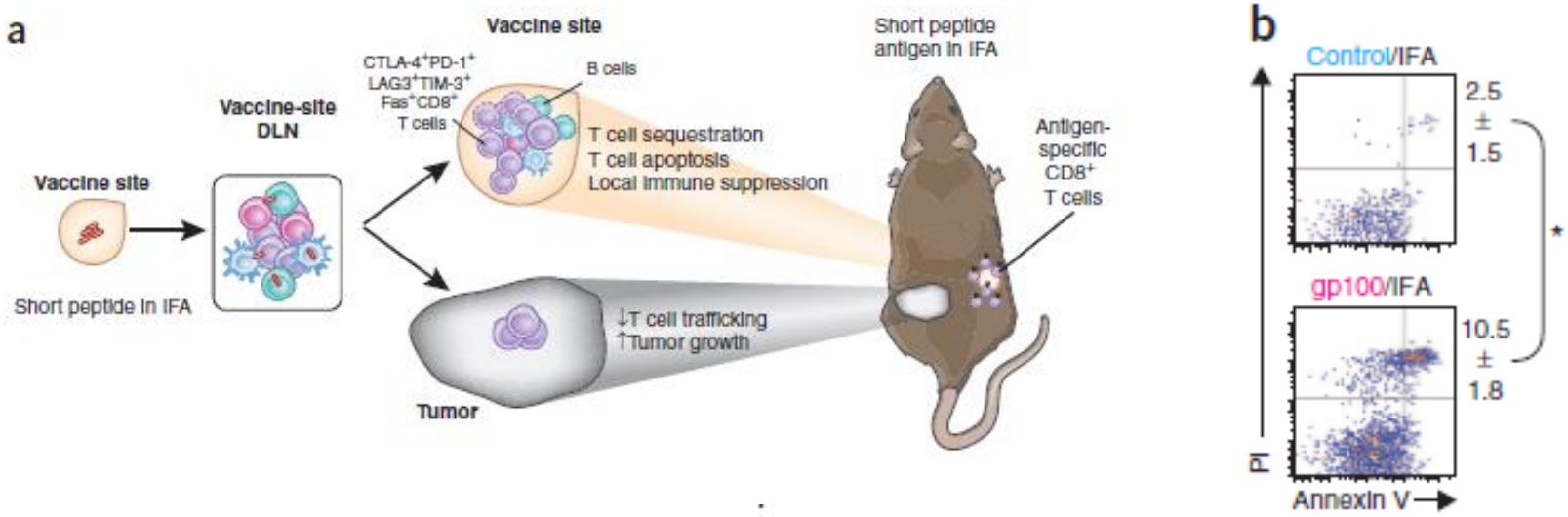
Source: adopted from Tacken et al., Nature Reviews Immunology 2007

- Exogenous antigens are presented on MHC class II molecules and induce CD4+ T cell responses. Endogenous antigens are generally presented on MHC class I molecules and engage CD8+ T cell response
- Therefore, exogenously loaded antigenic peptides/proteins used in previous cancer vaccines lead to the activation CD4+ T helper cells, which are incapable of killing tumor cells, and as a result the sole activation of CD4+ T cells fails to elicit an anti-tumor response
- Exogenous peptides can sometimes be presented on MHC class I receptors via a process known as cross-presentation; however, the induction of CTLs via cross-presentation is at least 10^5 times less efficient than direct presentation. According to Zinkemagel, cross-presentation is an experimental artifact as a result of large quantities of antigens used in the experiments
- Furthermore, certain peptide-protein vaccines generally have low immunogenicity and may result in tolerizing in the absence of an adjuvant
- One way to overcome these limitations is to use an approach that targets dendritic cells specifically
- IMDZ's ZVex platform exclusively targets DC and delivers the antigen (RNA form) via the DC-SIGN receptor that enables endogenous peptide loading.

Source: Zinkernagel et al, Frontiers in fimmu 2014

LEERINK

MINERAL OIL CARRIER USED IN PEPTIDE VACCINES LEADS TO T CELL SEQUESTRATION AT THE SITE OF VACCINATION

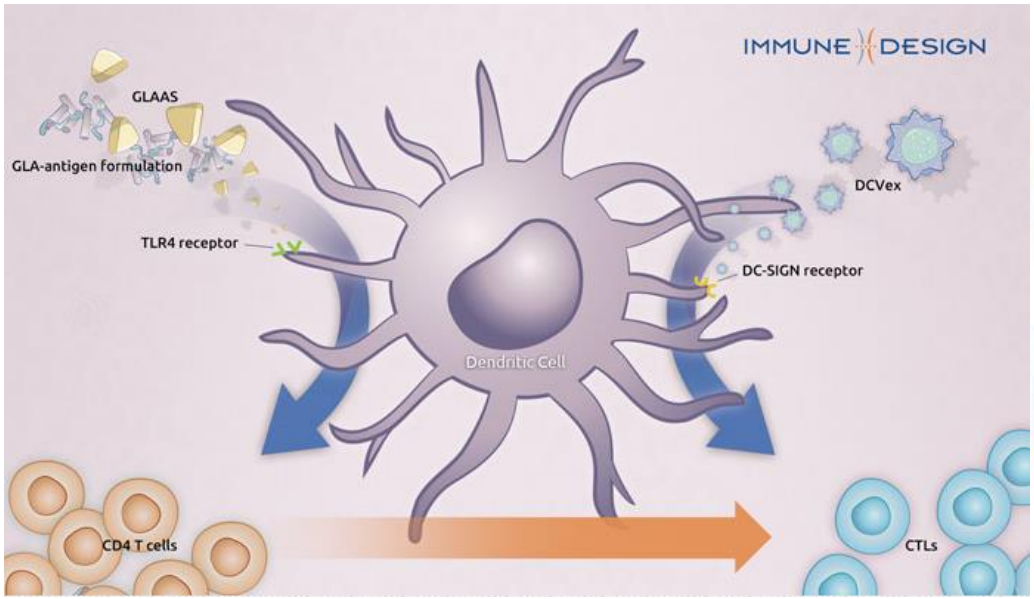


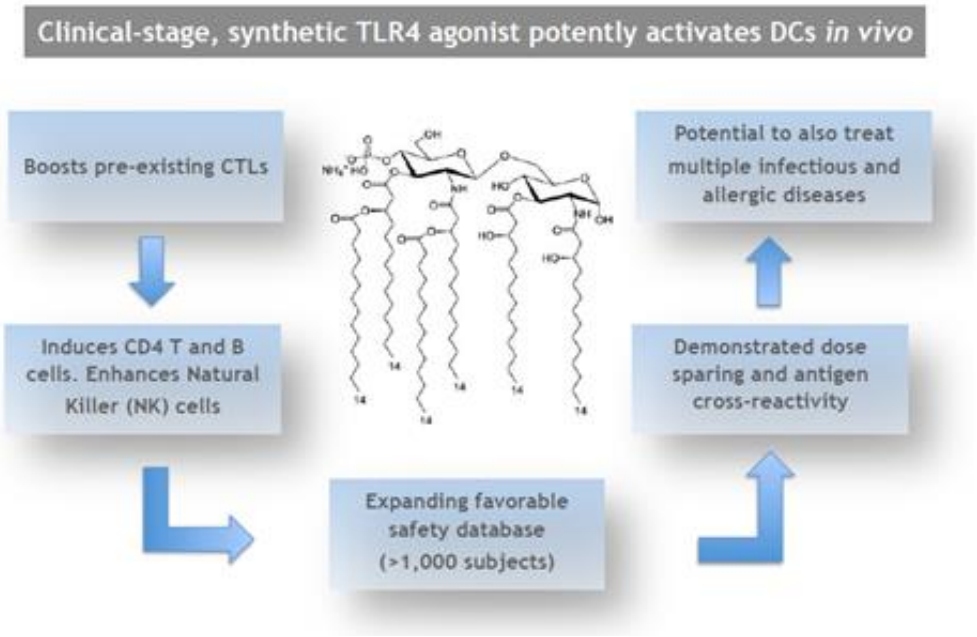
- Injection of peptide vaccines in a mineral oil-based carrier (IFA) results in sequestration of T cells at the site of injection due to the long-lived vaccine depot
- As a result, antigen-specific T cells do not migrate to the tumor
- The trapped prime T cells become dysfunctional and undergo antigen driven interferon-g (IFN-g) and Fas ligand (FasL) mediated apoptosis.

Source: Gnjatic, S et al., Nat. Med. 2013 (4)

In Addition to Its DC-targeting System, IMDZ Has Developed an Excellent Adjuvant

GLAAS™ SYNTHETIC TLR4 AGONIST PLATFORM PRODUCT LEADS TO ACTIVATION OF CD4+ T CELLS

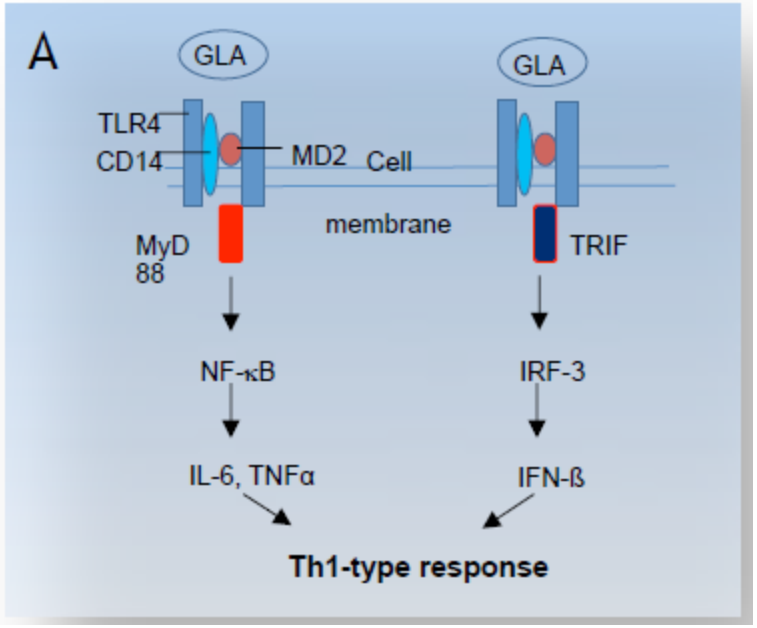


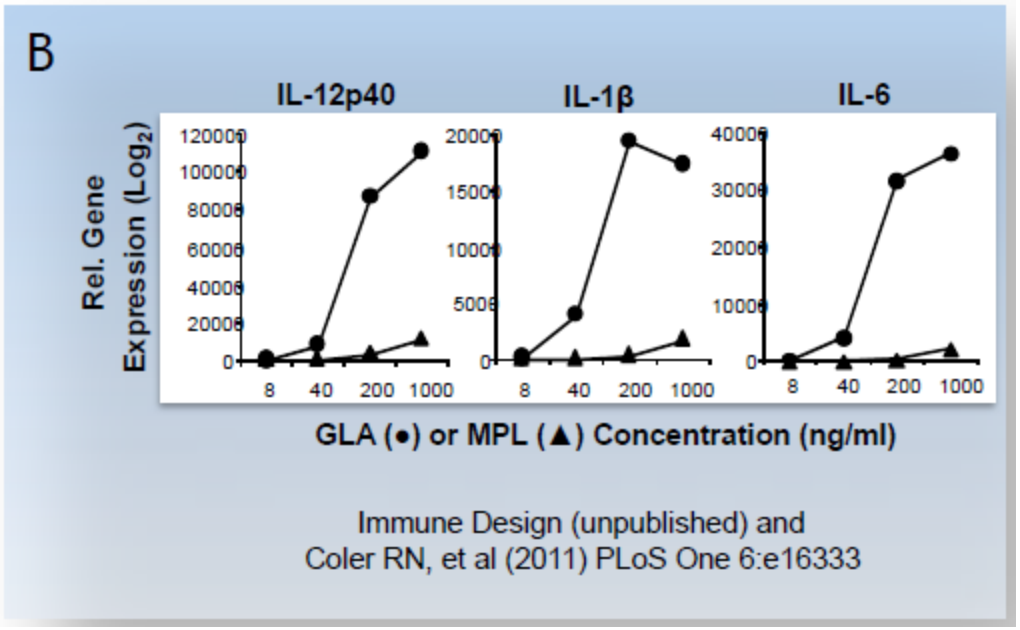


- GLAAS™ is a synthetic Glucopyranosyl (GLA) TLR4 agonist, which can be combined with recombinant full length tumor antigens, leading to the generation of tumor antigen specific T helper (Th1) CD4 T cells
- Th1 cells in turn lead to the further expansion of CTLs and trigger further DC activation and a humoral immune response via interaction with TLR4 receptor
- Has the ability to complement ZVex in the expansion of CTLs *in vivo* and as a stand-alone therapy
- Can be used to design products targeting both specific and endogenous antigens
- It can be manufactured to be 99% pure
- It has been tested in ~1,000 humans and has been shown to be safe.

Source: Company Reports

GLAAS™ CAN ACTIVATE CD4+ T CELLS VIA TWO INDEPENDENT PATHWAYS

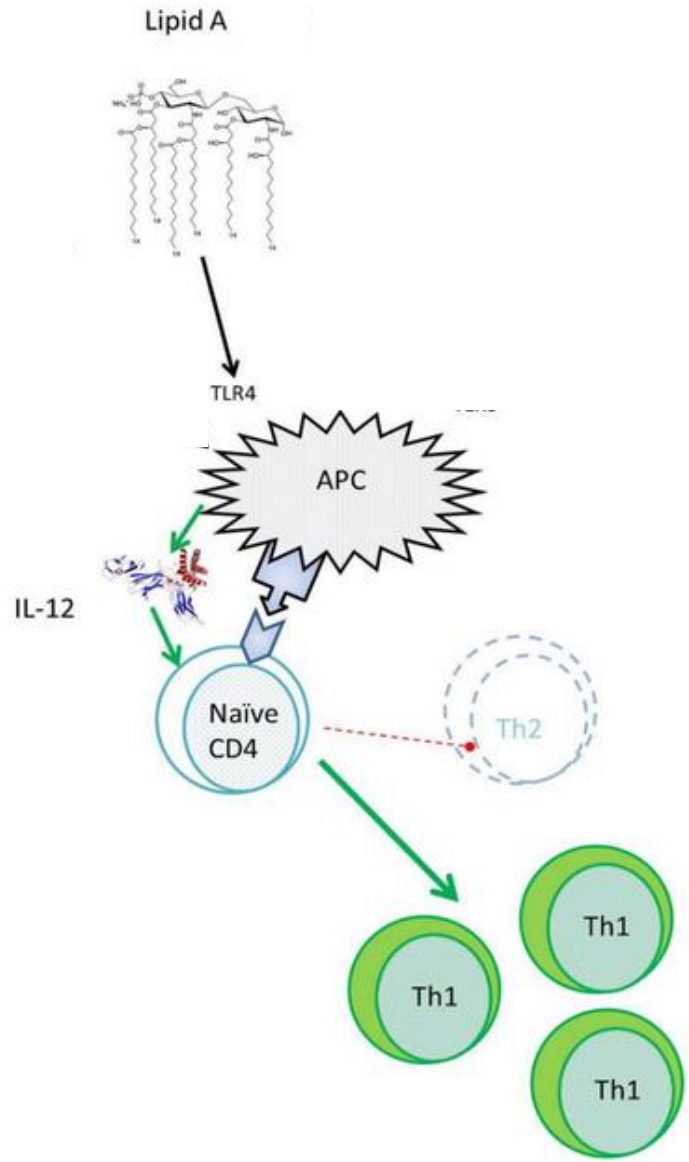




- GLAAS™ activates two pathways for maximal DC activation
- Pre-clinically, it appears to be ~100-1,000 fold more active than **MPL (GSK)**
- GLAAS™ induces the maturation of DCs in a dose dependent manner and leads to cytokine production in DCs in the absence of an antigen.

Source: Company Reports

CD4+ T HELPER CELL ACTIVATION CAN PROMOTE SUSTAINED CD8+ T CELL RESPONSES AND FORMATION OF CENTRAL MEMORY CD8 T CELLS



- GLAAS platform consists of a small synthetic molecule called glucopyranosyl lipid A, which selectively binds to the TLR-4 receptor and results in the activation and expansion of CD4 T helper cells
- CD4 T cells play an important role in boosting the anti-tumor by promoting the expansion of CTL and memory CD8 T cell memory formation.
- Unlike water adjuvants, it specifically targets and binds to a receptor on dendritic cells, which may lead to persistent responses
- It is differentiated from GSK's Monophosphoryl lipid A (MPL) lipid adjuvant that is comprised of the lipid A portion of Salmonella as it is a synthetic molecule and does not pose safety risks.

Source: Palucka et al., 2013 Immunity 39

ONGOING CLINICAL TRIALS EXAMINING THE ADJUVANT ACTIVITY OF TLR4 LIGANDS

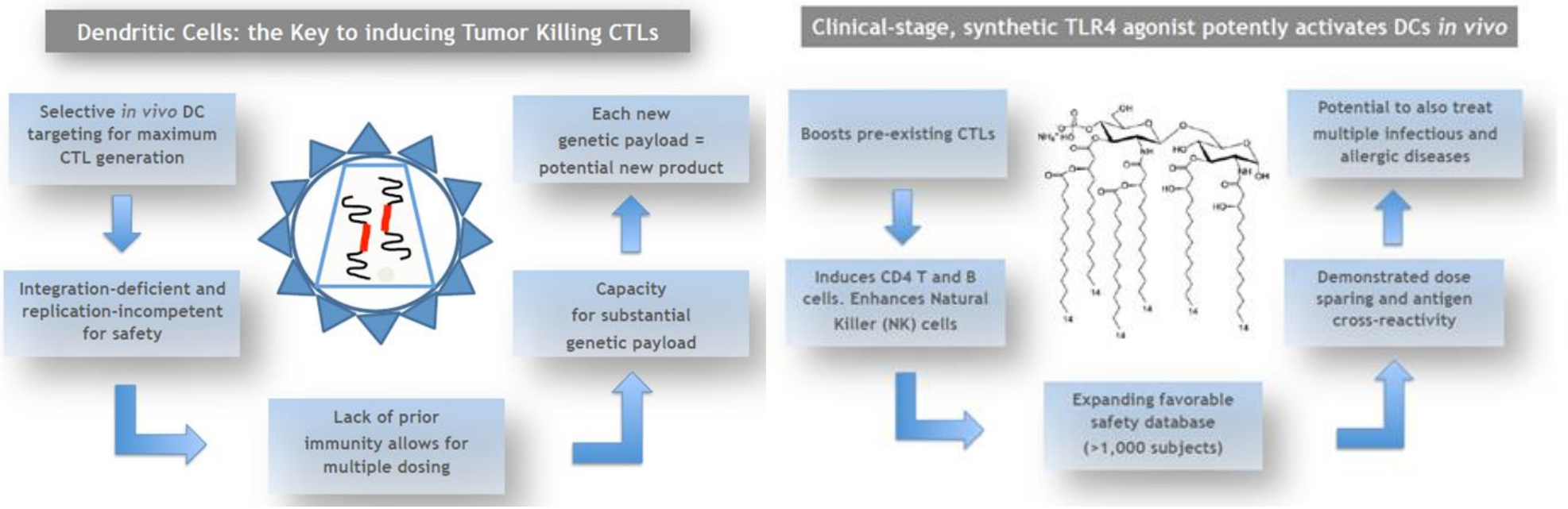
LEERINK

Treatment	Disease	Study Phase	Study population	Outcome Reference
Detox adjuvant + lysates from two melanoma cell lines	Melanoma	Phase II	139 melanoma patients	Clinical response rates were CR 3%, PR 5%, MR 4%, and PD 65%
Detox adjuvant + lysates from two melanoma cell lines	Melanoma	Phase III	140 melanoma patients	No difference in response rates or survival
Detox adjuvant + lysates from two melanoma cell lines	Melanoma	Phase III	553 melanoma patients	5-year relapse-free survival rate was 83% in patients who matched more than 2 of the M5[1]
Detox adjuvant + Stn-KLH	Breast cancer	Phase II	23 breast cancer patients	All patients developed Abs to STn
MPL + BLP25 + three lipids[2]	Lung cancer	Phase II	171 NSCLC patients	Median survival time extended to 17.4 vs 13.0 months (p=0.065)
MPL + BLP25 + three lipids[2]	Prostate cancer	Phase II	16 prostate cancer patients	50% had stable PSA
MPL + QS21) + MAGE-3 protein	MAGE-3 positive metastatic cancer	Phase I/II	57 cancer patients	96% developed anti-MAGE-3 Abs
AS02 (MPL + QS21) + MAGE-3 protein	MAGE-3 positive lung cancer	Phase II	17 NSCLC patients	Elicited strong MAGE-3 specific Ab and $CD4^+$ T-cell response

Source: Palucka et al., 2013 Immunity 39

Combination of Two Technology Platforms Potentially Allows Greater Immune Response

TWO DISCOVERY PLATFORMS DIFFERENTIATE IMDZ



- The ZVex platform comprises a first-in-class vector used to create compounds that leads to generation of antigen specific CD8 cytotoxic T cells *in vivo*
- The vector is an integration-deficient virus that carries genetic information about an antigen selectively in dendritic cells → Activation of CTLs
- The GLAAS platform is based on GLA that can be combined with a full length tumor antigen (protein)
- It is a synthetic molecules that binds to the TLR4 receptor on dendritic cells → Activation of CD4 T cells in either non-specific or in an antigen specific manner.

Source: Company Reports

COMPARING ZVex™/GLAAS™ TO OTHER APPROACHES

Vaccine Type	Compound	Modality	Adjuvant	Target Antigen	Target cells	Indication
Dendritic cell	Provenge (sipuleucel-T)	*ex vivo*	GM-CSF	PAP	dendritic cells	Prostate cancer
Protein/ peptide	rindopepimut	*in vivo*	GM-CSF	EGFRvIII	immune cells	glioblastoma
Oncolytic viruses	Talimogene laherparepvec (T-Vec)	*in vivo*	GM-CSF integrated into the viral vector	no specific antigen, viral injected into the tumor	tumor cells	melanoma, head and neck, pancreatic, breast, RCC
Delivery of genomic tumor antigens	LV 305 and CMB305	*in vivo*	GLA for CMB305 only	NY-ESO-1	dendritic cells	Sarcoma and NSCLC

Advantages of ZVex™ and GLAAS™

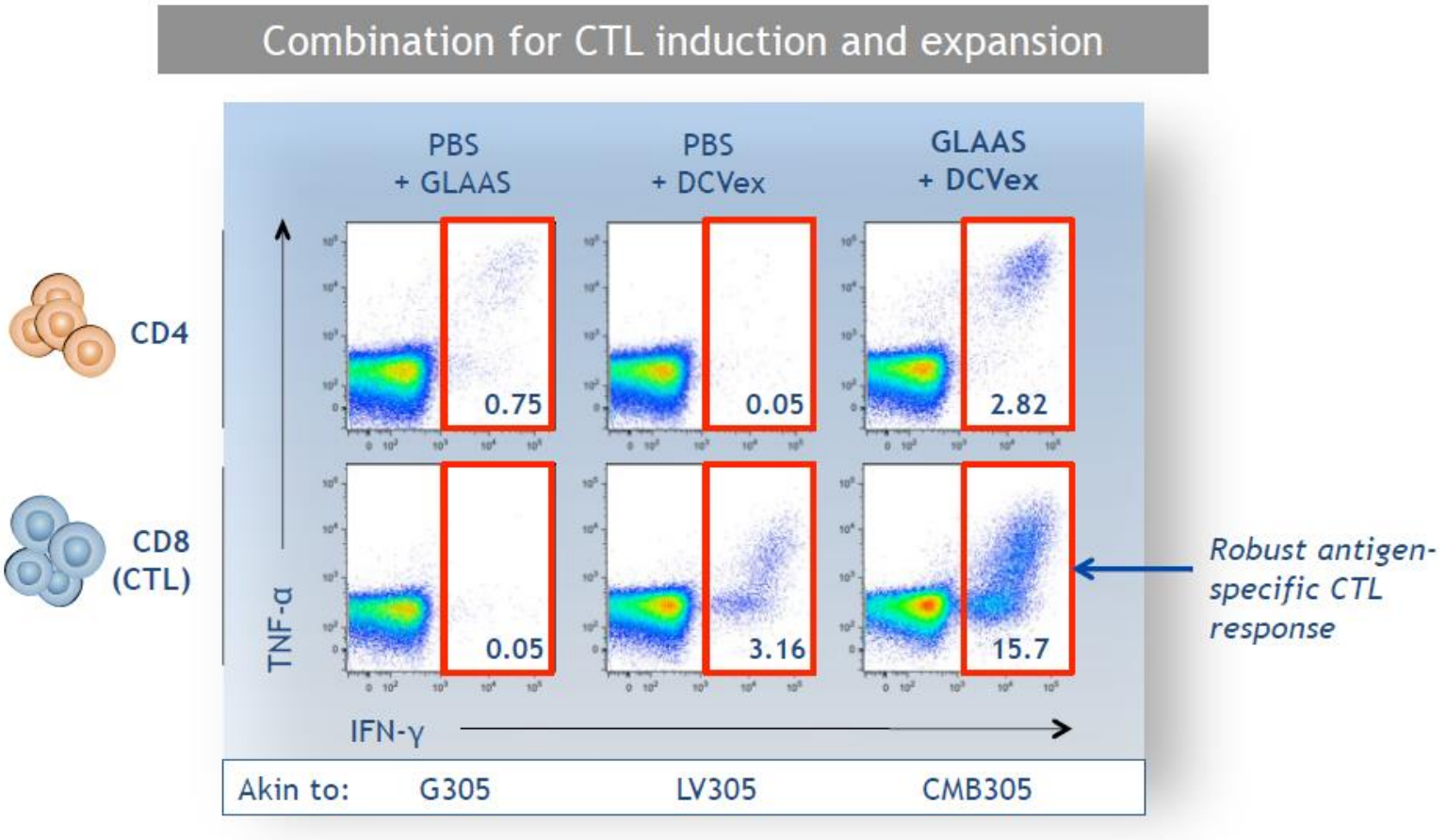
- Offer an *in vivo* off-the-shelf targeting approach
- Have the ability to generate, activate and expand CTLs (CD8+) and Th1 cells (CD4+)
- ZVex™ selectively targets DCs
- Ability to produce CTLs targeting multiple antigens due to their capacity for greater genetic payload

Disadvantages of ZVex™ and GLAAS™

- In the case of ZVex™ the need to identify tumor specific antigens.

Abbreviations: PAP- prostatic acid phosphatase. Source: Company Reports and Leerink Partners

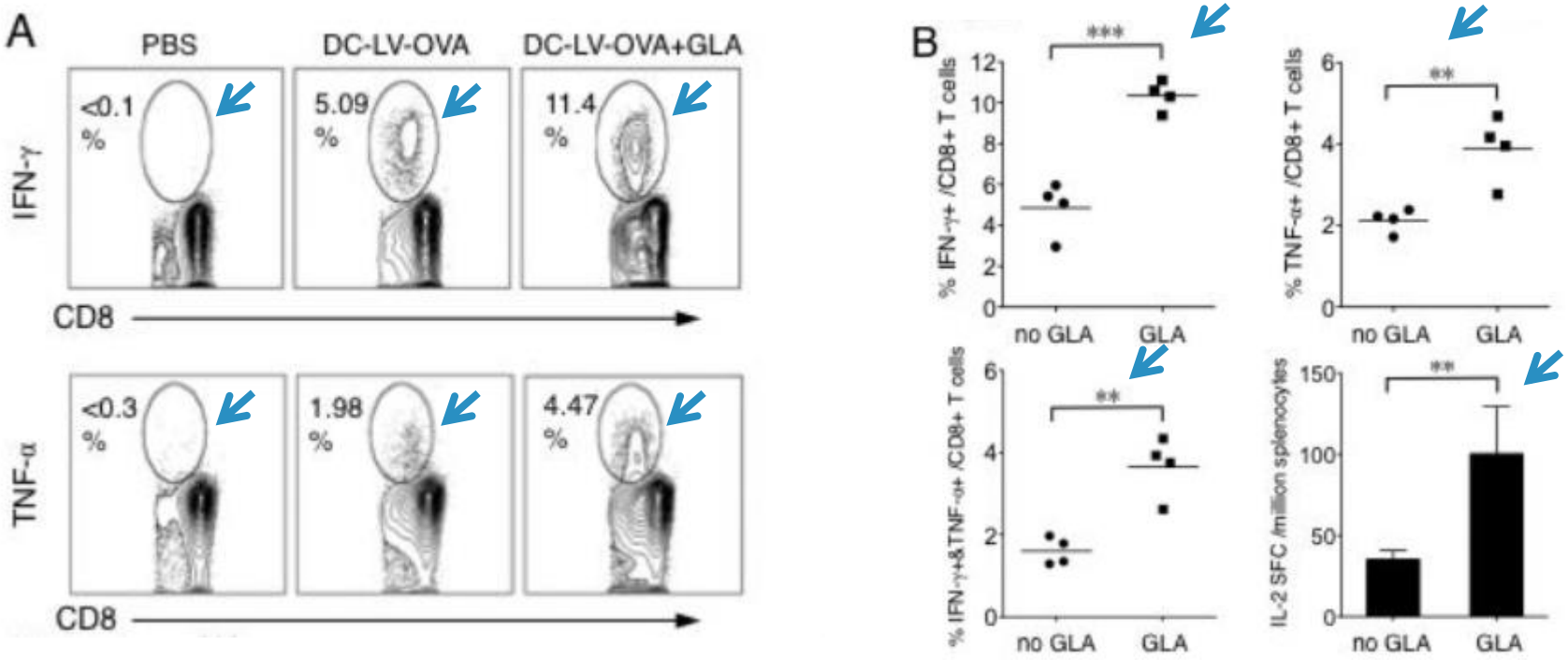
SYNERGISTIC PRIME BOOST: ZVex + GLAAS



- Combining ZVex and GLAAS may enhance the quality and number of CTLs and lead to the formation of central memory CD8 T cells
- Prime boost should also trigger an antigen specific humoral response
- KOLs believe that the prime boost will be the ideal combination in treating cancers.

Source: Company Reports

PRE-CLINICAL DATA SHOW SYNERGY BETWEEN ZVex AND GLAAS

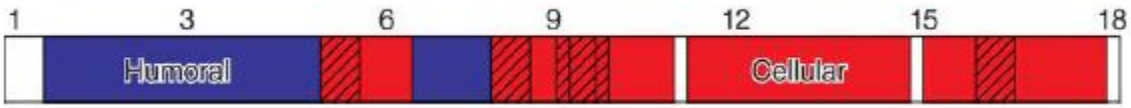


- GLA boosts the DC-LV (ZVex-derived agent) response *in vivo*
- Addition of adjuvants increases the % of CD8 T cells expressing TNF-α and IFN-γ, which are proxies for activated CTLs.

Source: Company Reports

NY-ESO-1 AS A TARGET

NY-ESO-1 : AN ATTRACTIVE TARGET FOR CANCER CELLS



Schematic representation of NY-ESO-1. Blue area is rich in epitopes recognized by antibodies. Red areas are rich in CD4 T-cell recognized HLA class II epitopes. These areas overlap in purple. Hatched areas represent HLA class I epitopes recognized by CD8 T cells.

- NY-ESO-1 was first discovered in cells from a patient with squamous cell carcinoma (SCC) of the esophagus
- It has been shown that NY-ESO-1 is expressed in a wide variety of cancers, with the highest frequency seen in synovial sarcoma, melanoma and epithelial ovarian cancer
- NY-ESO-1 has many advantages compared to other tumor antigens:
  (a)- NY-ESO-1 is highly immunogenic with an ability to elicit humoral and cellular immune responses
  (b)- NY-ESO-1 is more highly expressed in tumorigenic cells compared to normal tissue
- Additionally, studies have shown that NY-ESO-1 expression is associated with more advanced tumors and in some cases tumors of high grade
- One theoretical concern raised by a MEDACorp KOL is that the NY-ESO-1 is not essential for tumor growth, therefore the treatment may simply select for NY-ESO-1 negative cells
- Nonetheless, there appears to be some evidence of clinical activity for existing vaccines targeting NY-ESO-1
- IMDZ plans to target NY-ESO-1 in synovial sarcoma as an orphan indication and potentially NSCLC as a high incidence indication.

Source: Nichalaou et al., Imm and cell bio 2006 and Leerink Partners

NY-ESO-1 FREQUENCY OF EXPRESSION IN DIFFERENT TUMOR TYPES

Tumour type	Frequency of NY-ESO-1 expression		Frequency of LAGE-1 expression	Comment
	RT–PCR	IHC		
Acute lymphoblastic leukaemia	0/5 (0%)[148]	—		
Myeloid leukaemia	Acute: 0/52 (0%)[148] Chronic: 0/30 (0%)[148]			
Bladder transitional cell	20/62 (32%),[42] 15/43 (35%),[43] 7/16 (43%),[14] 4/5 (80%)[8]	2/14 (14%),[42†] 5/34 (15%),[43] 2/9 (22%),[4] 2/9 (22%)[41†]	17/34 (40%),[43] 7/16 (43%)[14]	Increased expression with higher grade disease[42]
Breast	13/129, (10%),[149] 13/98 (13%),[107] 3/12 (25%),[14] 10/33 (30%),[2] 37/88 (42%),[5] 12/27 (44%)[150]	1/37 (3%),[5†] 2/14 (14%)[8]	13/129 (10%),[149] 3/12 (25%)[14]	Low level expression in 68% of benign breast lesions, for example, fibro-adenoma[5]
Cholangiocarcinoma	(10%)[17]			
Colorectal	0/9 (0%),[14] 0/16 (0%),[8] 12/121 (10%),[45] 2/98 (20%)[149]	0/10 (0%)[41†]	0/9 (0%),[14] 2/98 (2%)[149]	
Endometrial		7/130 (6%)[151†]		
Gastric	0/16 (0%),[8] 8/102 (8%),[149] 12/101 (12%)[14]		8/102 (8%)[149]	
Head and neck SCC	3/45 (7%),[152] 3/15 (20%)[14]	0/10 (0%),[41†] 1/45 (2%)[152‡]	4/15 (27%)[14]	Expression seen only in high-grade tumours[152]
Hepatocellular carcinoma	0/21 (0%),[153] 12/49 (24%),[154] 17/62 (27%),[155] 2/7 (29%),[8] 31/73 (43%),[47] 28/42 (67%)[156]	25/132 (19%)[155]		A2-positive patients with spontaneous NY-ESO-1-specific CD8 T cells had no NY-ESO-1-expressing HCC[156]
Melanoma	15/62 (24%),[46] 6/21 (29%),[14] 23/67 (34%),[31] 10/23 (43%)[150]	17/70 (24%),[157†] 4/11 (36%),[41†] 64/120 (45%)[25†]	6/21 (29%)[14]	Including mucosal melanomas of the head and neck[157]

Source: Nichalaou et al., Imm and cell bio 2006 and Leerink Partners

NY-ESO-1 FREQUENCY OF EXPRESSION IN DIFFERENT TUMOR TYPES

Tumour type	Frequency of NY-ESO-1 expression		Frequency of LAGE-1 expression	Comment
	RT–PCR	IHC		
Multiple myeloma	35/60 (60%)[38]			Greater expression with higher stage or cytogenetic abnormality
Neuroblastoma	19/68 (28%),[158] 35/98 (36%)[45] 11/20 (55%)[35]	18/22 (82%)[35†]		
Non-Hodgkin's lymphoma	0/16 (0%),[14] 0/10 (0%)[8]		0/16 (0%)[14]	
Non-small-cell lung	3/15 (20%),[14] 11/51 (21%),[45,159] 27/518 (27%),[39] 20/63 (32%),[40] 17/43 (39%)[31]	13/52 (25%)[5†]	8/51 (15%),[13] 140/518 (24%),[149] 5/15 (33%)[14]	Increased expression with higher stage, node metastases[40]
Oesophageal squamous	11/46 (24%),[149] 41/123 (33%)[27]	44/213 (21%),[160] 18/56 (32%)[161†]		Less expression in poorly differentiated cancer[27].
Ovary	2/8 (25%),[8] 6/19 (32%),[44] 42/107 (39%)[28]	10/73 (14%),[46¶] 62/143 (43%)[28†]	22/107 (21%)[28]	
Pancreas	0/61 (0%),[34] 0/2 (0%)[2]			
Prostate	4/16 (25%),[2] 3/12 (25%),[14] 4/16 (25%),[31] 20/53 (38%)[41]	2/66 (3%),[162] localized 7/48 (15%),[162] HRPC 79/92 (86%)[29]	3/12 (25%)[14]	No correlation with PSA or Gleason score. Higher expression in metastatic disease.[29]
Renal	0/10 (0%),[2] 0/10 (0%),[14] 0/39 (0%),[163] 0/10 (0%)[31]	0/10 (0%)[4†]	0/10 (0%)[14]	The highest reported levels were seen in synovial sarcomas (80–100%)[5]
Soft tissue sarcoma	0/4 (0%),[2] 19/68 (28%),[158] 6/19 (32%),[14] 13/36 (36%)[7]	8/36 (22%),[7] 7/19 (47%),[158] 2/3 (66%),[4†] 20/25 (80%)[10†]	5/19 (26%)[14]	
Testicular: seminoma	0/1 (0%),[2] 6/34 (18%)[164]	0/17 (0%)[22¶]	2/34 (6%)[164]	Expression seen in carcinoma *in situ*[22]
Testicular: non-seminoma	0/7 (0%)[164]	0/12 (0%)[22¶]	0/34 (0%)[164]	
Thyroid (medullary)	2/5 (40%),[2] 2/5 (40%),[31] 15/23 (65%)[165]			
Uterus	0/8 (0%)[14]	6/19 (32%)[166¶]	0/8 (0%)[14]	

†ES121, ‡ES978, ¶D8.38. SCC, squamous cell carcinoma.

Source: Nichalaou et al., Imm and cell bio 2006 and Leerink Partners

LEERINK

SUMMARY OF CTL RESPONSES AND CLINICAL OUTCOMES OF OTHER NY-ESO-1 VACCINES IN DEVELOPMENT

Company/ Institution	Compound	Stage of Development	Indication	CD8 T cell levels	Efficacy
Celldex Therapeutics (CLDX)	CDX-1401	Phase I/II	Melanoma	CD8 and CD4 T cell responses increased in 56% of pts	13/45 pts experienced SD, with a median duration of 6.7 months (2.4+ to 13.4). In addition, 2 with melanoma experienced tumor regression of about 20% shrinkage in target lesions. Potential synergy with checkpoint inhibitors noted.
Roswell Park	rV-NY-ESO-1 + rF-NY-ESO-1	Phase II	Melanoma Ovarian cancer	Melanoma CD8 T cells increased from 40% pts-88% pts, ovarian cancer - 14%pts-45% pts	ORR in melanoma =9.5% (2/21), SD= 52% (11/21) mPFS= 9 mts (0–84) and mOS =48mts (3–106). In ovarian cancer patients who completed surgery and chemotherapy for primary disease (n=22), mPFS = 21 mts (95% CI, 16–29), mOS was 48 mo
Medizinische Klinik, Heamatologie Onkologie	NY-ESO-1 protein + CpG	Phase I	Prostate cancer	CD8+ T cells generation seen in 6/13 (46%) patients	SD=8/13 (62%), median time to progression was 4.75 mts (0-16) in all pts
Columbia University	recombinant NY-ESO-1 protein, Montanide ISA-51, and CpG	unknown	solid tumors (melanoma,, ovarian and breast cancer)	different levels of CD8 + T cells were seen in 9/18 (50%)	-

- The data from clinical trials with other NY-ESO-1 based vaccines do show generation of CD8+ T cells in patients. However, with the data so far it is difficult to assess the % increase of CTLs in a given patient, which may eventually be an important determinant for the clinical outcomes seen with NY-ESO-1 vaccine approaches
- In the Mediziniche Klinik Phase I study, no correlation was seen between immune activation and clinical outcomes.

Source: Valmori et al., PNAS 104 (21), 2007, Karbach et al., Clin Cancer Res 2011;17:861-870, Odunsi et al., PNAS 109(15), 2012, Dhodapkar et al., Sci Transl Med 6, C392014 and Leerink Partners

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PRELIMINARY DATA APPEAR TO SUGGEST CLINICAL SYNERGY BETWEEN AN NY-ESO-1 VACCINE AND CHECKPOINT INHIBITORS

Subject	CDX-1401 Dose Level / Adjuvants	Tumor Type	NY-ESO-1 Expression in Archived Tumor	NY-ESO-1 Cellular Response		NY-ESO-1 Humoral Response		Response to CDX-1401	Response to Anti-CTLA-4 mAb
				Baseline	Max Post-Treatment	Baseline	Max Post-Treatment		
01-0104	0.1 mg / topical resiquimod	Melanoma	+	-	+	-	-	SD	irPR
01-0206	1.0 mg / topical resiquimod	Melanoma	+	+	+++	+++	+++	SD	PR
01-0207	1.0 mg / topical resiquimod	Melanoma	+	-	-	++	+++	PD	PD
04-0304	3.0 mg / topical resiquimod	Melanoma	-	-	-	-	-	PD	PD
05-0507	1.0 mg / s.c. resiquimod	Melanoma	+	+++	+++	+++	+++	PD	PR
04-0605	1.0 mg / s.c. resiquimod + poly-ICLC	Melanoma	+	-	-	+	+	PD	CR

- Six melanoma patients received Yervoy within three months of receiving the last dose of CDX-1401, 4/6 (67%) patients achieved ORR, with one patient achieving a CR
- These responses compare favorably to the 11% ORR achieved in metastatic melanoma patients treated with Yervoy alone.
- In addition, 2 NSCLC patients were treated with an “investigational” checkpoint inhibitor, and both achieved partial responses
- These data lend further support to the potential of vaccines approaches in boosting the anti-tumor activity of checkpoint inhibitors.

Source: Dhodapkar et al., Sci Transl Med 6, C392014, CLDX press release

THE DIFFERENT NY-ESO-1 TARGETS IN DEVELOPMENT

Company	Compound	Mechanism	Indication	Stage of Development
Celldex Therapeutics (CLDX)	CDX-1401	monoclonal antibody	Melanoma	Phase I/II
Adaptimmune GlaxoSmithKline (GSK)	NY-ESO-1 (C259)	TCR	Melanoma, Multiple Myeloma (MM), Ovarian cancer, Sarcoma	Phase I/II Phase I (Sarcoma)
Aduro Biotech	ADU-623	vaccine	Brain cancer (malignant glioma, AA and GBM)	Phase I
Immune Design (IMDZ)	LV305, G305	vaccine	NSCLC, sarcoma and other solid tumors	Phase I
Takara Biotech	NY-ESO-1	TCR	Solid tumors	outside the US
Kite Pharma (KITE)	NY-ESO-1 (Kite)	TCR	Solid tumors	Phase II
Scancell Ltd. (SCLP)	SCIB2	vaccine	Cancer	Phase I

Source: Biomedtracker and Leerink Partners

PRELIMINARY CLINICAL DATA HAVE SHOWN AN EFFICACY SIGNAL

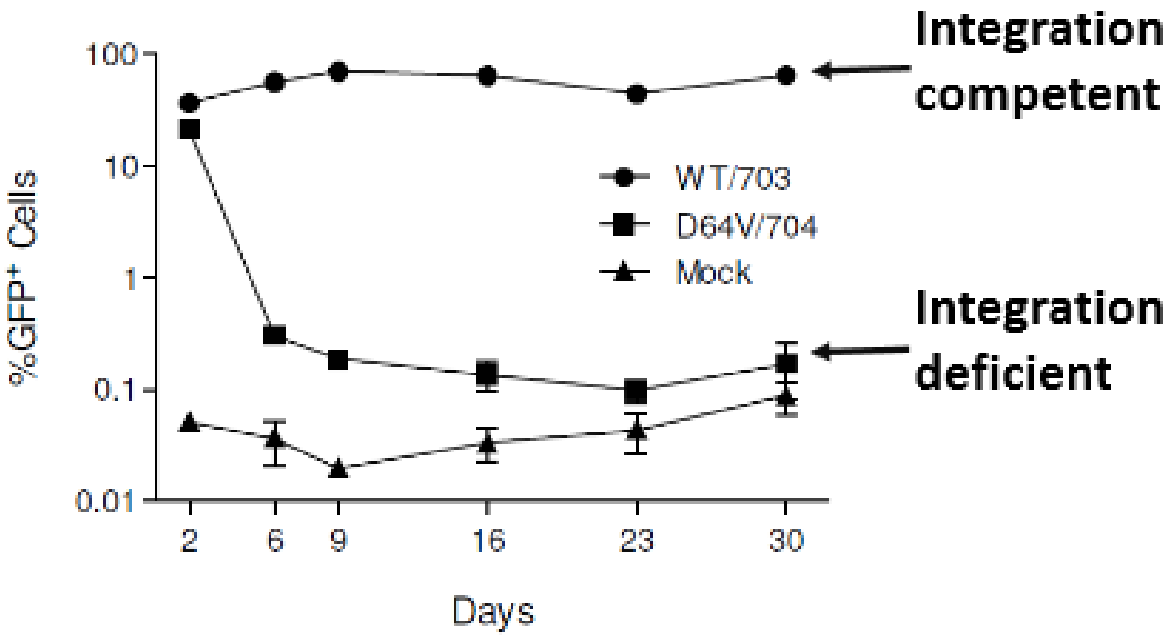
ENCOURAGING SIGNS OF INITIAL CLINICAL ACTIVITY

- IMDZ has three compounds -- LV305 (NY-ESO-1 delivered on ZVex), G305 (TLR4 agonist GLA + NY-ESO-1), and G100 (TLR4 agonist GLA) in Phase I
- Initial activity was seen in 1/3 patients with Merkel cell carcinoma (MCC) upon treatment with G100; the patient with local MCC showed a complete response. In a separate trial, a large reduction in biomarker CA125 (from 600 to 220) was seen in one ovarian cancer patient in first cohort of three patients on G305
- In 1Q:15, clinical and immune response data are expected from all three ongoing Phase I trials
- The immune response biomarker data to be presented will assess both the quality and the quantity of CD8+ T cells, CD4+ T cell, Tregs, NK cells and antibodies
- In addition, the data determining the fold induction of CD8+ T cells will be analyzed, and the different subsets (memory and effectors) of CD8+ T cells generated as a result of immunization will also be determined. These data will be important for determining the strength and the quality of the immune response induced
- There are also plans to initiate CM305 (LV305+ G305) Phase I trial in solid tumors in 1Q:15 if the safety profiles of LV305 and G305 are supportive. If clinical development remains on track, data from this trial are expected in 2H:15.

Source: Company reports

ZVex Design and Preclinical Data

ZVex™ VECTOR DOES NOT INEGRATE INTO TARGET CELLS

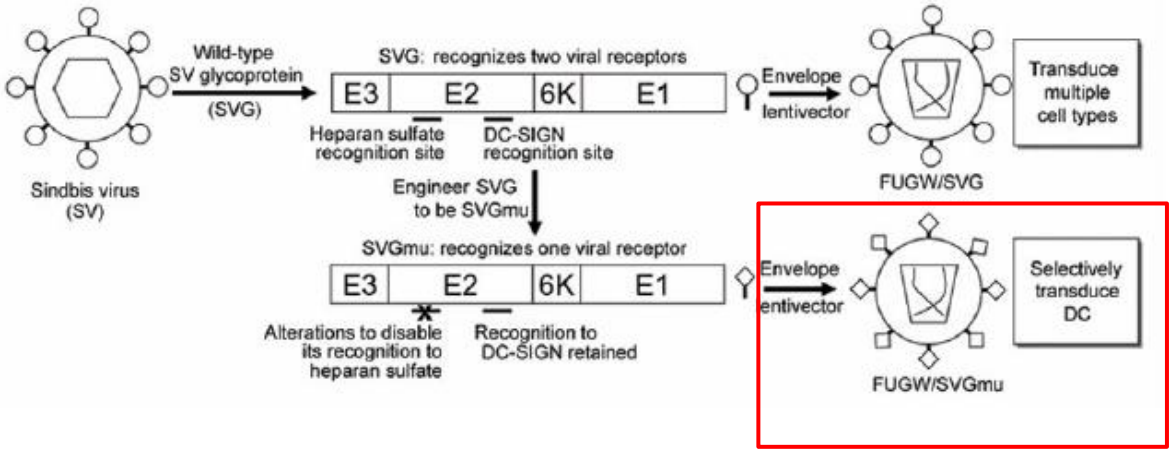


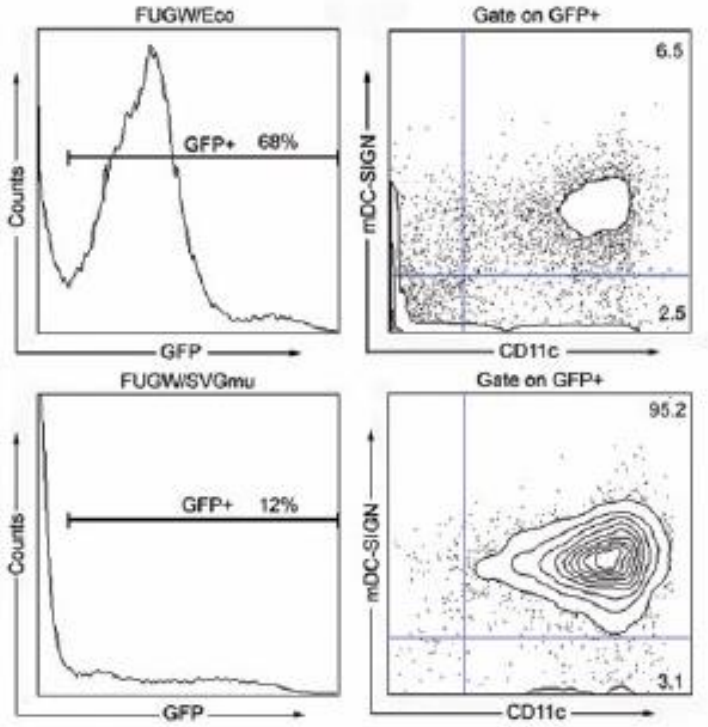
	Fold Reduction (versus WT/703)					
	Day 2	Day 6	Day 9	Day 16	Day 23	Day 30
D64V/704	1.71	187.63	439.38	462.64	448.10	385.65

- D64V/704 vector with a defective integrase fails to transduce HT1080 huDC-SIGN cells
- The lack of integration by the ZVex vector is considered safer for patients.

Source: Tareen et al., AACR 2014

ZVex™ VECTOR DESIGN ENABLES SPECIFIC TARGETING OF DENDRITIC CELLS

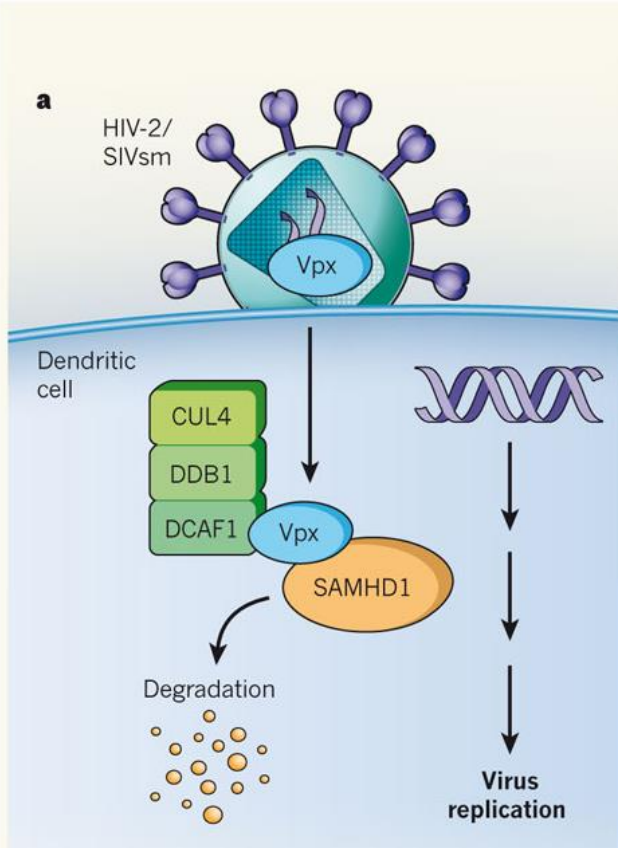


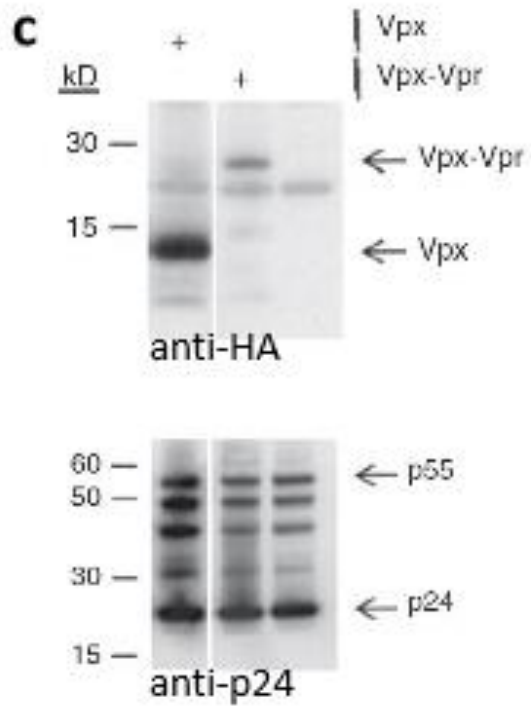


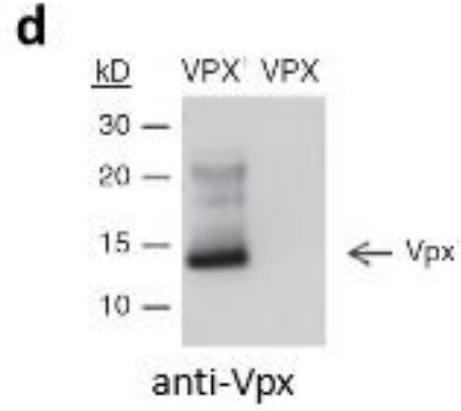
- ZVex™ lentiviral vector contains a Sindbis viral glycoprotein, allowing it to selectively target DC-SIGN expressing cells
- In addition, due to the rarity of Sindbis virus, most patients will not have prior immunity against ZVex
- Bone marrow cells isolated from B6 mice exposed to the fresh viral supernatant of FUGW/SVGmu show selective transduction of DCs.

Source: Tareen et al., AACR 2014, Yang et al., Nat. Biotechnol. 2008

ZVex™ VECTOR DESIGN INCLUDES Vpx, ENABLING TRANSDUCTION OF DENDRITIC CELLS





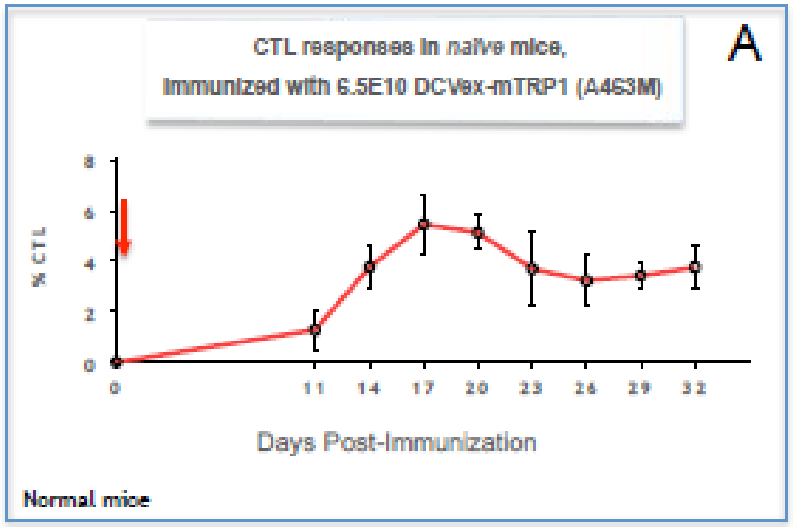


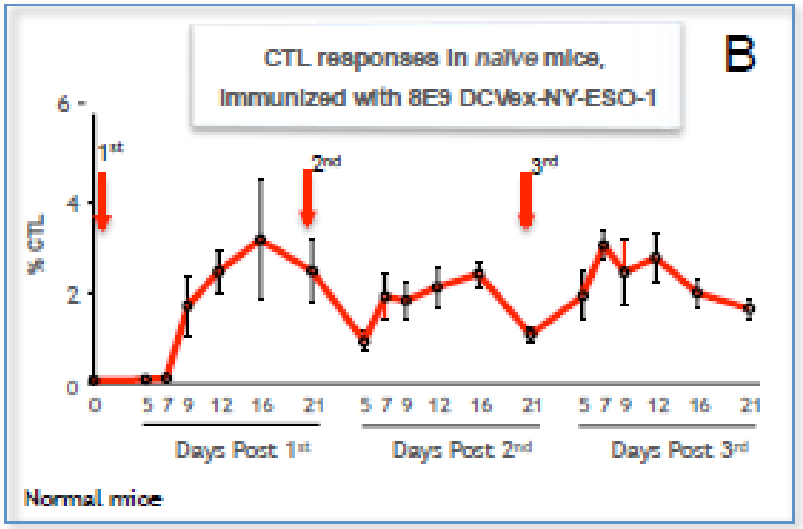
ZVex vector contains the Vpx protein

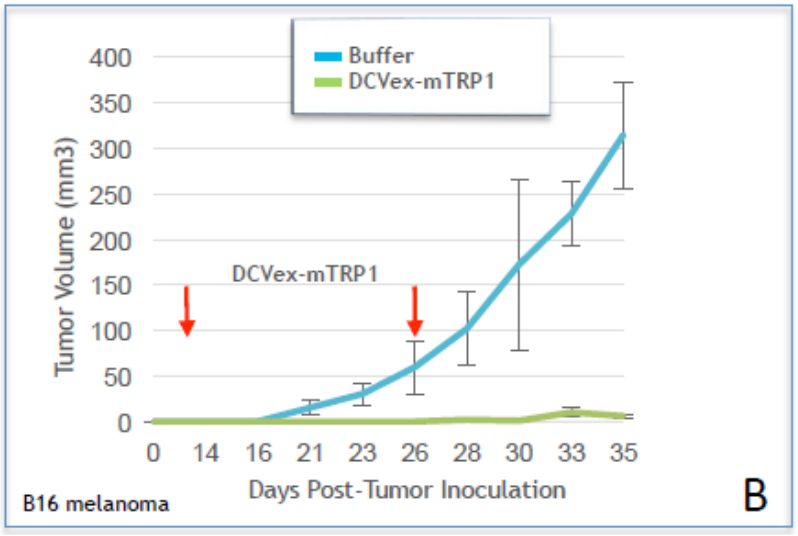
- The ZVex design includes Vpx protein that allows the NY-ESO-1 RNA to reverse transcribe and eventually translate into a protein
- Vpx enables this by degrading SAMHD1 together with CUL4–DDB1–DCAF1 protein complex.

Source: Tareen et al., AACR 2014, Lim and Emmerman

ZVex™: *In Vivo* TARGETING OF DENDRITIC CELLS APPEARS TO SHOW ANTI-TUMOR ACTIVITY PRE-CLINICALLY



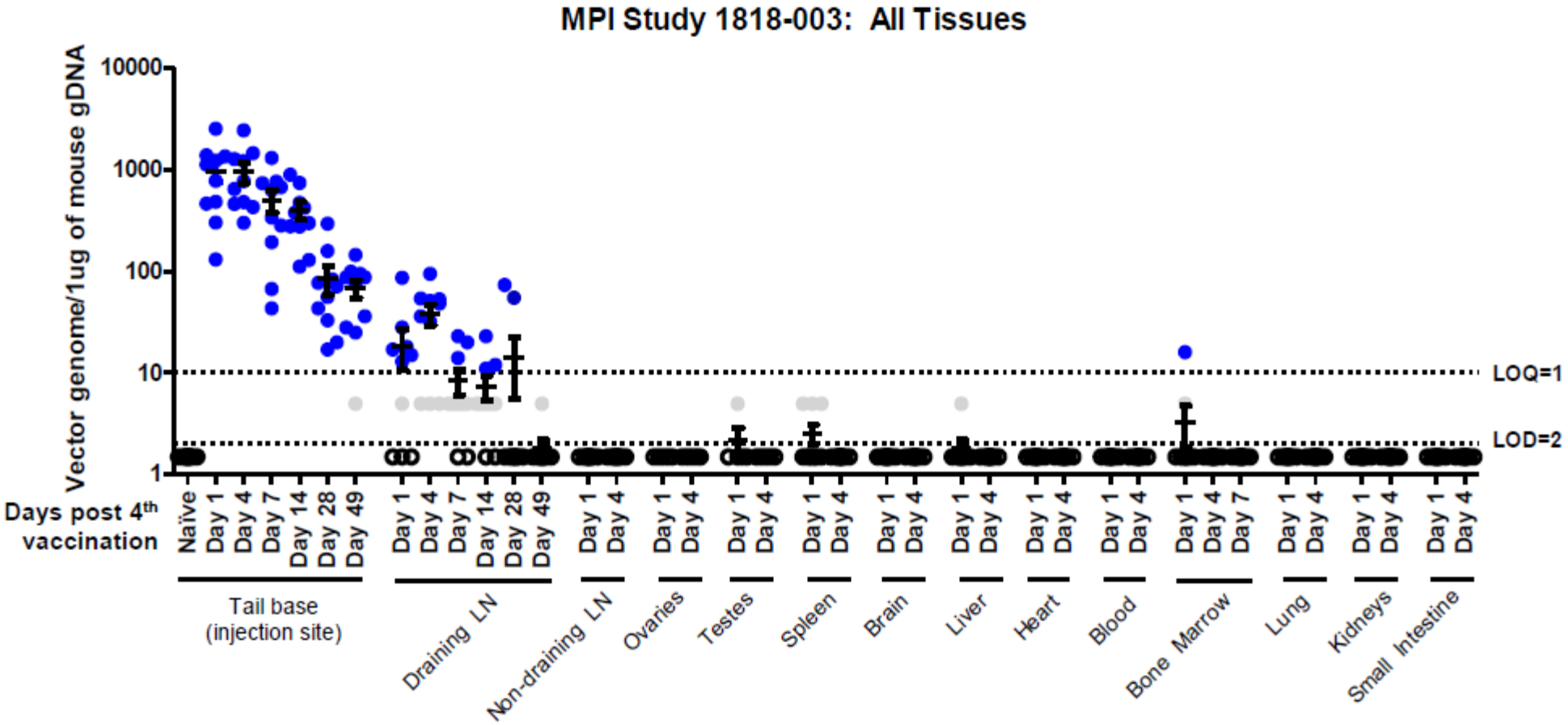




- Currently, the bar for generating CTLs in the blood is 0.1%; pre-clinical data show that ZVex + self melanocyte antigen (mTRP1) results in the generation of >1% of CTLs in normal mice
- ZVex can also be dosed repeatedly
- ZVex™ expressing TRP1 significantly inhibits tumor growth compared to the buffer control in B16 melanoma cells from mice
- Preliminary pre-clinical data suggest that ZVex-derived products can generate CTLs sufficiently and reduce the tumor burden in B16 melanoma models.

Source: Company reports

LV305 APPEARS CAPABLE OF MIGRATING TO DRAINING LYMPH NODES (LN)



- Given that ZVex uses an *in vivo* RNA approach, T cell trapping is not foreseen to be a problem
- In addition, DCs transfected with ZVex appear capable of migrating to the draining lymph nodes
- Tails of 5 BLB/c mice were injected 4 times (q2w) at the 5x108 dose
- LV205 measured at injection site and draining lymph nodes seven weeks after the last vaccination.

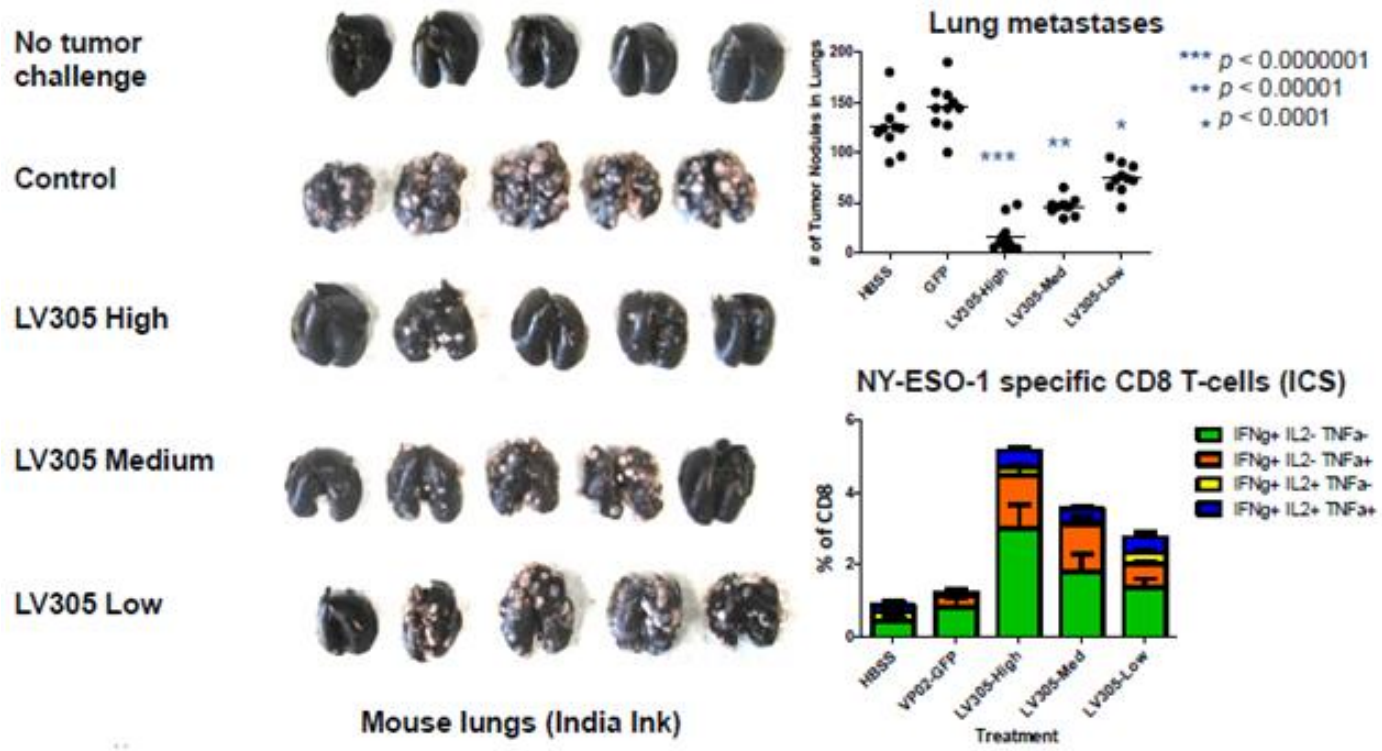
Source: Company Reports

PRE-CLINICALLY, LV305 REDUCES TUMOR BURDEN IN A DOSE-DEPENDENT MANNER

CHALLENGE
CT26/NY-ESO-1 cancer cells in mice to induce lung metastases

IMMUNIZATION
Single dose ID-LV305 injection three days after the challenge

RESULT
Dose dependent anti-tumor CTL response



- Treatment commenced on Day 3 after challenge
- T cell responses normally start between Day 3-7.

Source: Company reports

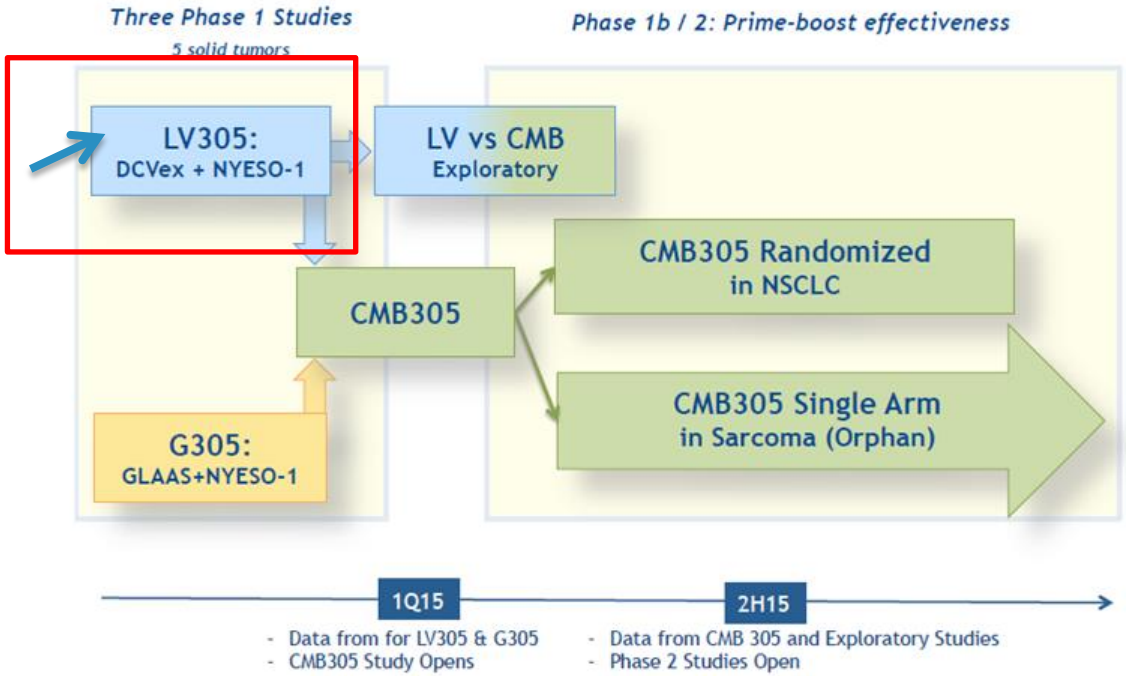
ONGOING CLINICAL TRIALS

IMDZ ONGOING TRIALS

Drug	Mechanism/ class	Trial Name/ ID	Status	Setting	Trial Design	n	Primary Endpoint	Trial initiation	Enrollment completion	Region	Primary completion date/ Inerim Data
ID-LV305	NY-ESO-1	NCT02122861	Phase I	NY-ESO-1 expressing melanoma, sarcoma, ovarian cancer, breast cancer NSCLC	ID-LV305	36	Safety	Apr. 2014	no	US	1Q:15
IDC-G305	NY-ESO- 1 endogenous antigens	NCT02015416	Phase I	NY-ESO-1 expressing melanoma, ovarian cancer,renal cell cancer ,NSCLC	IDC-G305 (NY-ESO-1 + GLA-SE)	30	Safety	Dec. 2013	no	US	Jul. 2014
G100 (GLA-SE)	endogenous antigens	NCT02035657	Phase I	Merkel cell carcinoma	G100 (GLA-SE)	10	Safety	Jan. 2014	no	US	1Q:15

Source: Company Reports, clinicaltrials.gov and Leerink Partners

UTILIZING THE THREE CANDIDATES TO TARGET NY-ESO-1 ENRICHED CANCERS



Tumor Type	Incidence (2014)	%NY-ESO-1
Synovial sarcoma	~900	80%
Melanoma	76,100	46%
Ovarian	21980	43%
Lung	224210	30%
Breast	235,030	15%

Source: Company Reports and Leerink Partners

LV305

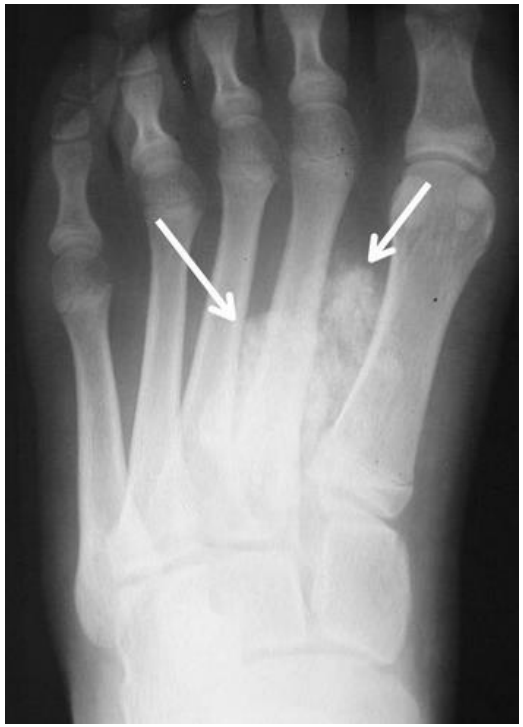
LV305 PHASE I IN PATIENTS WITH NY-ESO-1 EXPRESSING SOLID TUMORS

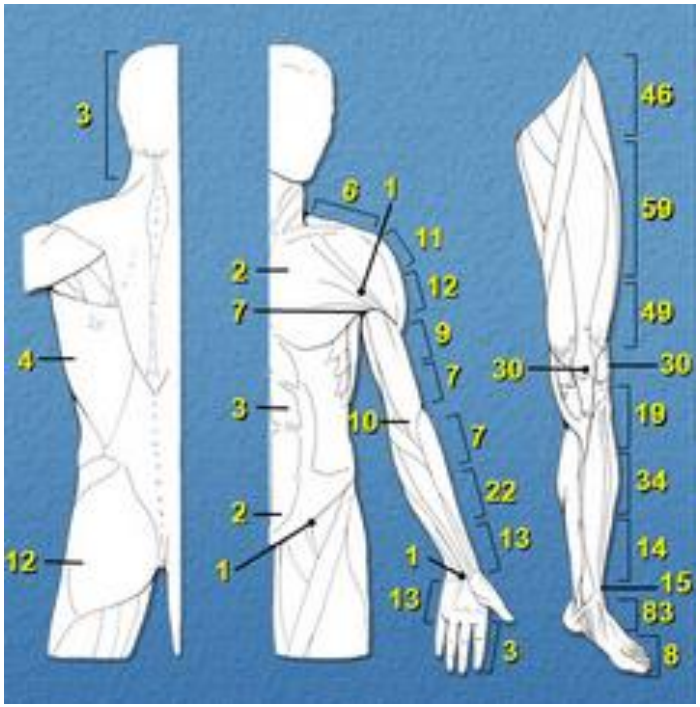
- LV305 Phase I dose-escalation study in ~9-18 patients (3+3 dose escalation design, each dose increasing by a log of 1)
- The doses will be administered intra-dermally starting at 1x 10^8, then to 1x10^9, 1x10^{10}. Anti-tumor activity in mice was seen at 1x 10^8
- Inclusion criteria include: locally advanced or metastatic melanoma, sarcoma, breast, melanoma, NSCLC and ovarian cancer
- Clinical benefit will be evaluated by analyzing response rates and disease progression via clinical and radiological assessments
- Efficacy will be assessed in an expansion cohort of patients with specific tumor types, which will comprise of ~20 patients
- Safety and immunogenicity data from the high-dose cohort in Phase I LV305 trial are expected in 1Q:15
- Data could be possibly presented at a medical meeting in 1H:15
- If LV305 exhibits an acceptable safety and efficacy profile, it will most likely be continued to be developed as a part of the CMB305 prime boost program
- IMDZ plans to develop a companion diagnostic for use in Phase II trials.

Source: Company reports and Leerink Partners

SYNOVIAL SARCOMA

SYNOVIAL SARCOMA IS AN ORPHAN INDICATION WITH A LARGE UNMET NEED





- Synovial Sarcoma is a rare form of soft tissue sarcoma that occurs in the joints of arms, legs and neck
- The standard of care includes surgery, chemotherapy and radiotherapy; currently no targeted therapies are available for the treatment of synovial sarcoma
- 5-year survival rates are ~25%, and 10-year survival rates are ~15%
- Synovial sarcoma is the indication of choice for IMDZ as it has one of highest expression of NY-ESO-1 antigen (~80%) and is an orphan indication as it affects ~900 people in the US annually.

Source: Nichalaou et al., Imm and cell bio 2006 and Leerink Partners

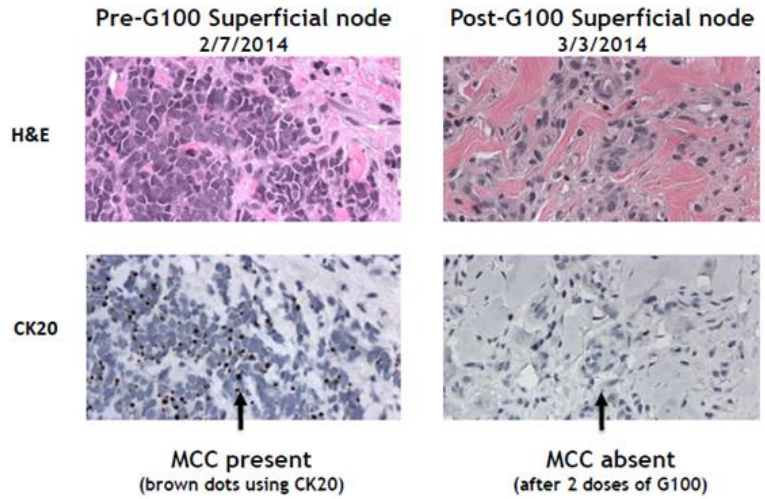
OTHER THERAPIES IN DEVELOPMENT FOR TREATING SYNOVIAL SARCOMA

Company	Compound	Mechanism	Stage of Development	Trial name/ ID
FHCRC/NCI	NY-ESO-1-specific T cells	T cell therapy	Phase I	NCT02059850
AdaptimmuneNCI	NY-ESO-1 T Cells	T cell therapy	Phase I	NCT01343043
Petrov Research Institute of Oncology	Autologous dendritic cell vaccine (NY-ESO-1 lysate)	Activating CTLs	Phase I/II	NCT01883518
Eisai/ EPZM	EPZ6438	Histone Methyltransferase (HMT)	Pre-clinical	-

Source: clinicaltrials.gov, Biomedtracker and Leerink Partners

G100

G100 MERKEL CELL CARCINOMA (MCC) TRIAL DESIGN AND INITIAL DATA



One complete response in loco-regional MCC

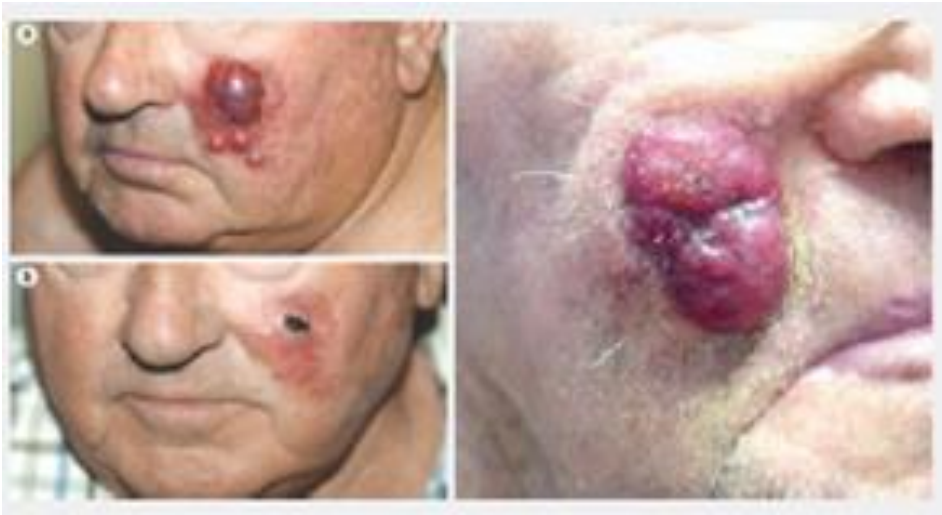
- Phase I proof of concept trial in MCC patients to evaluate safety and immunogenicity
- Patients with local and metastatic MCC receive 3 intra-tumoral doses of G100 (5ug/dose) one week apart
- Intra-tumoral injections were chosen as they are likely to cause antigen spreading from dying tumor cells and ultimately result in targeting of MCC tumor cells throughout the patient's body
- Reported **1 CR** (1/3), 2 metastatic patients did not respond, 4th patient with loco MCC just dosed, additional data from this trial is expected in 1Q:15

Next Steps

- Combine G100 with radiation therapy
- Phase I trial planned in NHL for 1Q:15.

Source: Mojica, P et al., JCO 25(9), 2007 and company reports

G100 WILL INITIALLY FOCUS ON MERKEL CELL CARCINOMA (MCC)- ORPHAN DRUG INDICATION

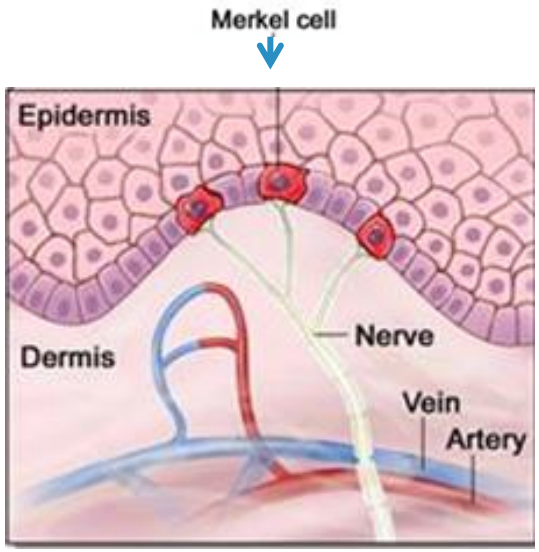


- About 1,500 new cases each year in the US, less than 50% of all MCC patients survive past five years
- Patients with small local tumors (<2 cm) have a 5-year survival rate of ~80%; however, once the tumor metastasizes the rate decreases to ~ 50%
- MCC recurs in nearly a third of the patients upon successful surgical removal of the local disease
- MCC is an orphan indication that represents a large unmet need as the current standard of care, which includes radiation and chemotherapy, is largely ineffective in advanced disease due to the short duration of responses
- Phase I trials for G100 in MCC evaluating safety and immunogenicity are underway.

Source: Mojica, P et al., JCO 25(9), 2007 and company reports

MERKEL CELL CARCINOMA

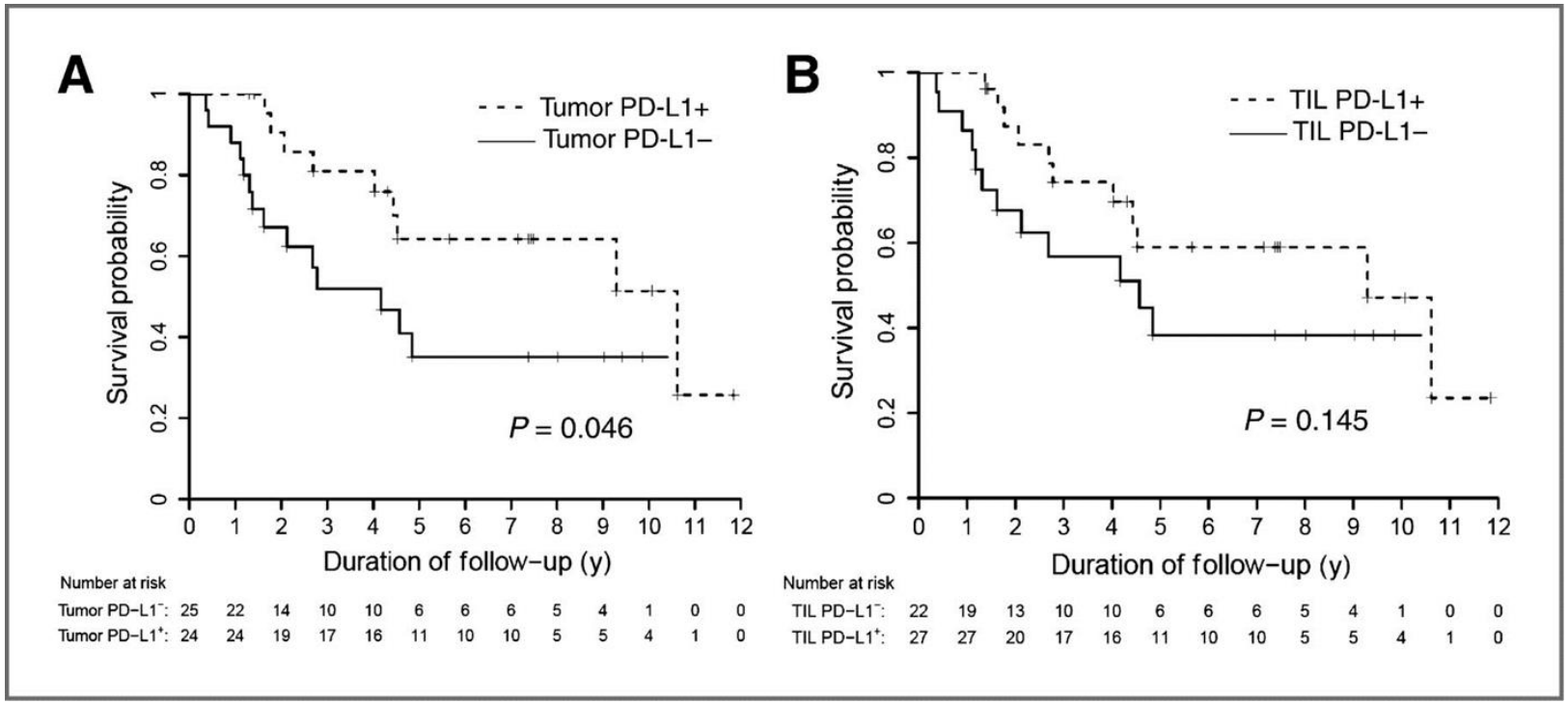
MERKEL CELL CARCINOMA (MCC)



- MCC is an aggressive cutaneous neuroendocrine cancer associated with polymavirus infection and UV exposure
- Approximately 80% of Merkel cell carcinomas are caused by oncogenic merkel cell polyomavirus (MCPyV)
- MCC most often occurs on the areas of the body most exposed to the sun -- such as the face, head, and neck
- MCC tends to grow fast and spreads quickly to nearby lymph nodes and later may spread to the brain, bones, liver or lungs
- MCC can be classified into four stages: Stage I and II are local disease with tumors being <2 and >2 cms in size, respectively. Stage III is regional nodal disease, and Stage IV is distant metastatic disease
- Patients who are immunosuppressed are ~15 times more likely to suffer from MCC.

Source: Mojica, P et al., JCO 25(9), 2007 and company reports

POSITIVE CORRELATION OF PD-L1 EXPRESSION WITH OVERALL SURVIVAL IN 49 PATIENTS WITH MCC



- Studies in MCC have demonstrated that patients with MCC that harbor tumor-infiltrating lymphocytes (TIL) show improved overall survival
- Kaplan-Meier survival curve shows improved survival for patients with MCC whose tumor cells showed membranous PD-L1 expression.

Source: Lipson E J et al., Cancer Immunol Res 2013;1:54-63

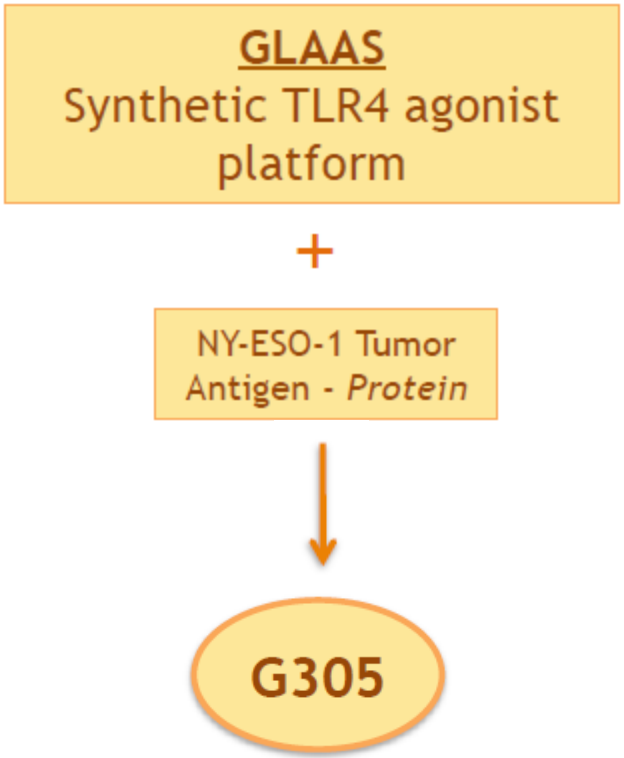
OTHER COMPOUNDS IN DEVELOPMENT TARGETING MERKEL CELL CARCINOMA

Company	Compound	Mechanism	Stage of Development	Trial name/ ID
Philogen S.p.A.	F16IL2	tenascin-C	Phase II	NCT02054884
Exelixis	Cabozantinib	VEGFR2, MET	Phase II	NCT02036476
EMD Serano	MSB0010718C	anti PD-L1	Phase II	NCT02155647
OncoSec Medical Incorporated	IL-2 vaccine	Immune stimulation	Phase II	NCT01440816
Novartis (NVS)	Pasireotide	Somatostatin analogue	Phase I	NCT01652547
Roche	MPDL3280	anti PD-L1	Phase I	NCT01375842
FHCRC/NCI	T cell vaccine	Adoptive immunotherapy	Phase I	NCT01758458
ImmunoGen	BB-10901	anti-CD56	Phase I	NCT00346385

Source: clinicaltrials.gov, Biomedtracker and Leerink Partners

G305

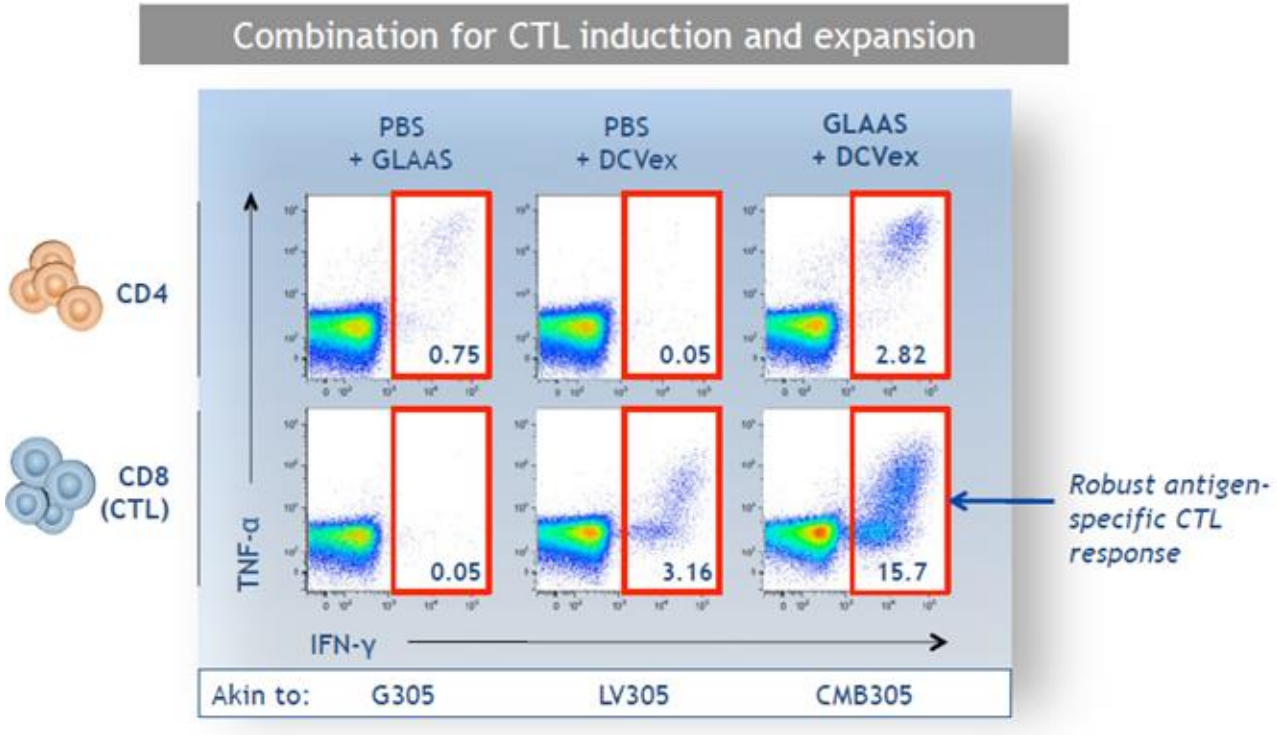
G305 WILL TARGET NY-ESO-1 ANTIGEN



- G305 is comprised of stable emulsion of GLA formulation and full-length NY-ESO-1 protein
- The Phase I safety and immunogenicity studies are targeting the same NY-ESO-1 positive five solid tumors as LV305 (locally advanced or metastatic melanoma, sarcoma, breast, NSCLC and ovarian cancer)
- A large reduction in biochemical marker CA125 (from 600 to 220) in an ovarian cancer patient in the first cohort of three patients on G305
- The first two cohorts should have complete enrollment in June 2014
- Phase I clinical data was initiated in Nov. 2013; data from this are expected to be available in 1Q:15.

CMB305

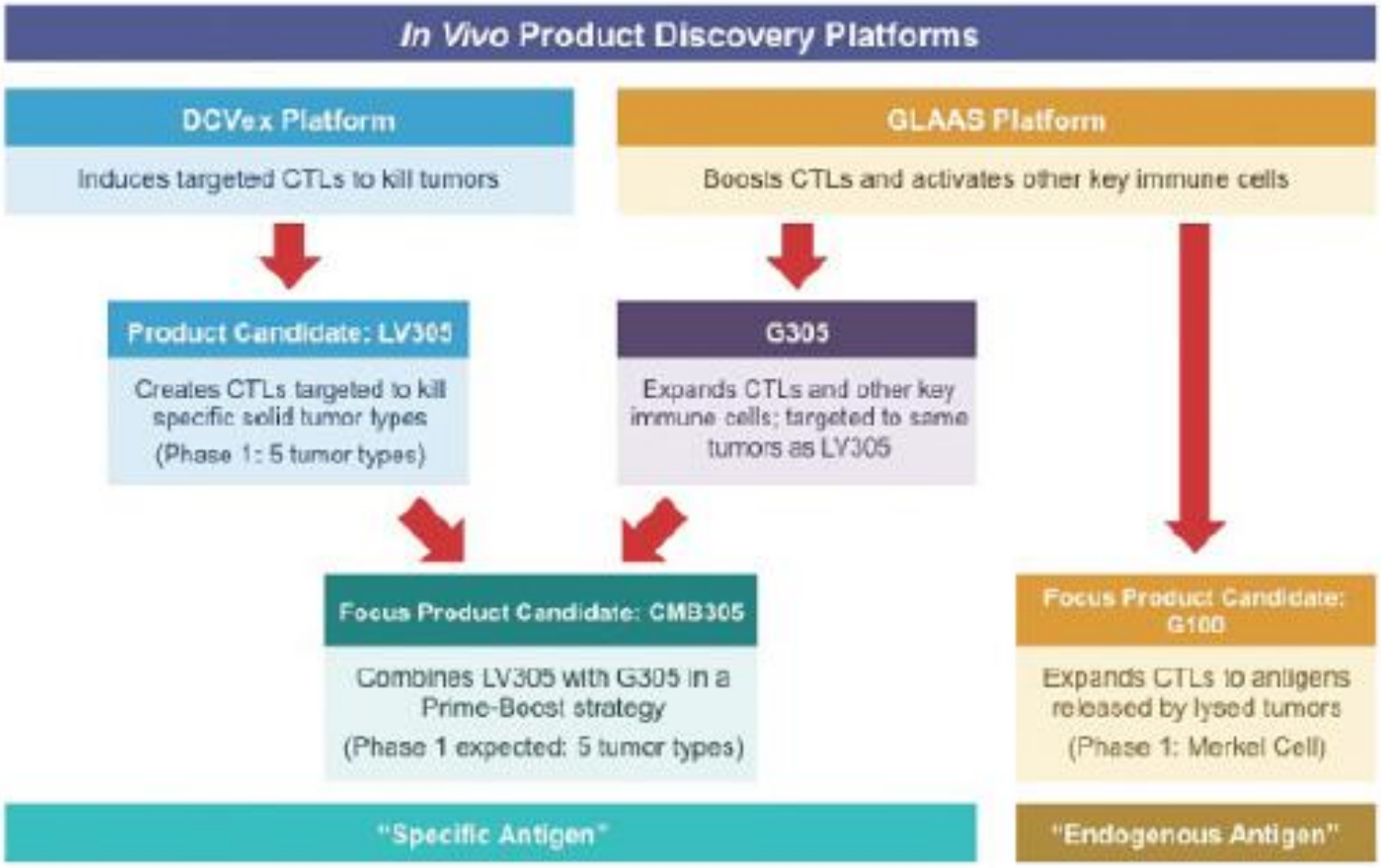
ADDITION OF GLASS TO ZVex HAS THE POTENTIAL TO ELICIT MORE ROBUST IMMUNE RESPONSES WHEN COMPARED TO SINGLE AGENTS



- CMB305 will combine **LV305** with **G305**
- A Phase I is expected to start in 1Q:15 to evaluate the safety and clinical benefit of combining the two agents; data from this trial are anticipated to become available in 2H:15
- Patients of similar tumor types as in the LV305 and G305 Phase I trials will be enrolled.

Source: Company reports

SUMMARY OF PRODUCTS AND DISCOVERY PLATFORMS



Source: Company Reports

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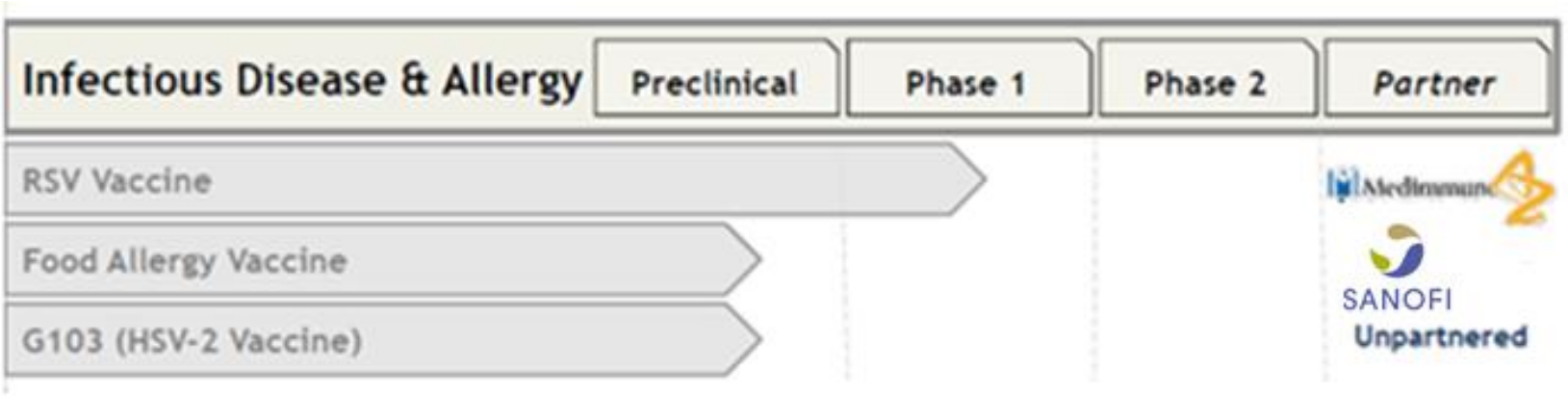
COMPARING ZVex™/GLAAS™ TO CART/TCR CELL THERAPIES

	CAR	TCR	DCVex™	GLAAS™
Modality	Personalized, adoptive, monoclonal T-cell therapy. Receptor is HLA-independent	Personalized, adoptive, monoclonal T-cell therapy. Receptor is HLA-dependent	Off-the-shelf, active *in vivo* immunization, active polyclonal T-cell stimulation	Off-the-shelf, active *in vivo* immune stimulation
Vector construction	High-affinity antibody fragment required. *Ex vivo* transduction of T-cells with integrating lentivirus or RNA	"Normal"-affinity T-cell receptor required. *Ex vivo* transduction of T-cells	Off-the-shelf product with public or proprietary TAAs, or customized antigen. *In vivo* transduction	Several off-the-shelf formulations available
Tumor Antigen Specificities	Surface-expressed native antigens (soluble antigens problematic due to competition). Single epitope, monoclonal CAR-T.	Any MHC-I presented antigen. Single epitope, monoclonal TCR-T.	Any MHC-I/II presented antigen. Full-length single or multiple antigens per vector. Polyclonal response. Customized TAA possible	Both specific, full-length antigen and antigen independent modalities
Targeted Tumors	Hematologic malignancies. Solid tumors: toxicity problem	Solid tumors: toxicity problem	Solid tumors and Hematologic malignancies	Solid tumors & Hem malignancies
Efficacy	Very effective in CLL (CD19). Many patients with CR for years. CR in 3/19 neuroblastoma (GD2)	PR in 3/11 PR melanoma and 4/6 synovial cell carcinoma (NY-ESO-1)	Strong preclinical data (B16F10 model). Strong CD8 responses	Best-in-class TLR4 agonist
Safety	Severe immune related toxicities reported	Severe immune related toxicities reported	No severe toxicities expected based on preclinical data and experience with other LV	Safe in multiple Ph1/2 (~1000 subjects dosed to date)
Next generation(s)	2nd gen. CAR-T: Co-stimulatory molecules (CD28, 41BB, OX40) 3rd generation: Multiple specificities, suicide switch	Co-stimulatory molecules; suicide switch	Co-stimulatory molecules (eg anti-CTLA4 antibody fragment). *Ex vivo* and *in vivo* transduction of T-cells	n/a

Source: Company Reports

INFECTIOUS DISEASES AND ALLERGIES

ONGOING PARTNERSHIPS FOR DEVELOPING VACCINES FOR INFECTIOUS DISEASES AND A SELECT FOOD ALLERGY



- IMDZ has three ongoing license agreements with MedImmune to use GLA for the development of vaccines for three different infectious diseases
- IMDZ entered into an exclusive licensing agreement with Sanofi to use the GLAAS platform for the development of a vaccine for a select food allergy (not disclosed).

Source: Company reports and IMDZ S-1

LITIGATION AND IP

LITIGATION

- IMDZ has an ongoing lawsuit with Theravectys SA ("TVS") filed in the Delaware Court of Chancery. In April 2014, TVS had voluntarily dismissed their claims but refiled the day after IMDZ started trading on the Nasdaq Global Market.
- The lawsuit involves IMDZ' former manufacturer, Henogen, SA. The claims are based on an exclusive contract TVS has with Henogen, SA to manufacture lentiviral vector, thereby preventing Henogen from using TVS' proprietary technology to manufacture products for a third party.
- TVS alleges that IMDZ impelled Henogen SA to violate the terms of the agreement by manufacturing and supplying IMDZ with lentiviral vectors. For this breach, TVS seeks monetary compensation and to refrain IMDZ from utilizing the service of Henogen SA.
- TVS claims include "tortious interference with contractual relations, misappropriation of trade secrets, unfair competition and unjust enrichment".
- IMDZ no longer uses Henogen SA's services for the manufacture of lentiviral vectors and has outsourced manufacturing to another company, which has already produced supplies for IMDZ.

Source: Company reports and IMDZ S-1

INTELLECTUAL PROPERTY

ZVex™

- ZVex has been granted patents to 2027 and application pending for extending the term

GLAAS™

- GLAAS discovery platform has also been granted patents to 2027 and application pending for extending the term

IMDZ also has a Prime Boost patent protecting cytotoxic CD8 T killer cell responses and it is valid through 2032.

Source: Company reports and IMDZ S-1

FINANCIALS

KEY FINANCIALS

- Shares offered at the time of IPO (7/24/14) – 4.5M
- Cash and cash equivalents (3/31/14)- $25M
- Cash burn ~$5M/quarter
- With IPO proceeds of ~$60M, cash runway expected by management to support operations into 2018
- Three separate license agreements with MedImmune, already received $4.5M
- Depending on the infectious indication, results of developmental-stage, regulatory and commercial milestones, MedImmune is obligated to pay an aggregate of $62.9M-76M
- In addition, IMDZ will receive mid-single-digit % royalties on net sales of licensed products
- IMDZ also entered into a licensing agreement for IMDZ's GLAAS platform with Sanofi to develop a therapy for a select food allergy
- ZVex and GLAAS were granted patents to 2027, applications pending for extending the term
- Prime Boost patent protecting CTL responses valid through 2032.

. Source: Company reports and Leerink Partners Research

MANAGEMENT

MANAGEMENT

- **Carlos Paya, M.D., Ph.D., Chief Executive Officer**

Previously served as the **President** of Elan Corporation, and before joining Elan served as the **Vice President** of Lilly Research Laboratories from 2001-2008.

- **Stephen R. Brady, JD, LLM, Chief Business Officer**

Previously served as **Chief Business Officer** for 3-V Biosciences, Inc. from 2011- 2013, and prior to that, he served as 3-V Bioscience, Inc.'s Vice President, Corporate Development, Strategy and Operations from 2010 -2011.

- **Wayne Gombotz, Ph.D., Chief Development Officer**

Previously served as Vice President Pharmaceutical Operations at Omeros Corporation from 2005-2011. Before joining Omeros Corporation, Dr. Gombotz held several executive management positions at various biotech companies.

- **Richard T. Kenney, M.D., FACP, Chief Medical Officer**

Previously served as Chief Medical Officer for Crucell Holland BV from 2012-2013. From 2009-2012, he was at various leadership positions at Vical Incorporated, which included Vice President, Clinical Development.

- **Jan H. ter Muelen, M.D., DTM&H, Chief Scientific Officer**

Previously served as Executive Director of Vaccine Research and Head of Department of Vaccine Basic Research at Merck Research Laboratories from 2008-2013.

- **Frank J. Hsu, M.D., Vice President, Head of Oncology**

Previously served as the Chief Medical Officer for Zyngenia, Inc. Prior to that, he was Senior Medical Director at Genzyme in the Transplant and Oncology Division for more than nine years.

- **Paul Rickey, Vice President, Finance & Administration**

Most recently he served as the Corporate Controller of Northstar Neuroscience from 2006-2009. Prior to that, he served as the Accounting Manager at Mobliss Inc. from 2004-2006.

Immune Design
(In '000s, except per share items)

	1QA	2QE	3QE	4QE	2014E	2015E	2016E	2017E	2018E	2019E	2020E
REVENUE:											
CMB305 (POS adjusted sales)	-	-	-	-	0	-	-	-	-	-	10,109
G100 (POS adjusted sales)	-	-	-	-	0	-	-	-	11,723	22,628	25,923
Other Product Sales	25				25						
Product Development and Licensing Agreements					0						
Contracts and Grants					0						
Product Royalties					0						
Milestone payments					0						
Other, net					0						
Total Revenue	**25**	**-**	**-**	**-**	**25**	**-**	**-**	**-**	**11,723**	**22,628**	**36,031**
OPERATING EXPENSES:											
Cost of product Sales	14								2,345	4,526	7,206
Research and Development	4,078	4,119	4,160	4,202	16,558	17,145	25,717	38,575	57,863	60,756	63,794
Sales General and Adminstrative	1,446	1,460	1,475	1,505	5,886	6,262	6,387	46,387	78,858	118,288	130,116
Royalties											
Amortization of Acquired Intangible Assets											
Total Operating Expense	**5,538**	**5,579**	**5,635**	**5,706**	**22,444**	**23,407**	**32,104**	**84,962**	**136,721**	**179,043**	**193,910**
Operating Loss	**(5,513)**	**(5,579)**	**(5,635)**	**(5,706)**	**(22,419)**	**(23,407)**	**(32,104)**	**(84,962)**	**(124,998)**	**(156,415)**	**(157,878)**
Investment, Interest and Other Income, Net	1										
Change in fair value of convertible preferred stock warrant liability	(2,711)										
Net Income before Taxes	(8,223)	(5,579)	(5,635)	(5,706)	(22,419)	(23,407)	(32,104)	(84,962)	(124,998)	(156,415)	(157,878)
Income tax rate%											
Income Tax											
Net Loss	**(8,223)**	**(5,579)**	**(5,635)**	**(5,706)**	**(22,419)**	**(23,407)**	**(32,104)**	**(84,962)**	**(124,998)**	**(156,415)**	**(157,878)**
Earnings per share	(0.81)	(0.54)	(0.36)	(0.36)	(1.42)	(1.41)	(1.11)	(2.92)	(3.02)	(3.02)	(3.02)
Shares Used in Calculating Basic and Diluted Net Loss per Share(pro forma)	10,139	10,240	15,522	15,677	15,834	16,641	28,808	29,096	41,387	51,801	52,319
Dilutive shares	10,139	10,240	17,344	17,517	17,692	18,595	30,781	31,089	43,400	53,834	54,372

Source: Company Reports and Leerink Partners Estimates

Disclosures Appendix

Analyst Certification

I, Howard Liang, Ph.D., certify that the views expressed in this report accurately reflect my views and that no part of my compensation was, is, or will be directly related to the specific recommendation or views contained in this report.

Distribution of Ratings/Investment Banking Services (IB) as of 06/30/14				
			IB Serv./Past 12 Mos.	
Rating	Count	Percent	Count	Percent
BUY [OP]	138	69.00	50	36.20
HOLD [MP]	62	31.00	2	3.20
SELL [UP]	0	0.00	0	0.00

Explanation of Ratings

Outperform (Buy): We expect this stock to outperform its benchmark over the next 12 months.

Market Perform (Hold/Neutral): We expect this stock to perform in line with its benchmark over the next 12 months.

Underperform (Sell): We expect this stock to underperform its benchmark over the next 12 months.The degree of outperformance or underperformance required to warrant an Outperform or an Underperform rating should be commensurate with the risk profile of the company.

For the purposes of these definitions the relevant benchmark will be the S&P 600® Health Care Index for issuers with a market capitalization of less than $2 billion and the S&P 500® Health Care Index for issuers with a market capitalization over $2 billion.

Important Disclosures

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