



Combining HS-110 and anti-PD-1 in NSCLC

September 1, 2015

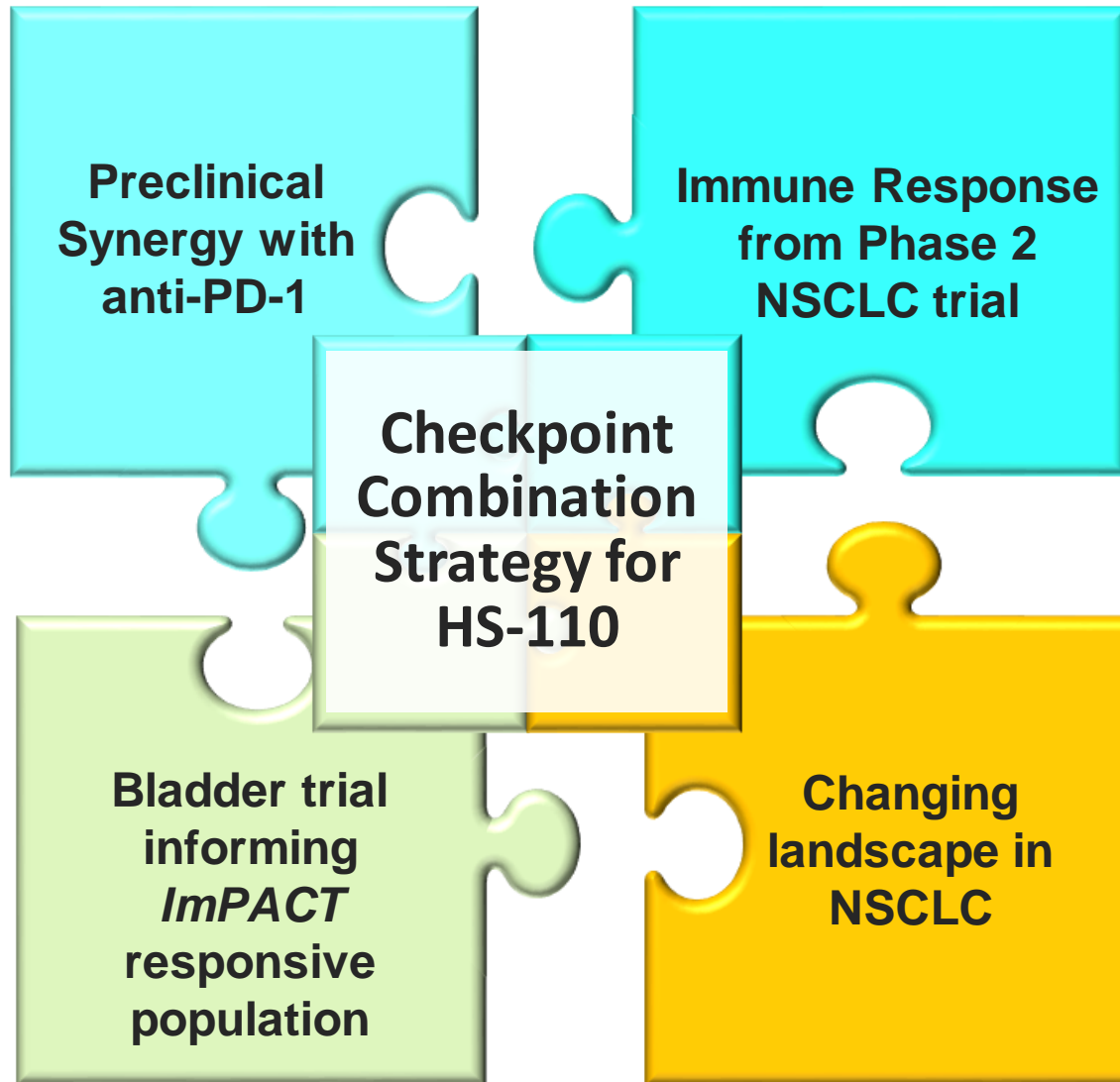
Forward Looking Statements

This presentation includes statements that are, or may be deemed, “forward-looking statements.” In some cases, these forward-looking statements can be identified by the use of forward-looking terminology, including the terms “believes,” “estimates,” “anticipates,” “expects,” “plans,” “intends,” “may,” “could,” “might,” “will,” “should,” “approximately” or, in each case, their negative or other variations thereon or comparable terminology, although not all forward-looking statements contain these words. They appear in a number of places throughout this presentation and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned discovery and development of drugs targeting cancer stem cells, the strength and breadth of our intellectual property, our ongoing and planned preclinical studies and clinical trials, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for our product candidates, our ability to partner our product development, the degree of clinical utility of our products, particularly in specific patient populations, expectations regarding clinical trial data, our results of operations, financial condition, liquidity, prospects, growth and strategies, the length of time that we will be able to continue to fund our operating expenses and capital expenditures, our expected financing needs and sources of financing, the industry in which we operate and the trends that may affect the industry or us.

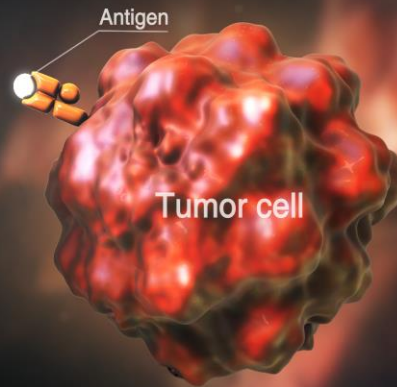
By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics, and healthcare, regulatory and scientific developments and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. Although we believe that we have a reasonable basis for each forward-looking statement contained in this presentation, we caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this presentation as a result of, among other factors, the factors referenced in the “Risk Factors” section of our Annual Report on Form 10-K for the year ended December 31, 2014 and our quarterly report on Form 10-Q for the subsequent quarters (collectively, our “SEC Filings”). In addition, even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in this presentation, they may not be predictive of results or developments in future periods. Any forward-looking statements that we make in this presentation speak only as of the date of such statement, and we undertake no obligation to update such statements to reflect events or circumstances after the date of this presentation, except as required by law.

You should read carefully the factors described in the “Risk Factors” sections of our SEC Filings to better understand the risks and uncertainties inherent in our business.

Checkpoint Combination Rationale

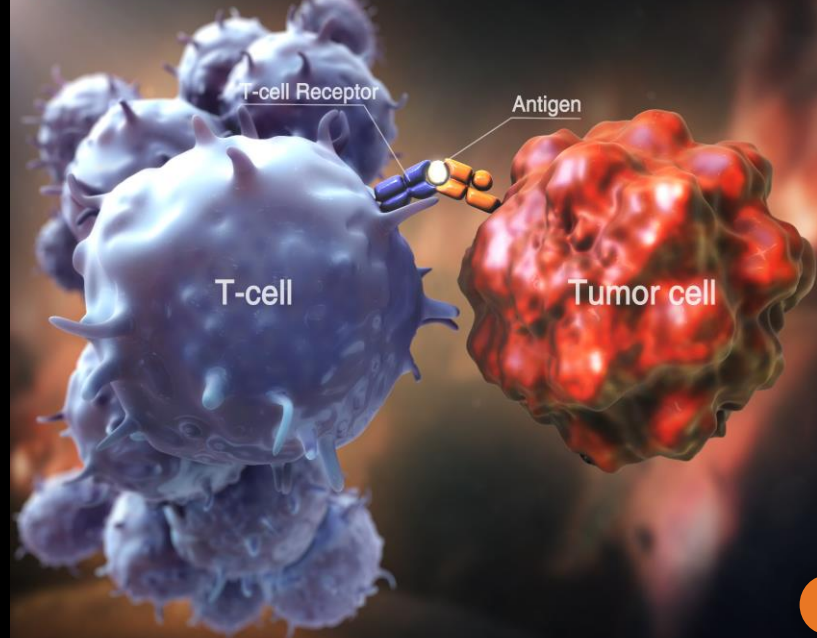


Tumor Cell Antigen Presentation



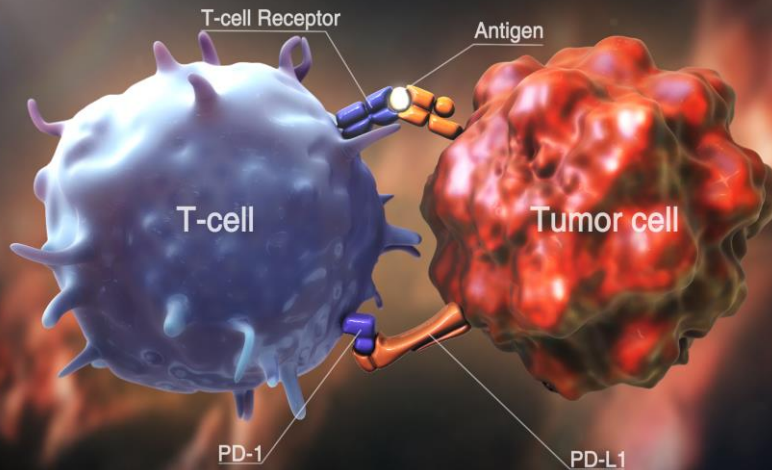
1

T-Cell Activation and Proliferation



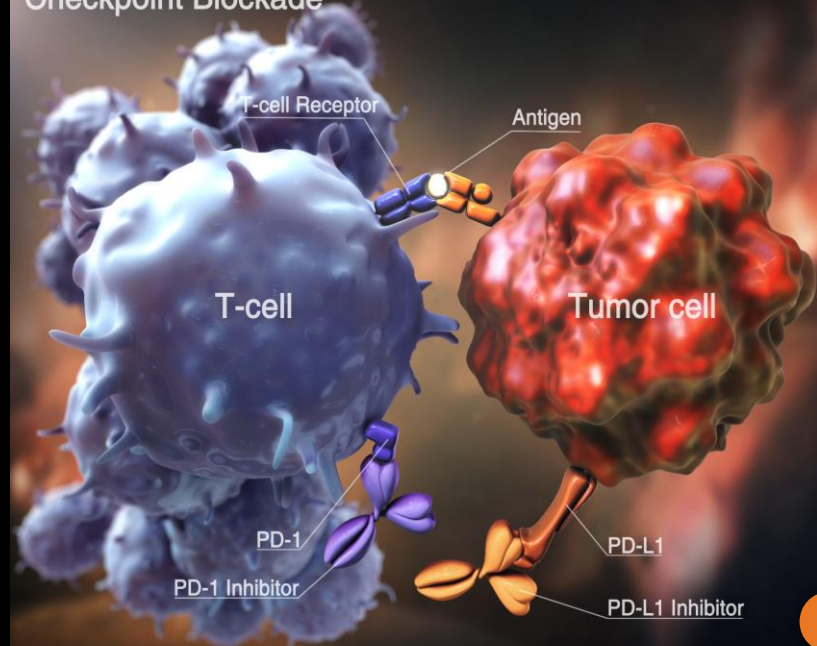
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Immune Evasion and T-Cell Exhaustion



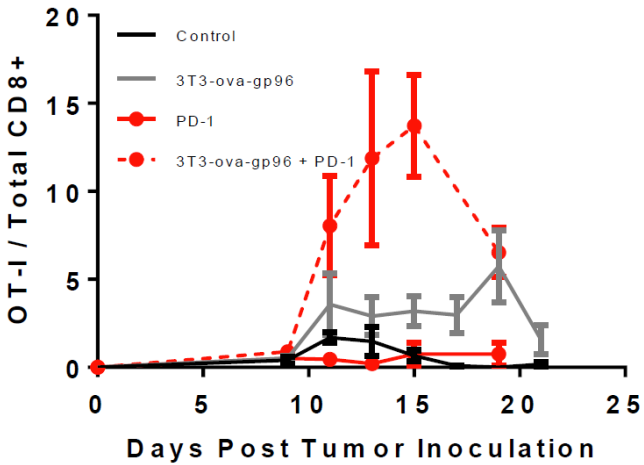
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Checkpoint Blockade

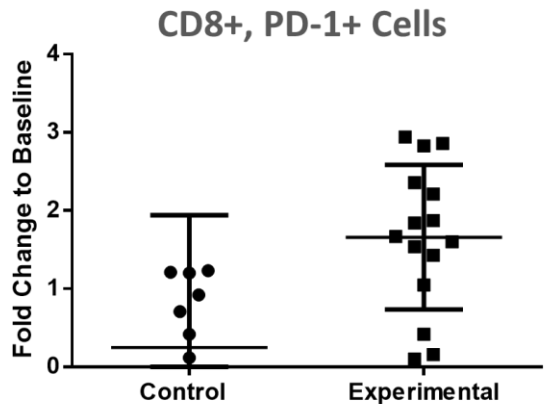


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Scientific Support for HS-110 & Nivolumab Combination

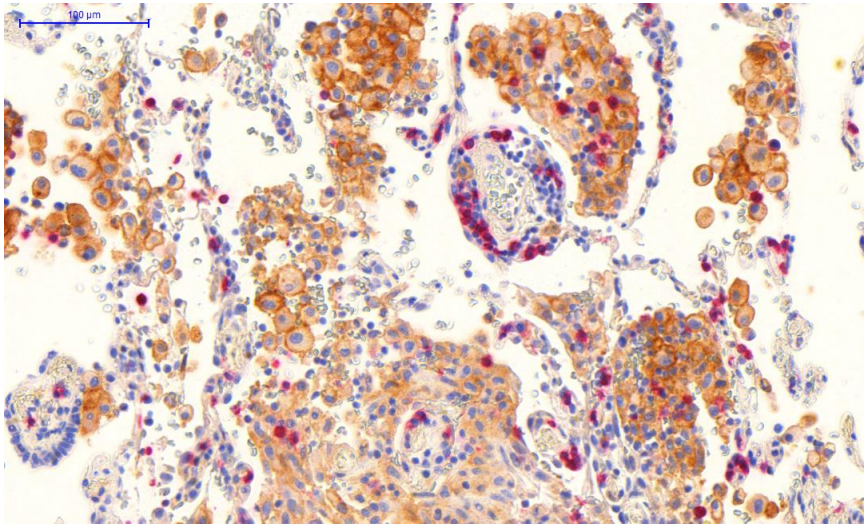


Schreiber T.H., et al. *Keystone* 2014



Cohen, R.B. et al, *ASCO* 2015

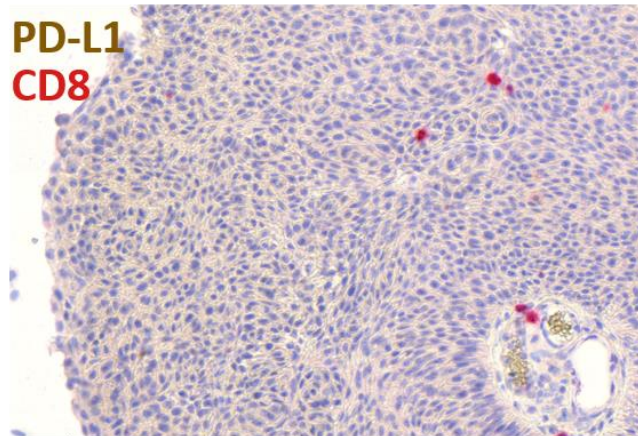
- 1. Pre-clinical studies demonstrate synergy between *ImPACT* vaccines and anti-PD-1
- 2. Phase 2 clinical data demonstrate that HS-110 treated patients upregulate PD-1 on CD8+ T cells
- 3. Phase 2 tumor biopsies show strong PD-L1 staining



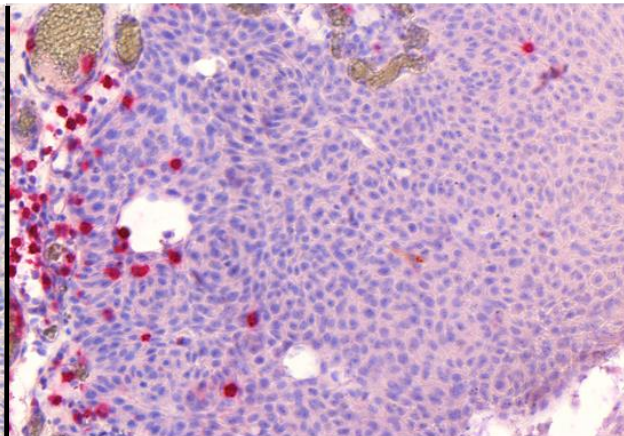
Phase 2 Tumor Biopsy from Patient Treated with HS-110

Bladder Cancer Patient Histology Data

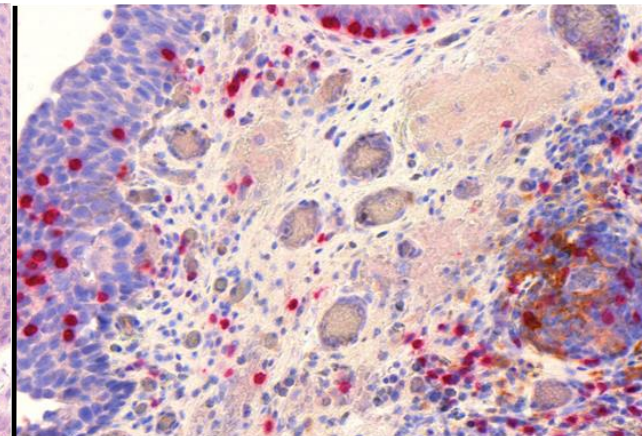
PD-L1
CD8



- 1** TIL:
- Low/Negative
PD-L1:
- Low/Negative



- 2** TIL:
- Mid/High
- Excluded from tumor
PD-L1:
- Positive or Negative



- 3** TIL:
- High
- Infiltrating tumor
PD-L1:
- Positive

Responder/non-responder phenotype emerging:

Responder: TIL⁻/PD-L1⁻

Non-responder: TIL⁺/PD-L1⁺

Design Intended to Broaden Responses to Nivolumab

T.H. Schreiber et al. / *Seminars in Immunology* 22 (2010) 105–112

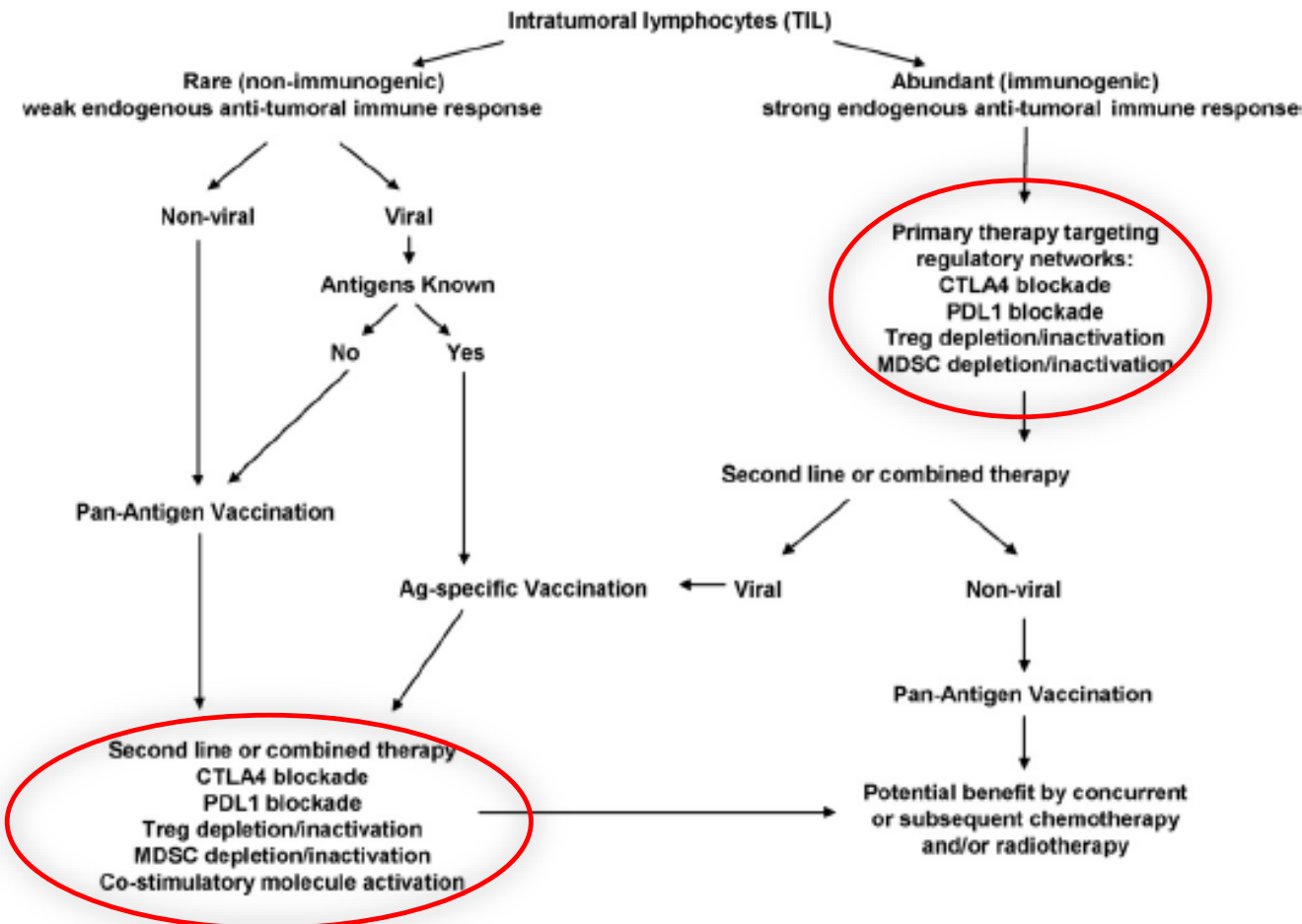
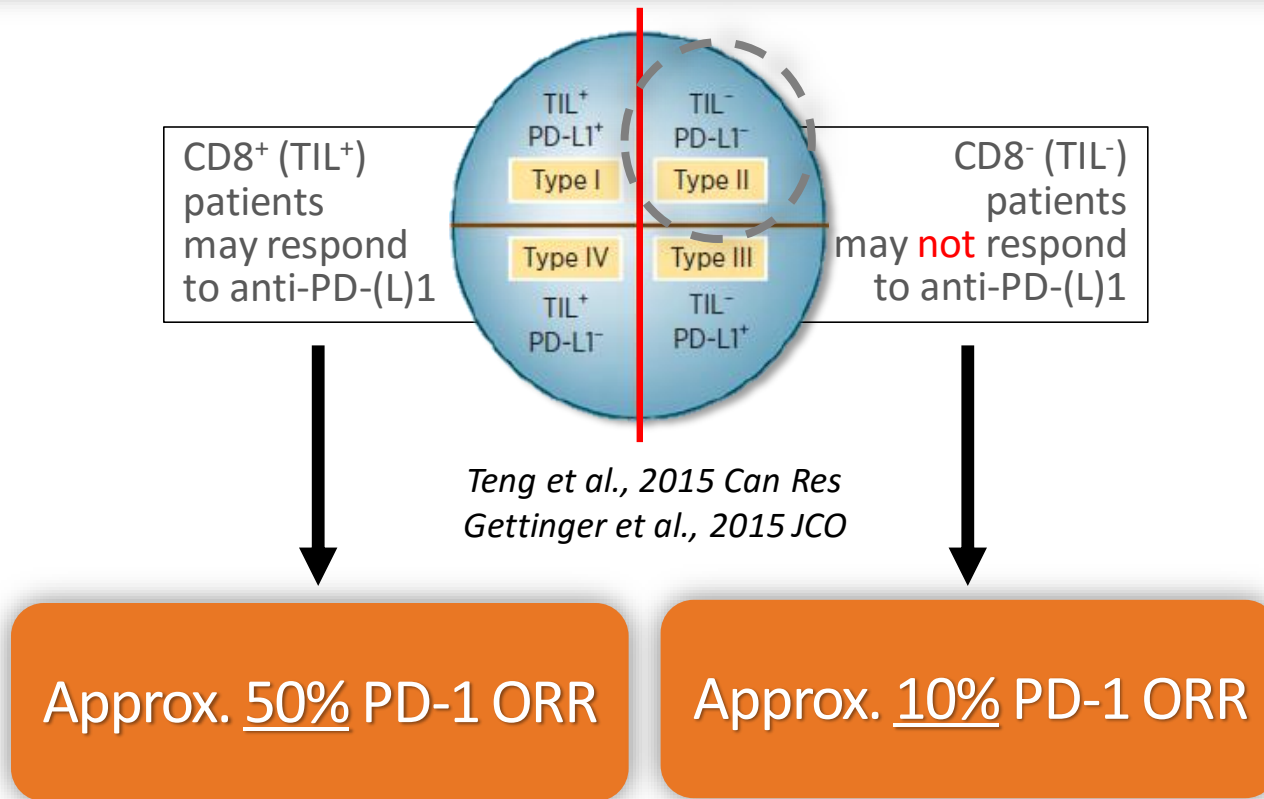


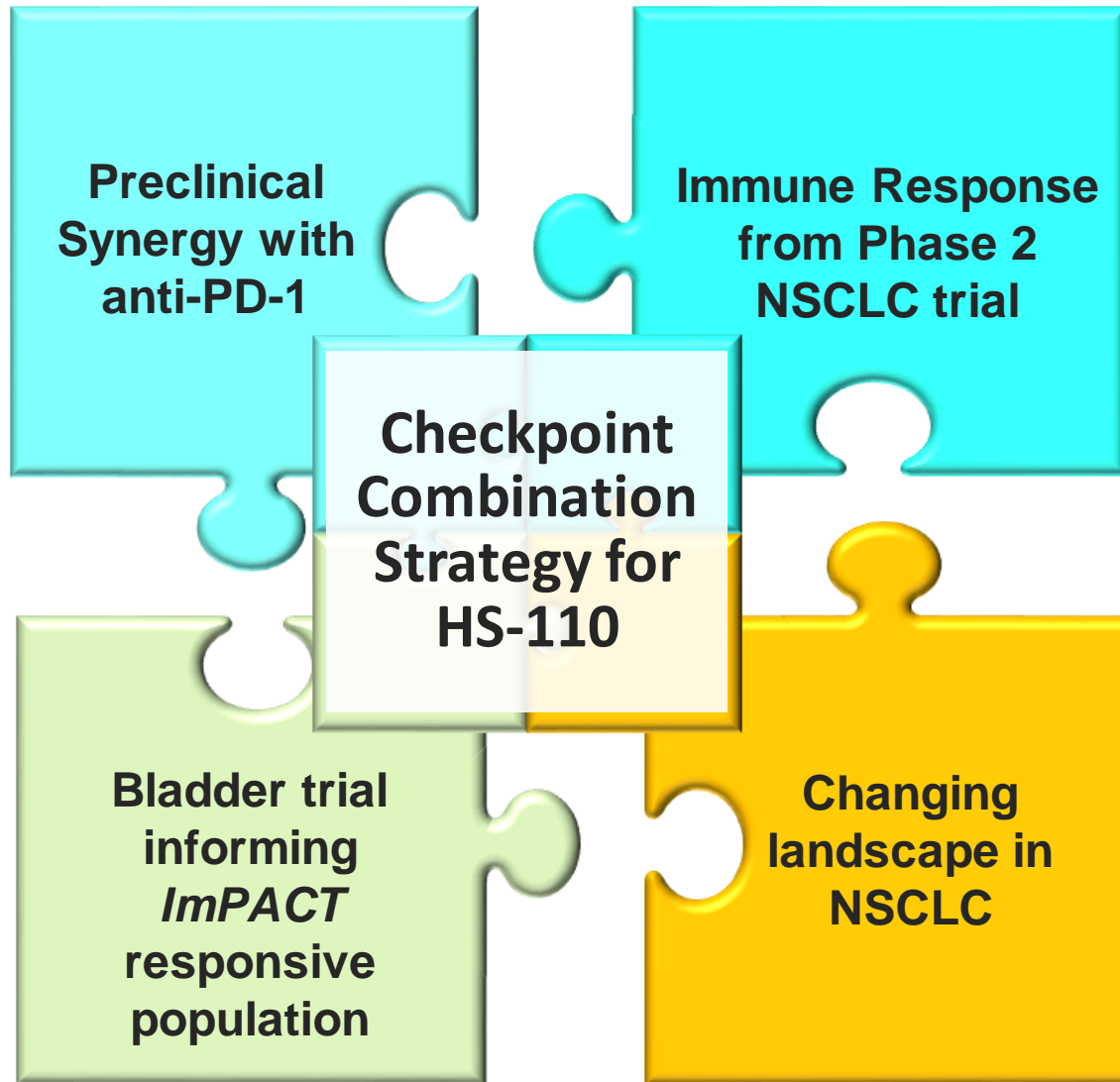
Fig. 2. Proposed flow chart for the application of therapeutic cancer vaccines.

Design Intended to Broaden Responses to Nivolumab

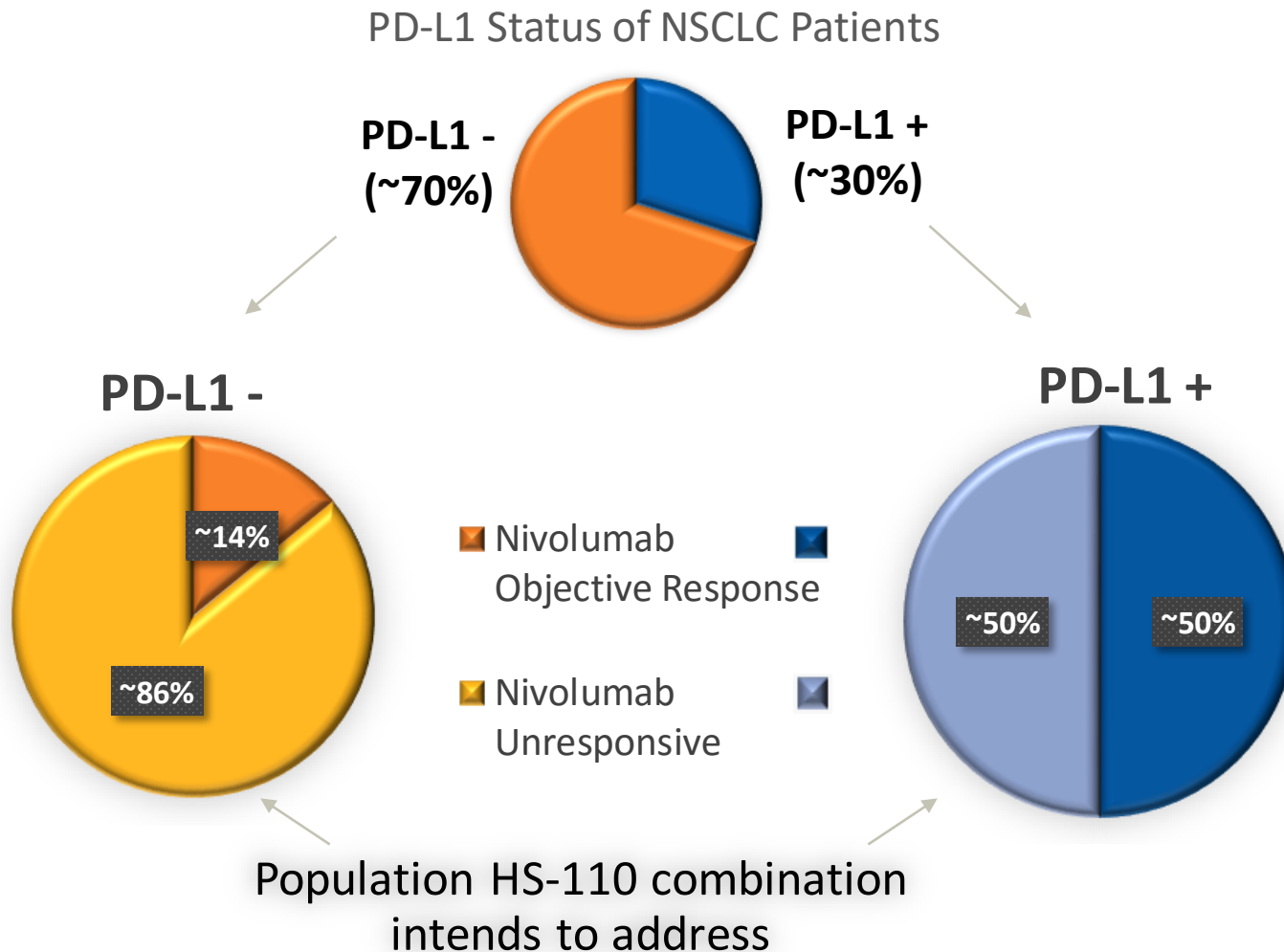
Estimated 45% NSCLC patients being underserved by single-agent anti-PD-(L)1 and may benefit from vaccine combination



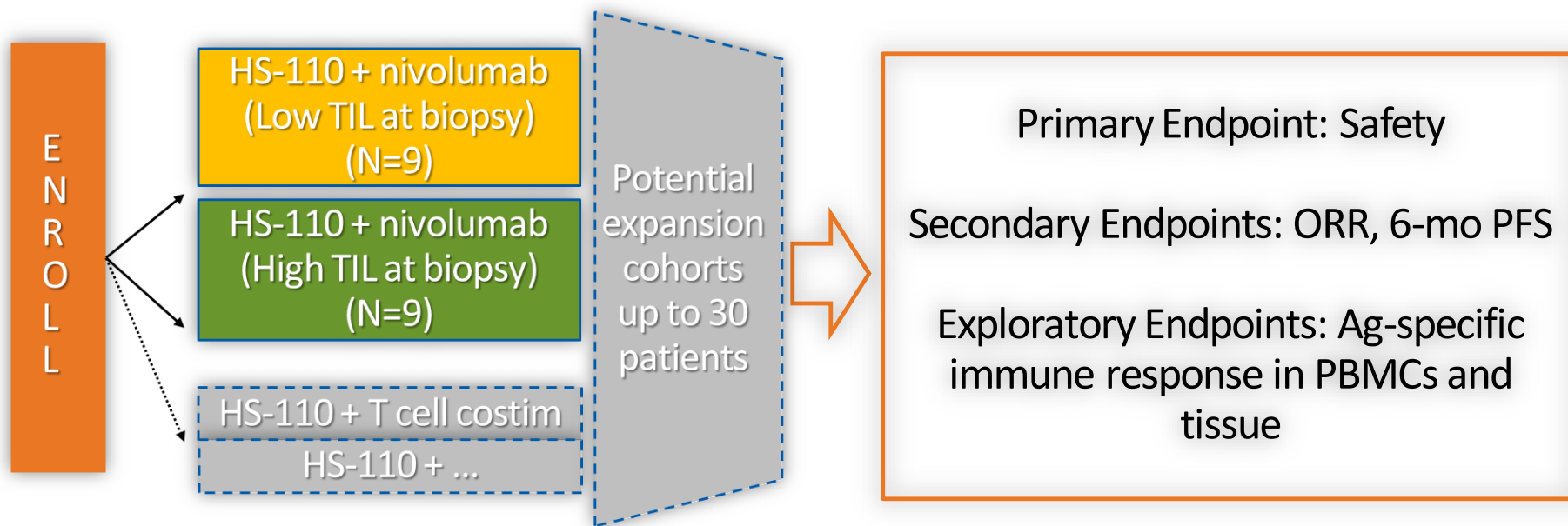
Checkpoint Combination Rationale



Response to Checkpoint Inhibitors by PD-L1 Status



DURGA Multi-arm Combination Trial



- Provides operational platform to:
 - React quickly to changing landscape
 - Leverage potential synergy with PD-1 mAb
 - Evaluate TILs as a potential biomarker to improve response rate (Yale Cancer Center's Translational Immuno-Oncology Laboratory collaboration)
 - Expand cohorts based on efficacy signal



Clinical Development Milestones

2H 2015	1H2016	2H2016
✓ 1 7 8	11 2 3	4 9 5 6 10

★ = NEW

	Milestone	Target Date
LUNG (NSCLC)	1 First dose combination with nivo in NSCLC (Durga)	31-Aug-2015
	2 Durga 18 pts enrolled	Q2 2016
	3 Durga immune response	Q2 2016
	4 Durga top-line readout for nivo (18 pts)	Q4 2016
	5 Ph 2 combo with cyclophosphamide readout (~65 pts)	Q4 2016
	6 Registration-directed trial initiation in NSCLC	Q4 2016
BLADDER (NMIBC)	7 Ph 2 Bladder Trial enrollment complete (75 pts)	Q3/Q4 2015
	8 Ph 1 Bladder Readout (10 pts)	Q4 2015
	9 Ph 2 Bladder Readout	Q4 2016
	10 Registration-directed trial initiation in NMIBC	Q4 2016
	11 Announce new <i>ComPACT</i> indication	Q1 2016

Summary



- First combination vaccine + nivolumab in NSCLC
- Strong preclinical/clinical rationale for combination
- Targeting patients unresponsive to checkpoints



- Data for nivo combo expected by end 2016
- Registration-directed trial initiation remains on schedule (end 2016/early 2017)
- Bladder program on track (readout Q4 2016)



- Cost savings from closing Ph 2 combination with cyclophosphamide to fund DURGA arms with nivolumab