CPI-444, an oral adenosine A2A receptor (A2AR) antagonist, demonstrates clinical activity in patients with advanced solid tumors

Leisha A. Emens[1], John Powderly[2], Lawrence Fong[3], Joshua Brody[4], Patrick Forde[1], Matthew Hellmann[5], Brett Hughes[6], Shivaani Kummar[7], Sherene Loi[8] Jason Luke[9], Daruka Mahadevan[10], Ben Markman[11], Ian McCaffery[12], Richard Miller[12], and Ginna Laport[12]

[1]Johns Hopkins University, Baltimore MD; [2]Carolina BioOncology Institute, Charlotte NC; [3]University of California, San Francisco, San Francisco CA; [4]Mount Sinai School of Medicine, New York NY; [5]Memorial Sloan Kettering Cancer Center, New York NY; [6]Royal Brisbane and Women's Hospital, Herston, Australia [7]Stanford University School of Medicine, Palo Alto CA; [8]Peter MacCallum Cancer Center, Melbourne, Australia; [9]University of Chicago, Chicago IL; [10]University of Arizona, Tucson AZ; [11]Monash Health, Victoria, Australia; [12]Corvus Pharmaceuticals, Burlingame CA

Forward Looking Statements

This presentation contains forward-looking statements, including statements related to the potential safety and efficacy of CPI-444, both as a single agent and in combination with anti-PD-1 and anti-PD-L1, the utility of biomarker data collected and the suitability of the dosing regimen selected for the Company's Phase 1/1b clinical trial of CPI-444. All statements other than statements of historical fact contained in this press release are forward-looking statements. These statements often include words such as "believe," "expect," "anticipate," "intend," "plan," "estimate," "seek," "will," "may" or similar expressions. Forward-looking statements are subject to a number of risks and uncertainties, many of which involve factors or circumstances that are beyond the Company's control. The Company's actual results could differ materially from those stated or implied in forward-looking statements due to a number of factors, including but not limited to, risks detailed in the Company's Annual Report on Form 10-K for the year ended December 31, 2016, filed with the Securities and Exchange Commission on March 10, 2017, as well as other documents that may be filed by the Company from time to time with the Securities and Exchange Commission. In particular, the following factors, among others, could cause results to differ materially from those expressed or implied by such forward-looking statements: the Company's ability to utilize biomarker data, select a suitable dosing regimen and demonstrate evidence of efficacy and safety for CPI-444 during its Phase 1/1b clinical trial; the accuracy of the Company's estimates relating to its ability to initiate and/or complete clinical trials; the results of early clinical trials may not be predictive of future results. Although the Company believes that the expectations reflected in the forward-looking statements are reasonable, it cannot guarantee that the events and circumstances reflected in the forward-looking statements will be achieved or occur, and the timing of events and circumstances and actual results could differ materially from those projected in the forward-looking statements. Accordingly, you should not place undue reliance on these forward-looking statements. All such statements speak only as of the date made, and the Company undertakes no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise. Additional information may be available in press releases or other public announcements and public filings made after the date of this presentation.

This presentation concerns products that have not yet been approved for marketing by the U.S. Food and Drug Administration ("FDA"). No representation is made as to their safety or effectiveness for the purposes of which they are being investigated.

Disclosure Information

AACR Annual Meeting 2017: Leisha A. Emens

I have the following financial relationships to disclose:

Consultant for: Vaccinex, Celgene, Bristol Meyers Squibb, AstraZeneca, Amgen, Syndax, Molecuvax, eTHeRNA, Peregrine, Bayer

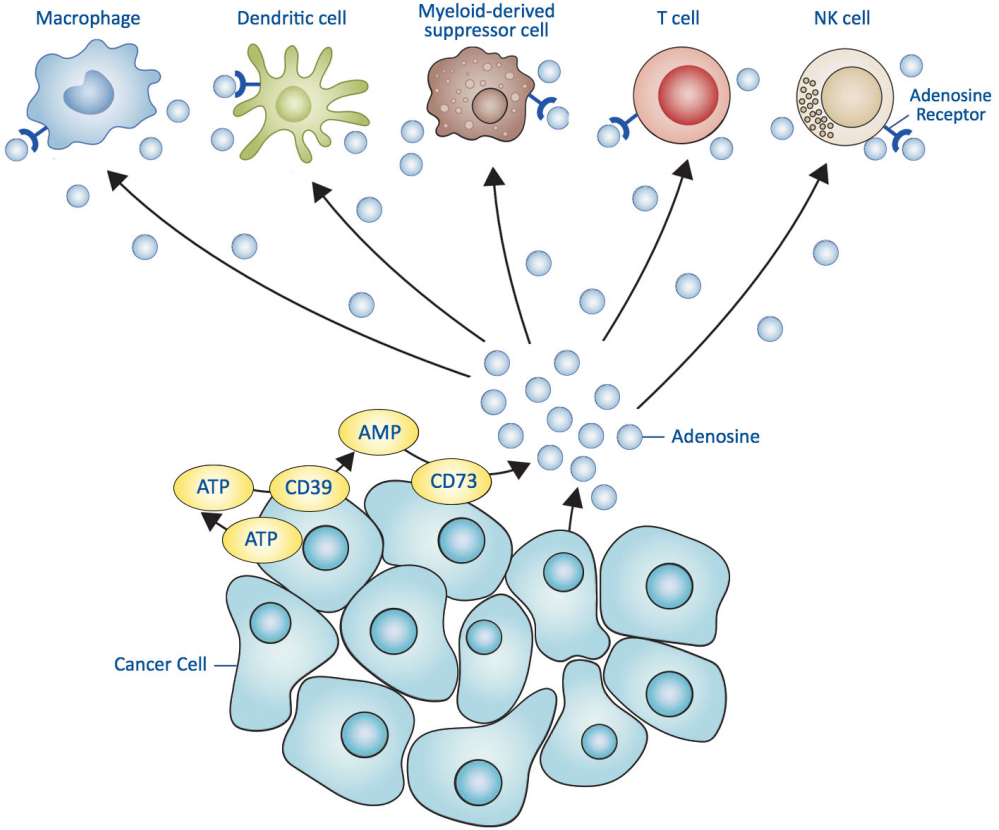
Grant/Research support from: Genentech/Roche, EMD Serono, Maxcyte, Merck, AstraZeneca, Aduro, Corvus

I will discuss the following off-label use and/or investigational use:

CPI-444 alone and combined with atezolizumab for advanced solid cancers.

Study funding provided by Corvus Pharmaceuticals.
Roche Genentech provided atezolizumab and support for biomarker analyses

Adenosine Signaling Suppresses Immunity in the Tumor Microenvironment



- PD-1/PD-L1 antibodies are effective immunotherapies with response rates ~20-30%
- Novel agents that enhance response or overcome resistance to immunotherapy are a high priority
- The adenosine pathway is a potential new immunotherapy target

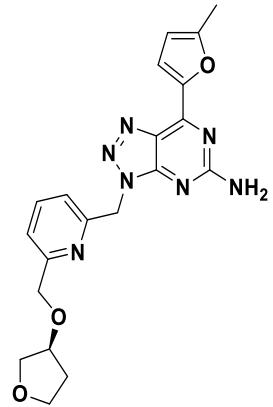
CPI-444: A Novel Inhibitor of the A2AR Pathway

- **Pharmaceutical Properties**
  - Molecular weight = 407Da
  - A2AR Ki= 3.5 nM
  - >55-fold selective over A1R, >400-fold A2BR and A3R
  - Oral bioavailability >50%
  - Plasma half life: ~10-14 hours

- **Single agent activity in multiple preclinical models***
  - Synergy with anti-PD-(L)1 and anti-CTLA-4 antibodies and other checkpoint inhibitors
- **Well-tolerated in early trials with healthy volunteers and ADHD patients**

- **This is the first evaluation of safety and clinical activity of an A2AR antagonist in patients with cancer**

CPI-444



*See Abstract #5598

A Phase 1/1b, Open-Label, Multicenter, Repeat-Dose, Dose-Selection Study of CPI-444 as a Single Agent and in Combination with Atezolizumab (atezo) in Patients with Selected Incurable Cancers

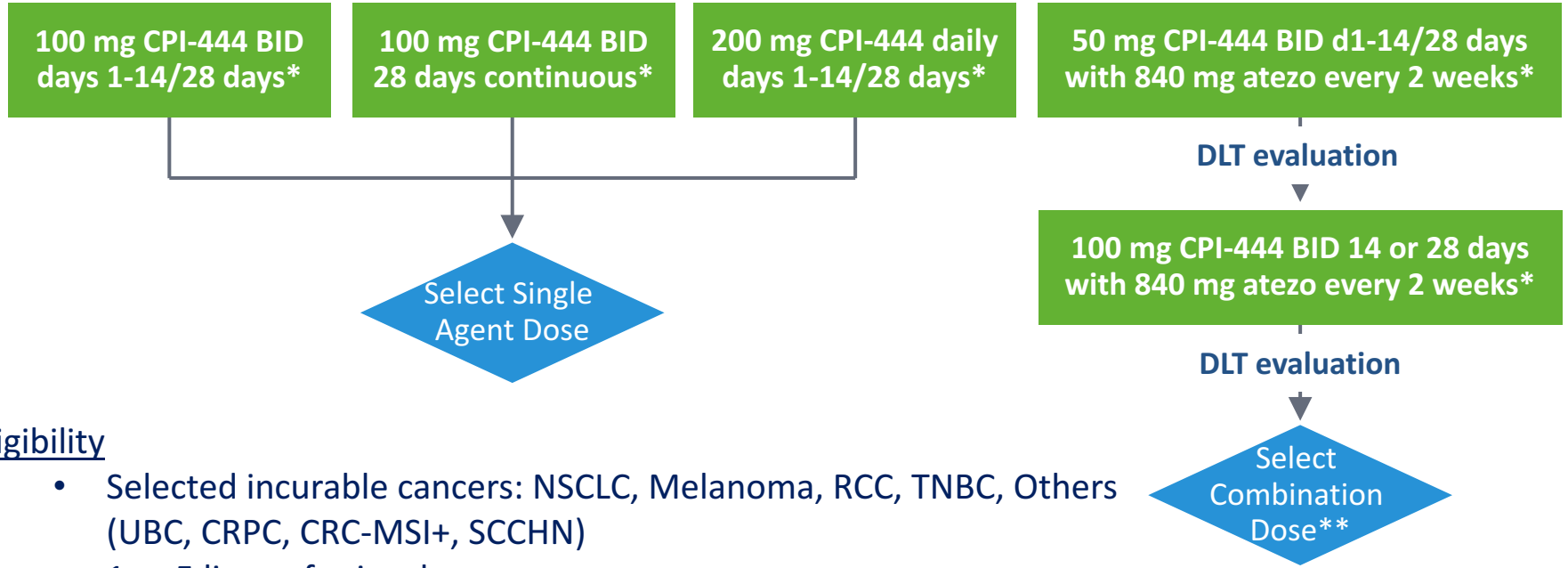
Primary Objectives

- Evaluate the safety of CPI-444 alone and with atezo
- Identify a recommended dose and schedule for CPI-444 alone and with atezo
  - Safety, PK and PD data*
- Measure the clinical activity of CPI-444 alone and with atezo
  - ORR, CBR and DOR*

*PK – pharmacokinetics; PD = pharmacodynamics; ORR = overall response rate; CBR- clinical benefit rate; DOR = duration of response

Trial Design: Step 1 Dose Selection

(Accrual completed)



Eligibility

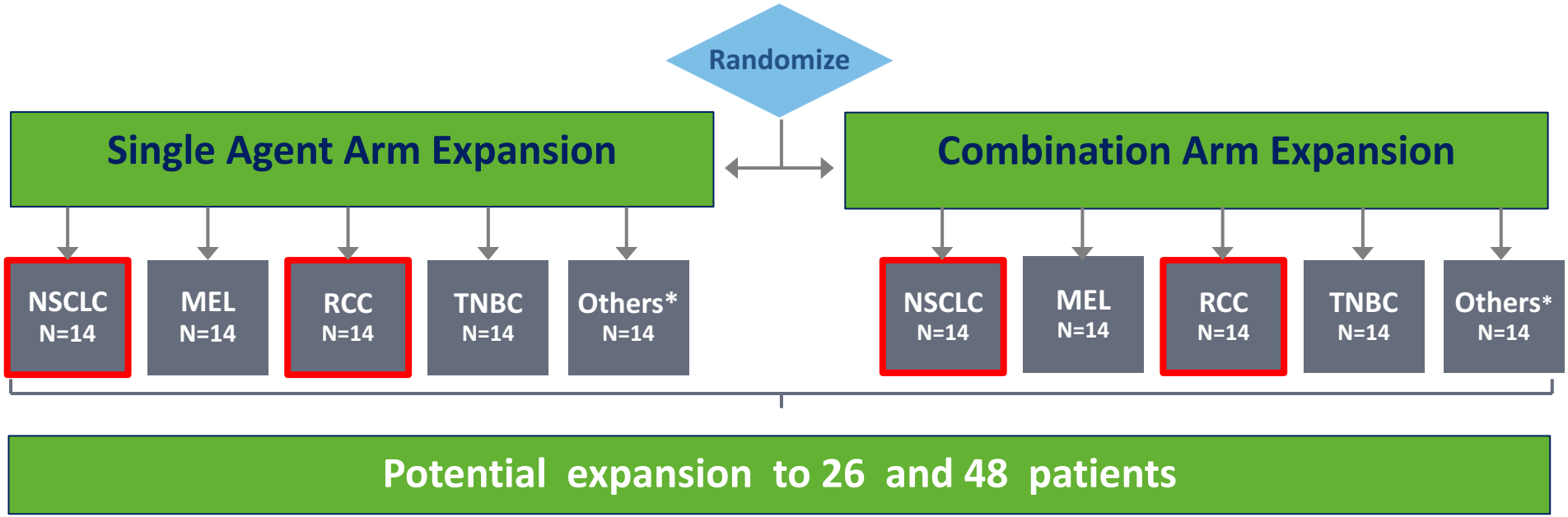
- Selected incurable cancers: NSCLC, Melanoma, RCC, TNBC, Others (UBC, CRPC, CRC-MSI+, SCCHN)
- 1 to 5 lines of prior therapy
- Stable, treated brain metastases allowed
- Resistant/refractory (R/R) to prior anti PD-1/PDL-1 allowed
- PD-L1, CD73, A2aR expression not required for enrollment

*1 cycle=28 days

***See Abstract #5593*

Trial Design: Step 2 Cohort Expansion by Disease

(Accrual ongoing)



*Others: CRPC, CRC-MSI, UBC, SCCHN

Patient Demographics/Disease Characteristics*

Median age, years (range)	**64 (36 – 85)**
Gender, n (%)	
Female	58 (51%)
Male	55 (49%)
ECOG performance status	
0	47 (42%)
1	66 (58%)
TNBC	32 (28%)
NSCLC	28 (25%)
MEL	14 (12%)
RCC	14 (12%)
Others	25 (23%)
Median # of prior regimens	2 (1–5)
Prior Chemotherapy	90 (80%)
Prior anti-PD1/PD-L1 exposure	
Naïve	50 (44%)
Resistant/Refractory	63 (56%)
Visceral metastases	102 (90%)
Liver	42 (37%)
Brain	10 (9%)

- Enrollment (n=113)
  - Step 1: n = 47 (33 single agent)
  - Step 2: n = 66 (26 single agent)
- Heavily pre-treated with extensive disease
- Over half with disease resistant/refractory to PD-1/PD-L1 antibodies

**Data cutoff: Mar 2017*

Treatment-Related Adverse Events (AE)

Adverse Events ≥ 5% Frequency (Gr 1/2)		
	Single Agent	Combo
Nausea	14%	13%
Pruritus	10%	9%
Fatigue	5%	7%
Abdominal Pain	5%	---
Rash	5%	---
Diarrhea	5%	---
Pyrexia	5%	7%
Decreased Appetite	5%	7%
Chills	5%	---

- Median duration of treatment: 9 weeks (range: up to 40+)
- 56% of patients experienced a treatment-related AE (any grade)
- No grade 3/4 AEs with single agent CPI-444
- Immune-related AEs seen only with combination of CPI-444 and atezo (n=1 for each):
  - -Pancreatitis (Gr 2)
  - -Autoimmune hemolytic anemia (Gr 3)
  - -Meningoencephalitis/thrombocytopenia (Gr 4)

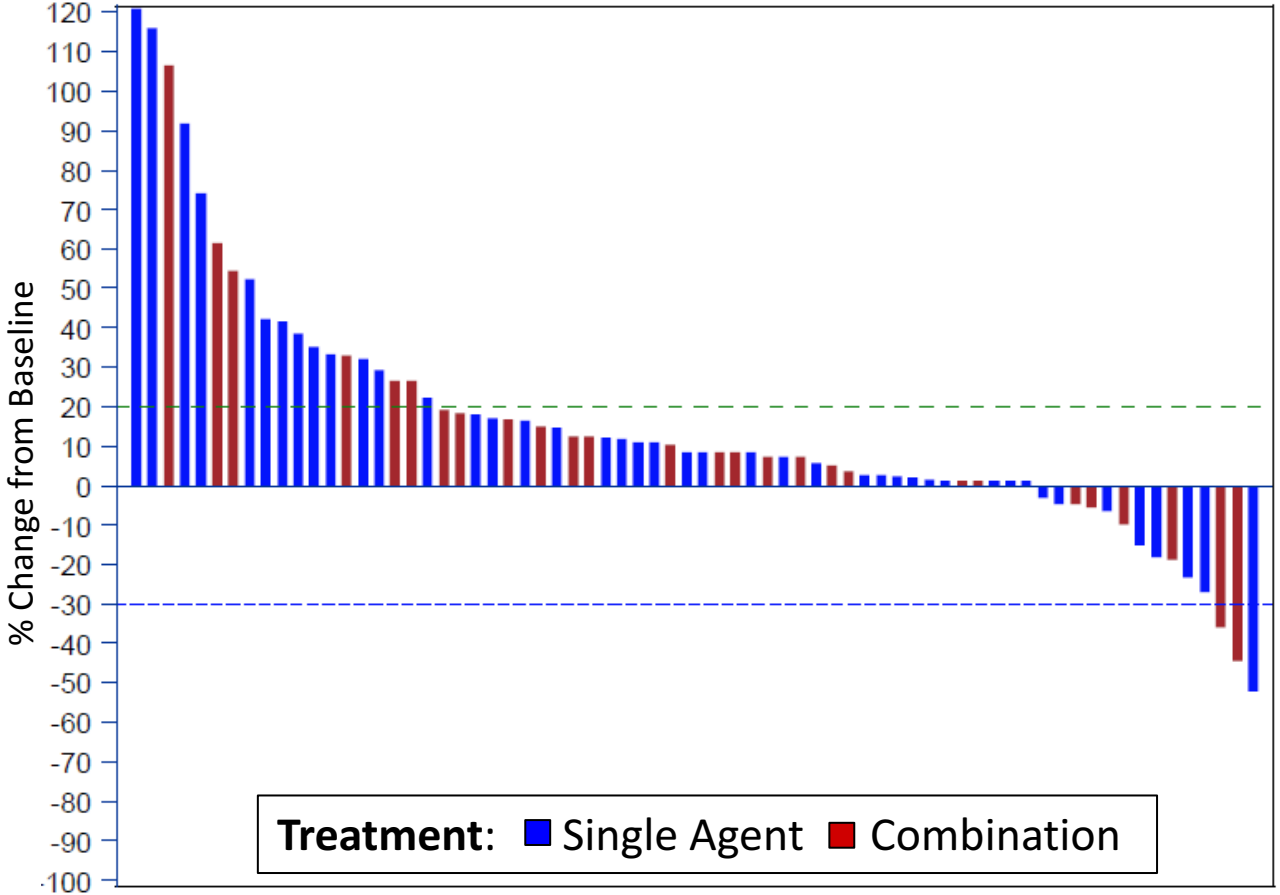
Overall Patient Outcomes

Disease Control Rate (CR, PR, SD) in Evaluable Patients

	CPI-444 (n=52)	CPI-444/ Atezolizumab (n=44)	All Subjects (n=96)
All subjects	20 (38%)	17 (39%)	37 (38%)
Prior PD-1/PD-L1 Experience			
Naïve	13/29 (45%)	5/18 (28%)	18/47 (38%)
Resistant/Refractory	7/23 (30%)	12/26 (46%)	19/49 (39%)
Disease Histology			
- NSCLC	4/14 (29%)	5/10 (50%)	9/24 (38%)
- MEL	2/5 (40%)	2/6 (33%)	4/11 (36%)
- RCC	3/5 (60%)	5/5 (100%)	8/10 (80%)
- TNBC	7/17 (41%)	3/14 (21%)	10/31 (32%)
- Others	4/11 (36%)	2/9 (22%)	6/20 (30%)

- Median follow up time for DCR: 16 weeks (range, 4-44 weeks)
- 23/37 of PR and SD patients remain on study

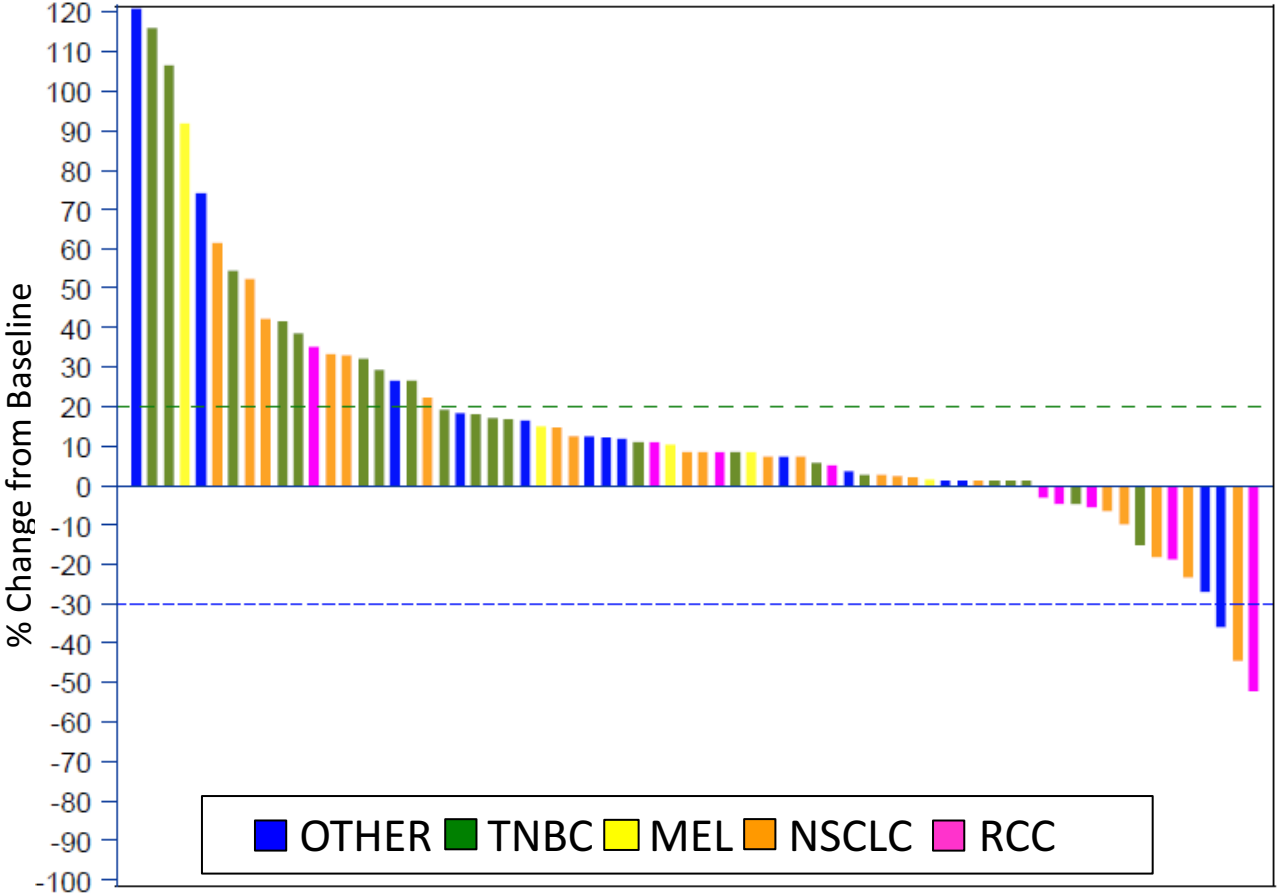
Clinical Activity: Overall Patient Population*



- SDs and PRs observed with CPI-444 alone and in combination with atezo

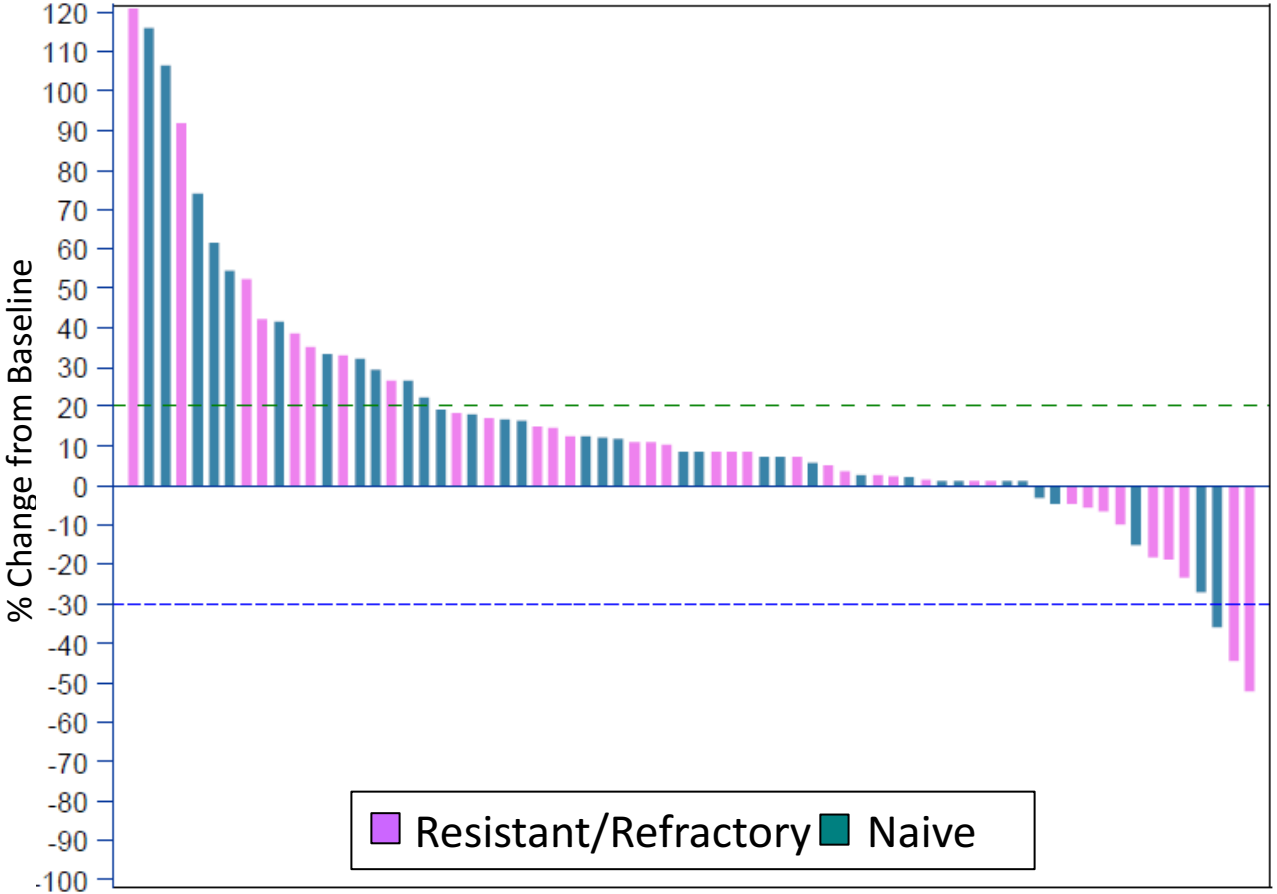
*Patients with disease evaluable by CT, n= 70

Clinical Activity: By Disease Type



- Tumor regression observed in RCC, NSCLC, TNBC, SCCHN and CRC

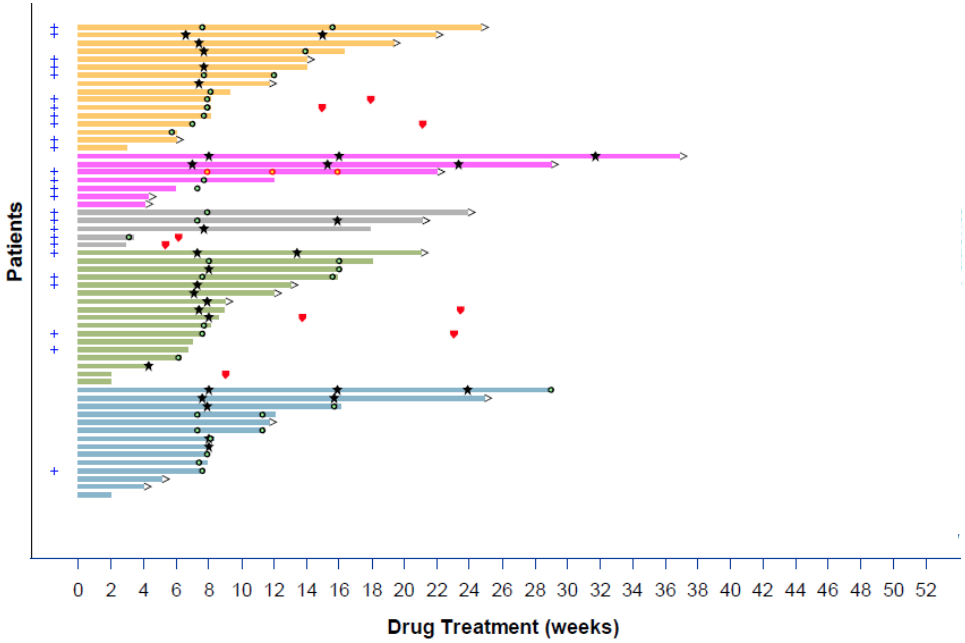
Clinical Activity by Prior PD-(L)1 Experience



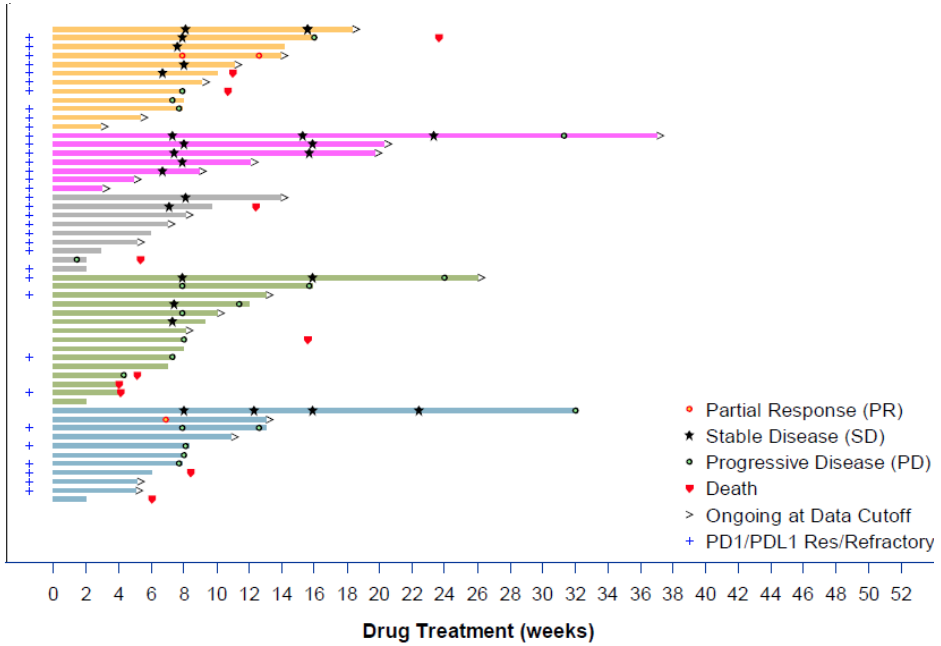
- CPI-444 has activity in patients resistant/refractory to PD-1 blockade
- 2 PRs and 7 minor regressions in PD-1 resistant/refractory patients
- 1 PR and 4 minor regressions in PD-1 naïve patients

Duration of Treatment

Single Agent CPI-444



CPI-444 Combined with Atezo

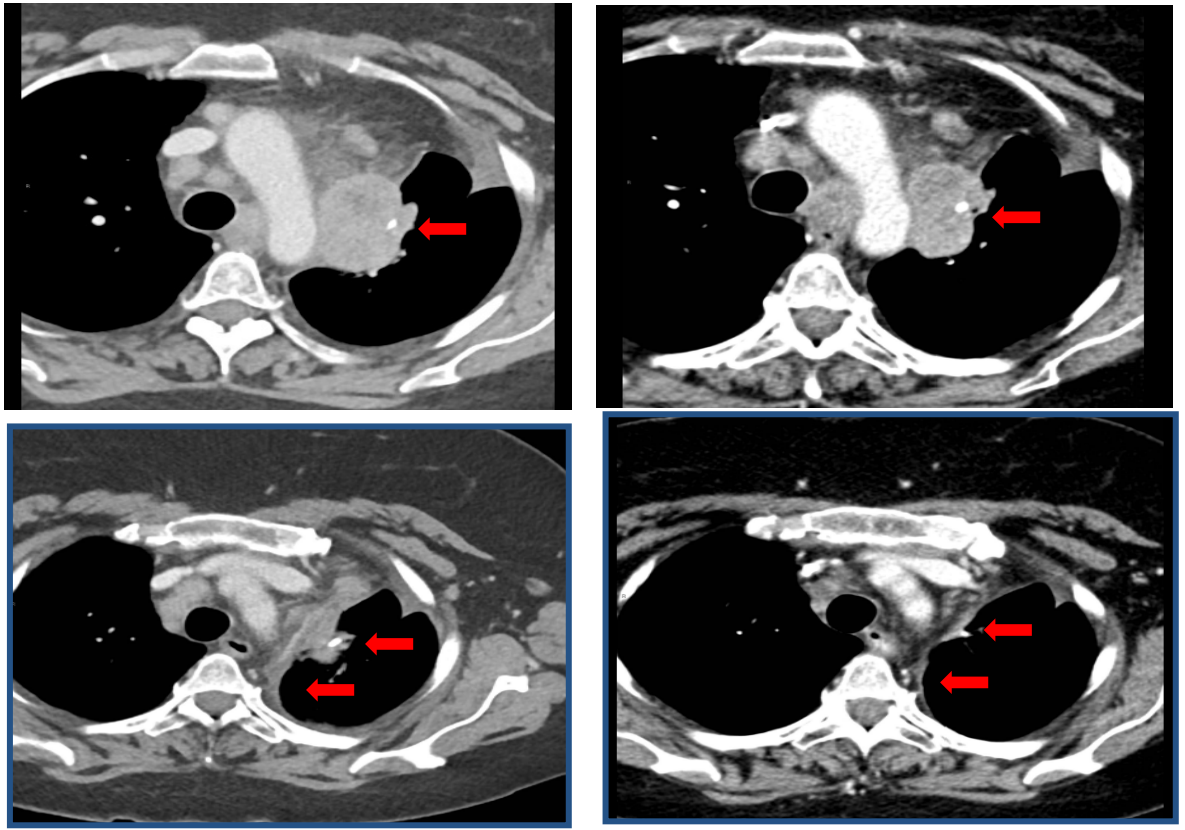


OTHER TNBC MEL NSCLC RCC

Tumor Regression in Nivolumab Refractory Lung Cancer

Single Agent CPI-444

- 2 prior chemotherapy regimens
- Refractory to nivolumab
- Started single agent CPI-444

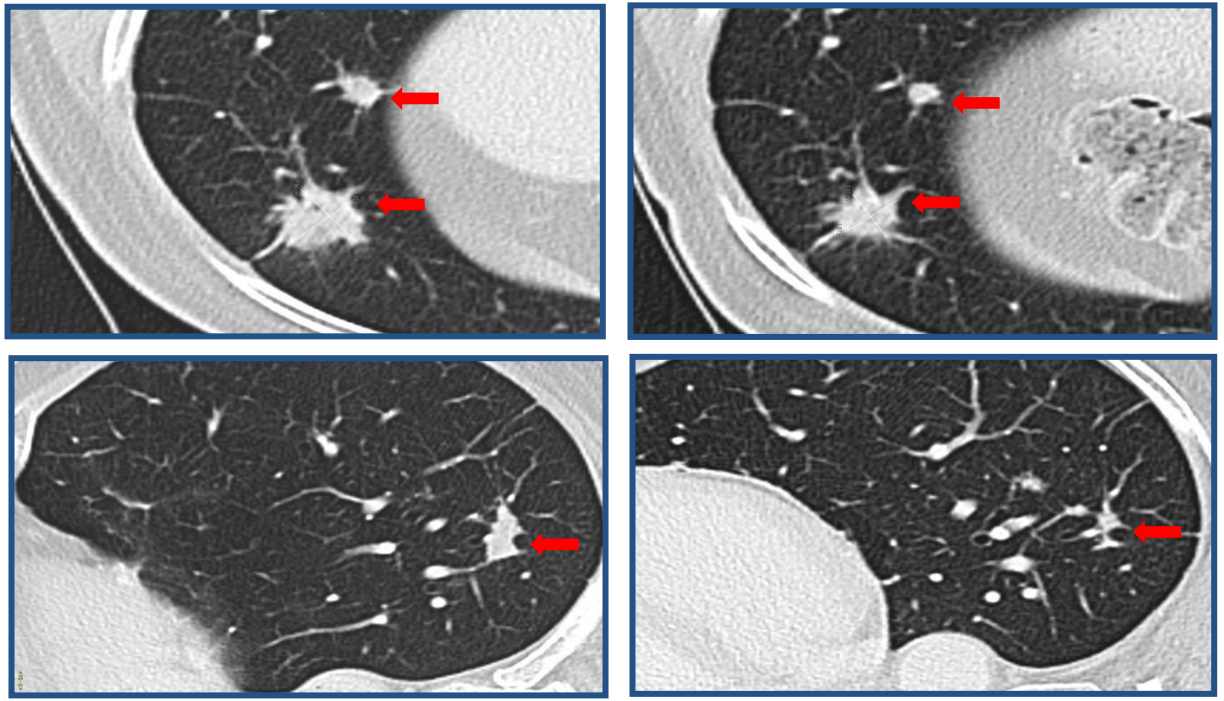


Pre-treatment **2 months of treatment**

Regression in Nivolumab Resistant Lung Cancer

Combination CPI-444/Atezolizumab

- 1 prior chemotherapy
- Responded to nivolumab, then progressed
- Started CPI-444 + atezo

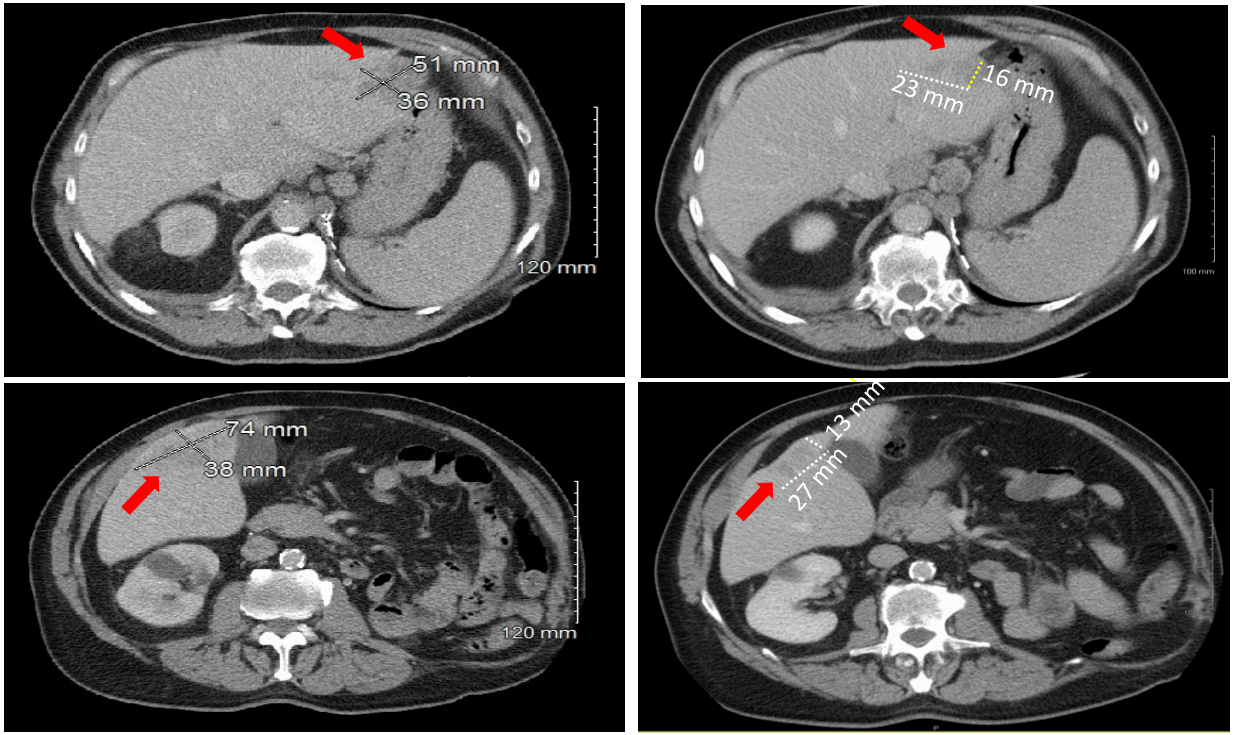


Pre-treatment **2 months on treatment**

Tumor Regression in Nivolumab Refractory Renal Cancer

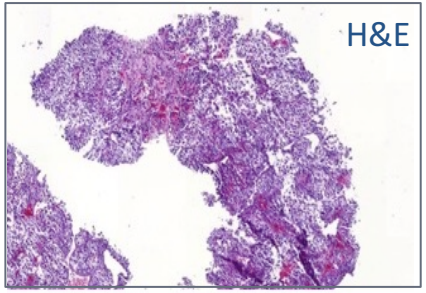
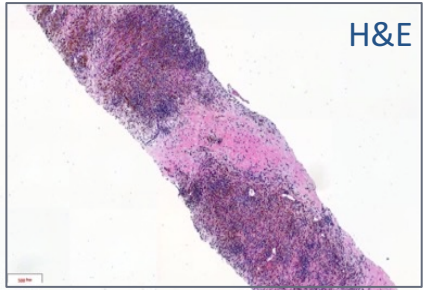
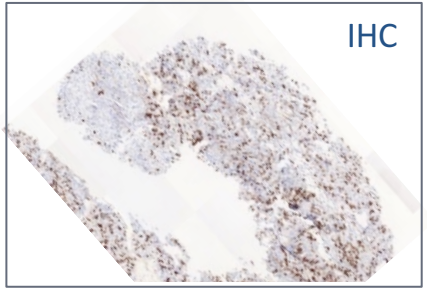
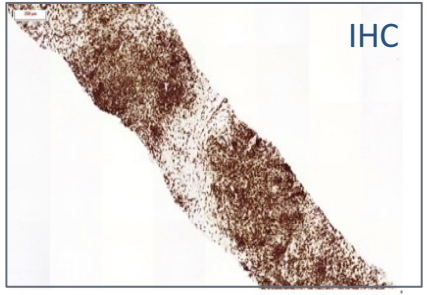
Single Agent CPI-444

- Five prior regimens including TKIs and mTOR inhibitor
- Tumor progression on nivolumab
- Started CPI-444



Pre-treatment **3 months of treatment**

Serial Biopsies of Liver Metastasis from PD-1 Refractory RCC Patient Treated with Single Agent CPI-444

Pre-treatment		Post treatment (2 months)	
Inflammatory Infiltrate in Tumor = 1%			Inflammatory Infiltrate in Tissue = 20%
CD8⁺ in tumor = 14%			CD8⁺ in tissue ≥70%; no tumor cells detectable

See Abstract #5593

Inflammation and CD8⁺ T Cell Infiltration After Progression on PD-1 Therapy Increased with Single Agent CPI-444 Therapy

Conclusions

- CPI-444 is well tolerated as a single agent and in combination with atezo
  - Most common Grade 1/2 toxicities: nausea, fatigue, pruritus
  - irAEs of hemolytic anemia (Gr3), meningoencephalitis (Gr4), and pancreatitis (Gr2) seen with combination therapy
- Selected dose of CPI-444 is 100 mg bid continuous
- Observed clinical activity:
  - As single agent and in combination with atezo in multiple tumor types in advanced cancer patients
  - In patients refractory/resistant to PD-1/PD-L1 blockade
  - 23/37 patients with PR/SD remain on study median 16 weeks
- Increased inflammation and $CD8^+$ T cells in biopsy observed in an anti PD(L)-1-experienced patients responding to single agent CPI-444

Acknowledgements

- **The patients and their families**
- **Participating Centers:** Carolina BioOncology Institute, Columbia University Medical Center, Cross Cancer Institute, Emory University, Indiana University, Johns Hopkins University, Juravinski Cancer Centre, Karmanos Cancer Center, Mary Crowley Cancer Research Centers, Medical College of Wisconsin, Memorial Sloan Kettering Cancer Center, Monash Health, Mount Sinai, Royal Brisbane and Women's Hospital, START, University of California at San Francisco Medical Center, University of Arizona Medical Center, University of Chicago Medical Center, University of Colorado Cancer Center, University of Pittsburgh, University of Washington, Washington University at Saint Louis
- **Colleagues at Corvus**
- **Colleagues at Roche Genentech**