UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d) of the
Securities Exchange Act of 1934
Date of Report (Date of earliest event reported): November 8, 2019

CORVUS PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-37719**	**46-4670809**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification Number)**

863 Mitten Road, Suite 102
Burlingame, CA 94010
(Address of principal executive offices, including Zip Code)

Registrant's telephone number, including area code: (650) 900-4520

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common Stock, Par Value $0.0001 per share	CRVS	Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR §230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2). Emerging growth company [X]

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. [X]

Item 8.01 Other Events.

On November 8, 2019, Corvus Pharmaceuticals, Inc. (“Corvus” or the “Company”) announced updated results from the first two arms of its Phase 1/1b trial evaluating CPI-006 as a single agent and in combination with ciforadenant. The updated data includes data from 24 patients who received CPI-006 given intravenously as monotherapy (at doses of 1, 3, 6, 12, 18 or 24 mg/kg every 21 days) and 16 patients who received the combination treatment of CPI-006 (1, 3, 6, 12 or 18 mg/kg every 21 days) plus a fixed dose of ciforadenant (100 mg twice daily). These patients had advanced, refractory disease (12 had colorectal cancer, six had renal cell cancer, six had pancreatic cancer, six had prostate cancer, five had head and neck cancer, three had non-small cell lung cancer, one had bladder cancer and one had sarcoma), and had failed a median of four prior therapies. The key highlights from the updated CPI-006 clinical results include:

- Pharmacokinetic studies showed a dose-dependent increase in CPI-006 plasma exposure, with doses of 6 mg/kg and higher producing sustained plasma levels of CPI-006 and doses of 12 mg/kg and higher achieving complete and sustained occupancy of CD73 on peripheral blood lymphocytes.
- Biopsies revealed penetration of CPI-006 and complete occupancy of CD73 in tumors at doses of 18 mg/kg, which is the selected dose for continued expansion of the study.
- In vitro results revealed that CPI-006 induced B-cell differentiation into both plasmablasts and memory B-cells, promoted secretion of immunoglobulin M (IgM), and class switching of the IgM to produce immunoglobulin G (IgG).
- In vivo results demonstrated that treatment with CPI-006 produced changes in blood B-cell and T-cell levels, highlighted by a reduction in circulating B-cells within 30 minutes of treatment, with a partial return by 21 days, and with returning B-cell levels heavily enriched with memory B-cells. These changes are consistent with the in vitro findings that suggest that CPI-006 induces a humoral adaptive immune response.
- A specific analysis of the B-cell receptor repertoire (the range of B-cell receptors expressed by the total B-cell population) revealed that several patients exhibited the induction of new memory B-cell clones in blood following treatment with CPI-006, with clonal frequencies as high as 1%, supporting a very strong antibody immune response comparable or exceeding that seen when patients receive vaccinations. These findings are consistent with antigen driven clonal expansion of B-cells.
- In evaluable patients receiving 6 mg/kg and higher in the protocol defined, pre-specified disease specific cohorts, tumor regression was seen in four of nine patients: mCRPC (one of two patients; reduction of 18.2%), RCC (two of five patients; reduction of 7.0%, 21.3%) and NSCLC (one of two patients; reduction of 5.8%).
- A patient with metastatic prostate cancer that had previously failed multiple anti-androgen therapies and chemotherapy received over 19 cycles (a cycle equals 21 days) of CPI-006 monotherapy at a dose of 6 mg/kg and showed reduction in tumor volume and a reduction in bone pain.
- CPI-006 was well tolerated at all dose levels, with no dose-limiting toxicities. Grade 1 infusion reactions were detected (N=3 patients) and mitigated with premedication with acetaminophen and antihistamine. Grade 3 or 4 toxicities included a grade 3 anemia (N=1) and a grade 3/4 diarrhea (N=1).

The Company also announced updated data on the Adenosine Gene Signature. The key highlights from the updated data include:

- The Adenosine Gene Signature was examined in 32 patients with advanced refractory renal cell cancer, including 21 that were positive for this biomarker and 11 that were negative for this biomarker. In patients with a positive biomarker result, 17% had a partial response (PR) and many had tumor regression that did not meet the response evaluation criteria in solid tumors (RECIST) for PR. In patients with a negative biomarker result, there were no responses. In the 21 patients in the Adenosine Gene Signature positive group, 9 patients had tumor regression; 4 patients had no change in tumor size and 8 patients had tumor progression as best response; no patients in the negative group showed tumor reduction. There was a statistically significant correlation of the Adenosine Gene Signature with tumor response, p=0.008.
- A positive Adenosine Gene Signature was also associated with duration of response. Six of 21 patients had progression free survival (PFS) exceeding 40 weeks, with a plateau on the curve, and all of these patients were Adenosine Gene Signature positive, including four patients who had failed prior therapies with anti PD(L)-1.
- CPI-006 blocks CD73 enzymatic activity and prevents conversion of adenosine monophosphate (AMP) to adenosine leading to an elevation of AMP levels.
- AMP induces gene expression changes nearly identical to the Adenosine Gene Signature due to its ability to bind to and activate the adenosine A2A receptor, producing similar effects to that of adenosine binding to the A2A receptor.
- CD73 antagonists preserve AMP and thereby amplify the AMP gene expression signature.

- Ciforadenant (which has been shown to inhibit adenosine binding to A2A receptor) blocks both AMP and adenosine induced gene expression changes.
- This suggests that use of CPI-006 (which has been shown to inhibit adenosine production) in combination with ciforadenant could be a more effective way to block the immunosuppressive effects of A2A receptor signaling.

Item 7.01 Regulation FD Disclosure.

On November 8, 2019, the updated results from the CPI-006 trial discussed above were presented in an oral session at the Society for Immunotherapy of Cancer (SITC) Annual Meeting in National Harbor, Maryland by Jason J. Luke, M.D., principal investigator of the trial and Director of the Cancer Immunotherapeutics Center at UPMC Hillman Cancer Center and Associate Professor of Medicine at the University of Pittsburgh School of Medicine. A copy of the presentation is furnished as Exhibit 99.1 to this Current Report and is incorporated herein by reference.

On November 8, 2019, the updated data on the Adenosine Gene Signature discussed above were presented in a poster session by Stephen Willingham, Ph.D., Corvus Senior Scientist. A copy of the poster is furnished as Exhibit 99.2 to this Current Report and is incorporated herein by reference.

The information in this Item 7.01 of this Current Report on Form 8-K (including Exhibits 99.1 and 99.2) shall not be deemed "filed" for purposes of Section 18 of the Securities Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that Section, or incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Forward-Looking Statements

To the extent that statements contained herein or in the presentations attached hereto as Exhibits 99.1 and 99.2 are not descriptions of historical facts regarding Corvus, they are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, including statements related to the potential safety and efficacy of CPI-006 and ciforadenant (CPI-444), the Company's ability to develop and advance product candidates into and successfully complete preclinical studies and clinical trials, including the Company's Phase 1/1b clinical trial of CPI-006, the utility of biomarker data collected and the suitability of dosing regimen selected for clinical trials and the potential utility of the Adenosine Gene Signature to identify patients that are most likely to respond to therapies targeting the adenosine pathway. Such forward-looking statements involve substantial risks and uncertainties that could cause the Company's clinical development programs, future results, performance, or achievements to differ significantly from those expressed or implied by the forward-looking statements. For a description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of the Company in general, see Corvus' reports filed with the Securities and Exchange Commission ("SEC"), including its Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, filed with the SEC on October 29, 2019, as well as other documents that may be filed by the Company from time to time with the SEC.

Item 9.01 Financial Statements and Exhibits.

Exhibit No.	Description
99.1	Presentation by Jason J. Luke, M.D., principal investigator of the trial and Director of the Cancer Immunotherapeutics Center at UPMC Hillman Cancer Center and Associate Professor of Medicine at the University of Pittsburg School of Medicine.
99.2	Poster presented by Stephen Willingham, Ph.D., Corvus Senior Scientist.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

CORVUS PHARMACEUTICALS, INC.

Date: November 8, 2019

By: /s/ Leiv Lea
Leiv Lea
Chief Financial Officer


SITC 2019
Gaylord National Hotel
& Convention Center
Nov. 6-10
NATIONAL HARBOR, MARYLAND
sitc
Society for Immunotherapy of Cancer

SITC 2019
Gaylord National Hotel & Convention Center Nov. 6-10
NATIONAL HARBOR, MARYLAND

Immunobiology and Clinical Activity of CPI-006, an Anti-CD73 Antibody with Immunomodulating Properties in a Phase 1/1b Trial in Advanced Cancers

Luke JJ, Merchan J, Harshman LC, Marron T, Powderly J, Barve M, LoRusso P, Johnson M, Hotson A, Gittelman R, Munneke B, Buggy J, Willingham S, Piccione E, Mobasher M, Miller R

Disclosures

Jason J. Luke: University of Pittsburgh Medical Center, Pittsburgh

The following relationships exist related to this presentation:

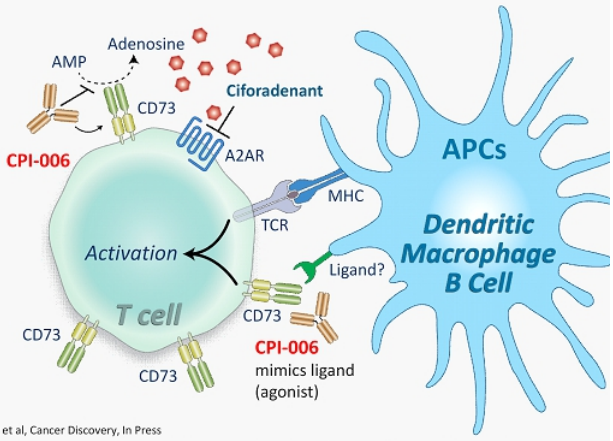
- **Data and Safety Monitoring Board:** TTC Oncology
- **Scientific Advisory Board:** 7 Hills, Actym, Alphamab Oncology, Mavu, Pyxis, Springbank, Tempest
- **Consultancy**: Abbvie, Akrevia, Array, Astellas, AstraZeneca, Bayer, Bristol-Myers Squibb, Compugen, EMD Serono, Ideaya, Immunocore, Incyte, Janssen, Leap, Merck, Mersana, Novartis, RefleXion, Silicon, Vividion
- **Research Support:** (all to institution for clinical trials unless noted) AbbVie, Agios (IIT), Array (IIT), Astellas, Boston Biomedical, Bristol-Myers Squibb, CheckMate (SRA), Compugen, Corvus, EMD Serono, Evelo (SRA), Five Prime, FLX Bio, Genentech, Immatics, Immunocore, Incyte, Leap, MedImmune, Macrogenics, Necktar, Novartis, Palleon (SRA), Merck, Springbank, Tesaro, Tizona, Xencor
- **Travel**: Akrevia, AstraZeneca, Bayer, Bristol-Myers Squibb, EMD Serono, Immunocore, Incyte, Janssen, Merck, Mersana, Novartis, RefleXion
- **Patents**: (both provisional) Serial #15/612,657 (Cancer Immunotherapy), PCT/US18/36052 (Microbiome Biomarkers for Anti-PD-1/PD-L1 Responsiveness: Diagnostic, Prognostic and Therapeutic Uses Thereof)

Corvus Pharmaceutical Inc. is the sponsor of this study.

Background

CPI-006 is an Anti-CD73 with Adenosine Independent Immunomodulatory Properties

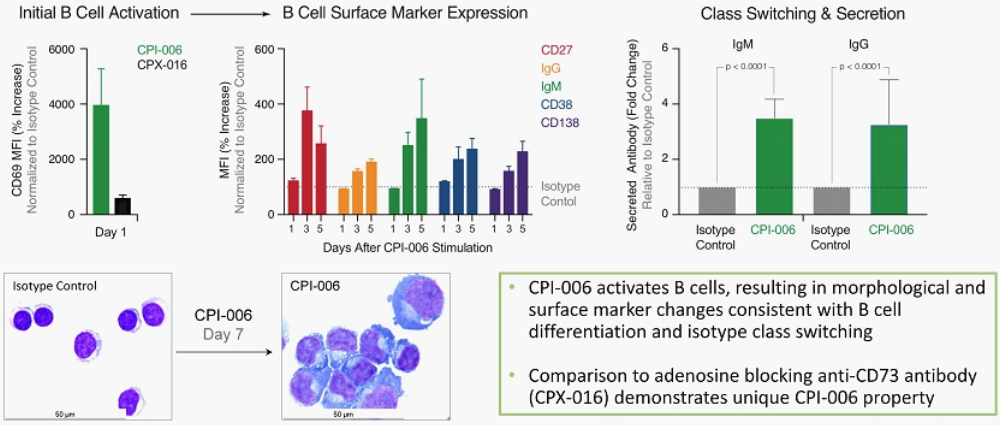
- CD73 is an ectoenzyme present on many tissues including subsets of T and B cells
  - Converts AMP to adenosine
  - Functions in lymphocyte adhesion, migration and activation[1]
- CPI-006 is a humanized IgG1 Fcγ receptor deficient anti-CD73 with unique properties[2]
  - Blocks catalytic activity
  - Has agonistic immunomodulatory activity on CD73 positive cells that are **adenosine independent**
  - Increases expression of CD69, HLA-DR, etc. on APC
- Early results from Ph1 dose escalation trial demonstrate lymphocyte activation and effects on trafficking[2]
- Ciforadenant (CPI-444) is an adenosine 2A receptor (A2AR) antagonist with reported anti-tumor activity in mCRPC, RCC and NSCLC[3]
  - Adenosine gene signature in tumor correlates with response in RCC



[1]Resta & Thompson, Cell Signaling, 1997 [2]Luke, ASCO Annual Meeting, 2019 [3]Fong et al, Cancer Discovery, In Press

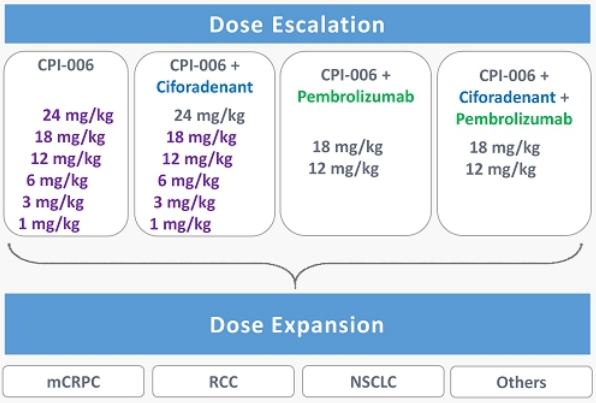
CPI-006 is an Anti-CD73 with Unique Properties

CPI-006 induces B cell differentiation: isotype switching and immunoglobulin secretion in vitro



- CPI-006 activates B cells, resulting in morphological and surface marker changes consistent with B cell differentiation and isotype class switching
- Comparison to adenosine blocking anti-CD73 antibody (CPX-016) demonstrates unique CPI-006 property

CPI-006-001 Clinical Trial Design



Design
- Phase 1/1b dose escalation/dose expansion in disease specific cohorts
- CPI-006 every 3 weeks; fixed dose of ciforadenant

Eligibility
- Cancers progressed on 1-5 prior therapies
- CD73 expression: required in expansion, not in dose escalation
- Adenosine gene signature not used to select patients

Objectives
- Primary: Safety and tolerability
- Secondary: PK/PD, efficacy, biomarkers

Biomarker Assessments
- Tumor markers, cytokines, etc.

Doses explored to date & planned doses

See Poster P434, Saturday Nov 9th

Patient Characteristics

Total Patients N=40	CPI-006 (N = 24)	CPI-006 + Ciforadenant (N=16)
Age (yrs), median (range)	62 (46, 78)	67 (36, 86)
Gender, male N (%)	18 (75)	12 (75)
No. of prior therapies, median (range)	4 (1, 6)	4 (2, 7)
Histologies	**N**	**N**
Renal Cell Cancer	2	4
Non-small cell lung cancer	2	1
Prostate Cancer	5	1
Colorectal Cancer	7	5
Head and Neck Cancer	3	2
Pancreatic Cancer	3	3
Sarcoma	1	0
Bladder Cancer	1	0

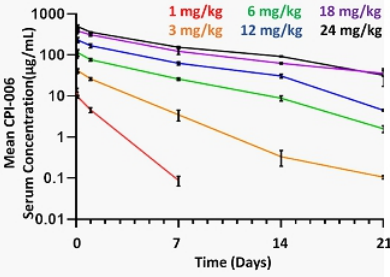
Adverse Events

Adverse Events N (%)	CPI-006 Monotherapy (N=24)		CPI-006 + Ciforadenant (N= 16)	
	All Grades	Grade 3 or 4	All Grades	Grade 3 or 4
Patients with any TEAE	18 (75.0)	4 (16.7)	12 (75.0)	2 (12.5)
Anemia	1 (4.2)	1 (4.2)	2 (12.5)	1 (6.3)
Lymphopenia	2 (8.3)	1 (4.2)	0 (0.0)	0 (0.0)
Colitis	0 (0.0)	0 (0.0)	1 (6.3)	1 (6.3)
Diarrhea	1 (4.2)	0 (0.0)	3 (18.8)	1 (6.3)
Nausea	4 (16.7)	0 (0.0)	2 (12.5)	0 (0.0)
Vomiting	3 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)
Chills	11 (45.8)	0 (0.0)	3 (18.8)	0 (0.0)
Fatigue	3 (12.5)	0 (0.0)	3 (18.8)	0 (0.0)
Pyrexia	2 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Infusion related reaction	3 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)
Liver enzymes increased (AST & ALP)	1 (4.2)	1 (4.2)	0 (0.0)	0 (0.0)
Blood creatinine increased	0 (0.0)	0 (0.0)	2 (12.5)	0 (0.0)
WBC decreased	1 (4.2)	0 (0.0)	3 (18.8)	0 (0.0)
Decreased appetite	1 (4.2)	0 (0.0)	1 (6.3)	0 (0.0)
Hyponatremia	1 (4.2)	1 (4.2)	0 (0.0)	0 (0.0)
Tumor pain	2 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Headache	2 (8.3)	0 (0.0)	1 (6.3)	0 (0.0)
Pruritus	2 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Hypertension	1 (4.2)	0 (0.0)	2 (12.5)	0 (0.0)

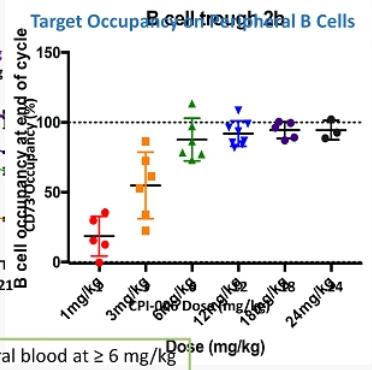
Treatment related adverse events: Any grade 3 or 4 events, or 2 or more all grades

Pharmacokinetics and Receptor Occupancy

Serum Pharmacokinetics



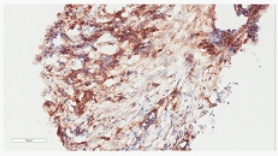
Target Occupancy on Peripheral B Cells



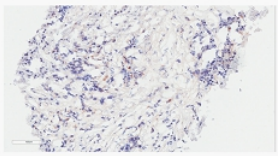
Tissue Occupancy

(18 mg/kg CPI-006)

CD73 with non-cross blocking antibody (total CD73)



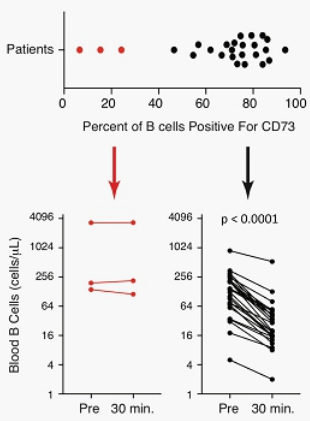
CD73 with CPI-006 demonstrates sites occupied



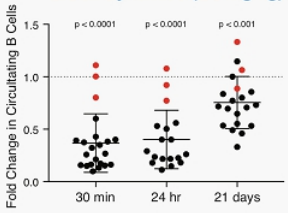
- Sustained CD73 occupancy of peripheral blood at ≥ 6 mg/kg
- Full tumor occupancy observed at ≥ 18 mg/kg

Treatment Induces Rapid Changes in Blood B and T Cells

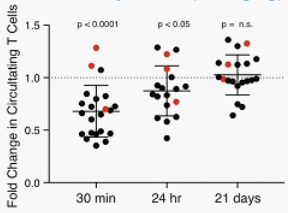
Distribution of CD73^{POS} B Cells in Patients



B Cell Dynamics (≥ 6 mg/kg)



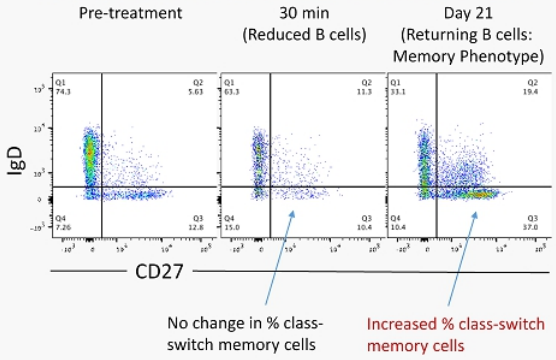
T Cell Dynamics (≥ 6 mg/kg)



- Changes in B cells (but not T cells) appear to be CD73 expression dependent
- B cell numbers partially return by 21 days; T cells fully return

Increase in Memory B Cells in Returning Lymphocytes

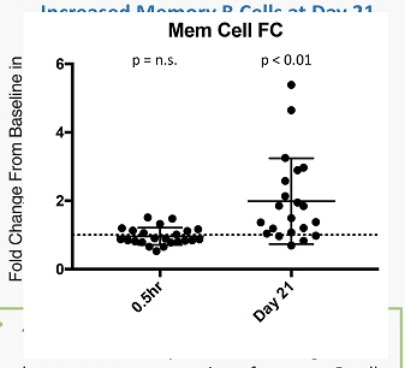
Peripheral Blood Gated on CD19+ and CD20+ B Cells



No change in % class-switch memory cells

Increased % class-switch memory cells

Increased Memory B Cells at Day 21

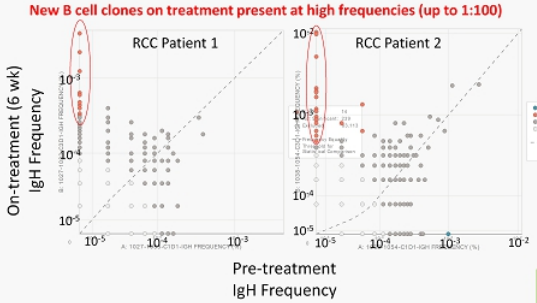


- have a greater proportion of memory B cells
- These findings are consistent with a humoral adaptive response

Significant Expansion of New B and T cell Clones

Differential Abundance Plots of B cell Clonal Expansion

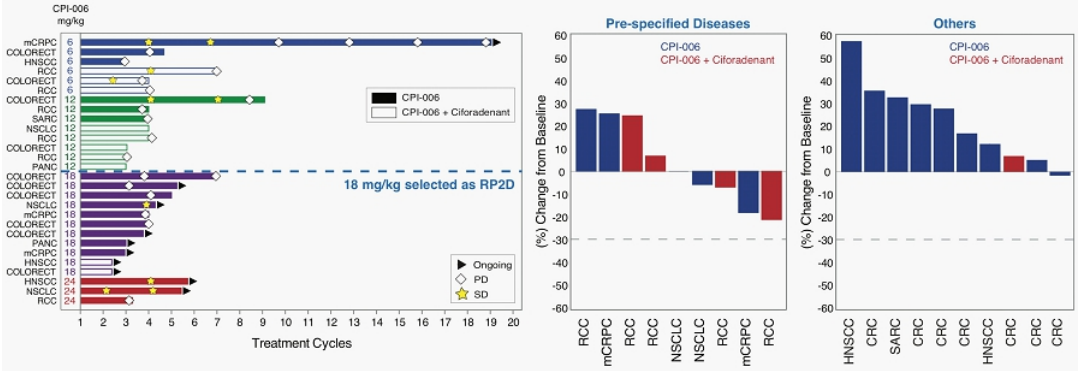
New B cell clones on treatment present at high frequencies (up to 1:100)



Cohort	Number of Patients with B Cell Expansion	Number of Patients with T Cell Expansion
CPI-006 monotherapy	5 of 7	2 of 4
-006 + radenant	2 of 4	1 of 4
Total	7 of 11	3 of 8

- Generation of prevalent B and T cell clones on therapy
- Consistent with antigen-driven clonal selection
- No change in serum immunoglobulins observed

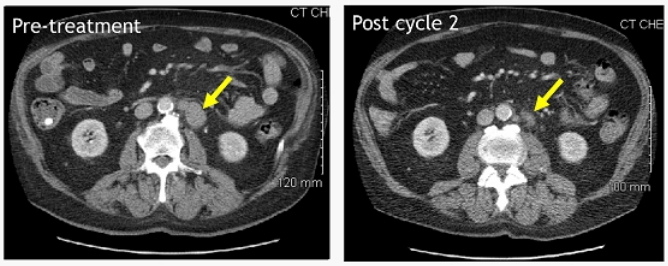
Response Assessments



- Response assessments in patients receiving ≥ 6 mg/kg dose

Tumor Reduction in a Prostate Cancer Patient

CPI-006 monotherapy



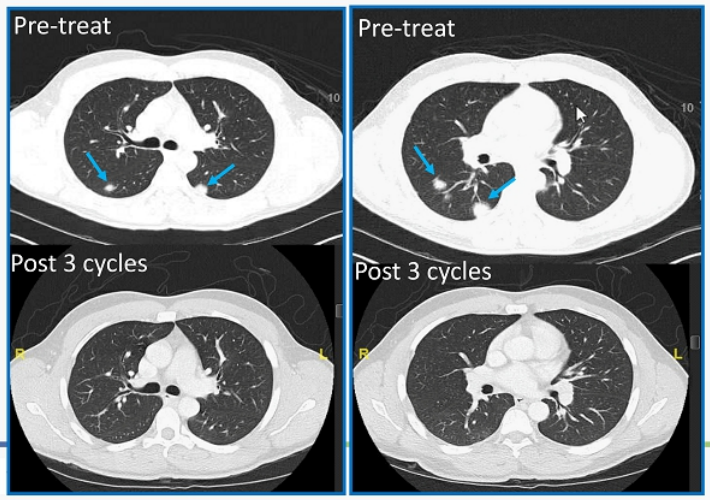
- 72 year old man with widely metastatic prostate cancer; previous therapies include leuprolide/bicalutamide, abiraterone, enzalutamide and docetaxel

- Decrease in target lesion in patient receiving 6 mg/kg monotherapy, treatment ongoing through 19 cycles

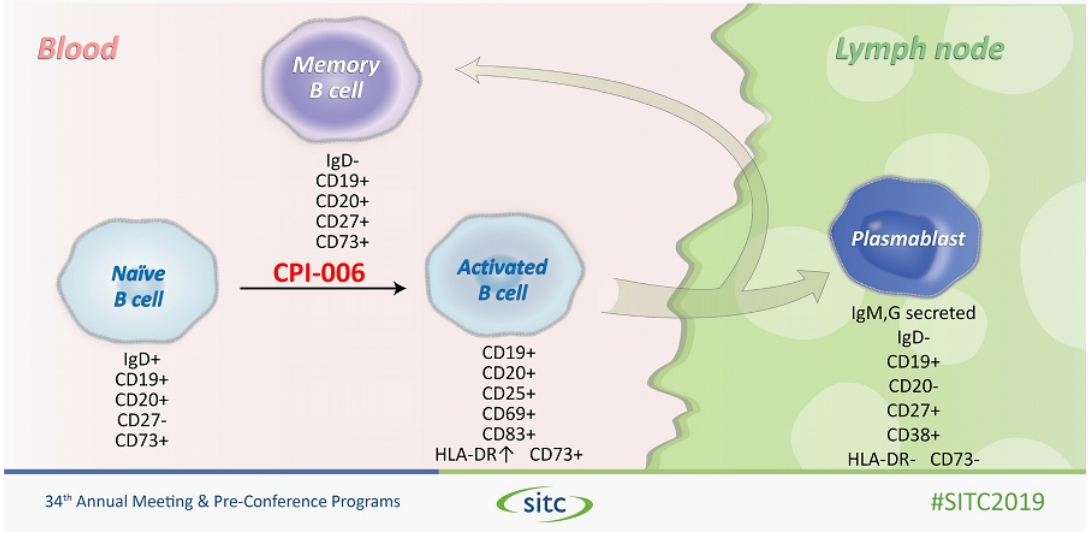
Responding Pulmonary Metastases in RCC Patient

CPI-006 6 mg/kg plus ciforadenant combination

- 36 year old male presented in 2015 with renal mass and bone metastases
- Failed TKI, nivo and nivo/ipi with increase pulmonary mets
- Regression of multiple biopsy proven pulmonary metastases on CPI-006 + ciforadenant



Model for CPI-006 Effects on Cells



Conclusions

- CPI-006 has novel immunomodulatory activities:
  - Induces differentiation of B cells, class switching, secretion of immunoglobulin (in vitro), and generation of memory B cells
  - Increases expression of CD69 and other markers consistent with increased antigen presentation by APCs
- The optimum and well tolerated dose of CPI-006 is 18 mg/kg
- Treatment with CPI-006 induces redistribution of T and B cells with an increase in returning memory B cells and expansion of new B cell clones
- Changes in lymphocytes are consistent with induction of adaptive humoral immunity
- Tumor regression observed in RCC and prostate
- *Treatment with CPI-006 may represent an opportunity to identify novel anti-tumor antibodies*

Acknowledgements

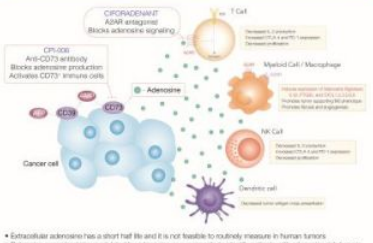
- **The patients and their families**
- **Participating Centers and Investigators**: *Dana Farber Cancer Institute, Medical College of Wisconsin, Monash Health, Mount Sinai Icahn School of Medicine, University of California San Francisco Medical Center, University of Chicago, University of Miami, University of Oklahoma, Yale University, Carolina BioOncology Institute, City of Hope, Mary Crowley Cancer Research, Roswell Park Cancer Institute, Sarah Cannon Research Institute*
- **Colleagues at Corvus**

Adenosine and AMP Gene Expression Profiles Predict Response to Adenosine Pathwa Therapies and Indicate a Need for Dual Blockade of CD73 and A2AR with CD73 Inhibitors

Willingham S, Hotson A, Hsieh J, Munneke B, Kwei L, Mobasher M, Buggy J, Miller R
Corvus Pharmaceuticals, Burlingame CA, USA

CORVU PHARMACEUTIC

ADENOSINE INHIBITS ANTI-TUMOR IMMUNITY



- Extracellular adenosine has a short half life and it is not feasible to routinely measure in human tumors
- Determine genes/proteins modulated by adenosine as a surrogate to identify patients with adenosine rich tumors

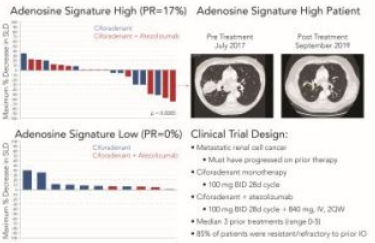
ADENOSINE INDUCES A SPECIFIC GENE SIGNATURE

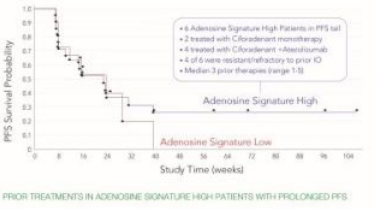
HUMAN PBMCs STIMULATED WITH NECA, A STABLE ADENOSINE ANALOG

ADENOSINE SIGNATURE - NANOSTRING

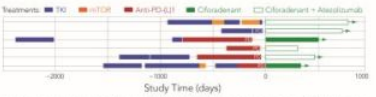
	Adjusted p Value	Function
IL2A	1.44E-04	Increases angiogenesis and reduces CD8+ T cell infiltration
SLC11A1	1.27E-03	Natural resistance-associated macrophage protein 1
CXCL2	1.27E-03	MIP2a: macrophage inflammatory protein 2, alpha
CXCL7	1.27E-03	PPBP: Pro-Platelet Basic Protein
CXCL6	1.40E-03	GCP2: Granulocyte chemotactic protein 2
CXCL3	1.40E-03	Controls migration and adhesion of monocytes
IL-6	1.48E-03	Pro- and anti-inflammatory cytokine
IL-1α	1.73E-03	Inflammation
CXCL5	1.96E-03	IL-8: Neutrophil chemotactic factor
CXCL5	1.98E-03	Attracts and activates neutrophils
THBS1	2.29E-03	Multiple functions. Inhibits angiogenesis & immune regulation
IL-1β	2.38E-03	Inflammation
PTGS2	2.65E-03	COX-2. Elevated during inflammation and cancer
IL2A	2.73E-03	Cell survival and proliferation. Activates STAT1/3
CXCL1	3.92E-03	Neutrophil chemoattractant
CD80	5.21E-03	B7-2: Costimulatory signal for T cell activation and survival
CLEC5A	5.82E-03	Interacts with DAP-12 and may play a role in cell activation
CD14	6.24E-03	Expressed by myeloid cells

SIGNATURE CORRELATES WITH TUMOR RESPONSE



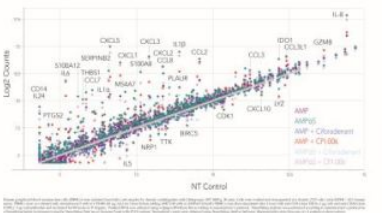


PRIOR TREATMENTS IN ADENOSINE SIGNATURE HIGH PATIENTS WITH PROLONGED PFS



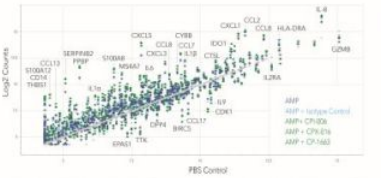
AMP INDUCES ADENOSINE-LIKE GENE SIGNATURE

AMP INDUCED GENE SIGNATURE IS NEARLY IDENTICAL TO ADENOSINE SIGNATURE
AMPαS IS A NON-HYDROLIZABLE FORM OF AMP - IT DOES NOT FORM ADENOSINE



CD73 ANTAGONISTS AMPLIFY AMP SIGNATURE

CD73 ANTAGONISTS INHIBIT ADENOSINE FORMATION, BUT CONSEQUENTLY PRESERVE AMP
PRESERVED AMP AMPLIFIES ADENOSINE-LIKE GENE SIGNATURE SUGGESTING AMP SIGNALS THROUGH A2AR



CPI-006 AND CPX-516 ARE ANTI-CD73 ANTIBODIES. CP-1653 IS A CD73 SMALL MOLECULE INHIBITOR

AMP IS AN ADENOSINE RECEPTOR AGONIST

AMP AND AMPαS AGONIZE A2AR, BUT ARE WEAKER THAN ADENOSINE

A2AR	EC50 (nM)	n
NECA	0.17	n = 2
ADENOSINE	2.7	n = 4
AMP	235.2	n = 4
AMPαS	228.6	n = 4

A2BR	EC50 (nM)	n
NECA	1.3	
ADENOSINE	10.8	
AMP	227.3	
AMPαS	427.3	

A1	EC50 (nM)	n
NECA	2.8	n = 2
ADENOSINE	11.9	n = 4
AMP	237.5	n = 4
AMPαS	418.2	n = 4

A3	EC50 (nM)
NECA	1.7
ADENOSINE	12.9
AMP	199.0
AMPαS	240.1

CIFORADENANT NEUTRALIZES AMP & AMPαS

CIFORADENANT BLOCKS AMP AND AMPαS SIGNALING AT A2AR

A2AR	IC50 (nM)	n
ADENOSINE	4.0	n = 4
AMP	4.7	n = 2
AMPαS	7.1	n = 2

A2BR	IC50 (nM)
ADENOSINE	171.2
AMP	204.8
AMPαS	210.2

A1	IC50 (nM)	n
ADENOSINE	200.9	n = 4
AMP	111.4	n = 2
AMPαS	92.8	n = 2

A3	IC50 (nM)
ADENOSINE	516.0
AMP	231.7
AMPαS	315.1

CONCLUSIONS

- A2AR agonists induce a specific gene signature in human immune cells. This "Adenosine Signature" is by inflammatory myeloid cytokines and chemokines.
- **Updated clinical data confirms original reports that expression of the Adenosine Signature corre tumor regression in an ongoing Ph 1/1b trial in patients with advanced/refractory RCC.**
- **High Adenosine Signature expression has a statistically significant correlation with tumor respon**
- The Adenosine Signature may be used as a predictive biomarker to select patients most likely to respond with agents that antagonize adenosine production or signaling.
- AMP induces gene expression changes nearly identical to the Adenosine Signature in human imm suggesting AMP can activate and signal through adenosine receptors. CD73 antagonists further a AMP-associated gene expression changes as a consequence of preserving AMP.
- AMP is an agonist of adenosine receptors. AMP agonism of A2AR and A2BR can be blocked by ciforad
- These data suggest treatment with CD73 antagonists will benefit from concomitant blockade of A2AR t the resultant induction of AMP mediated gene expression changes.