IO-001 study, AACR abstract: First in human study with EOS100850, a novel potent A_{2A} antagonist, shows excellent tolerance and clinical benefit in immune resistant advanced cancers.

Laurence Buisseret[1], Sylvie Rottey[2], Johann De Bono[3], Manon Mossakowski[4], Brant Delafontaine[2], Thubeena Manickavasagar[3], Nuria Kotecki[1], Chiara Martinoli[5], Manfred Schneider[5], Olivier de Henau[5], Joanne Lager[6], Jean-Pascal Machiels[4]

1. Institut Jules Bordet, Universite Libre de Bruxelles, Brussels, Belgium. 2. Department of Medical Oncology, Drug Research Unit Ghent, Universitair Ziekenhuis Ghent, Ghent, Belgium. 3. Division of Clinical Studies, The Institute of Cancer Research, Sutton, UK; Royal Marsden National Hospital Trust, Sutton, UK. 4. Department of medical oncology and head and neck surgery, Cancer center, Cliniques universitaires Saint-Luc and Institut de Recherche Clinique et Experimentale (Pole MIRO), Universite catholique de Louvain, Brussels, Belgium. 5. iTeos Therapeutics SA, Gosselies, Belgium 6. iTeos Therapeutics Inc., Cambridge, MA, USA

iTeos Therapeutics

Author Disclosure Information

- L. Buisseret: AstraZeneca; Bristol-Myers Squibb; Roche
- S. Rottey: None
- J. de Bono: Astra Zeneca; Bayer; Boehringer Ingelheim; Genentech/Roche; Merck Sharp & Dohme; Pfizer; Sanofi Aventis; Astellas; GSK; Janssen; Cellcentric; Daiichi; Genmab; Merck Serono; Menarini/Silicon Biosystems; Orion; Sierra Oncology; Taiho; Vertex Pharmaceuticals
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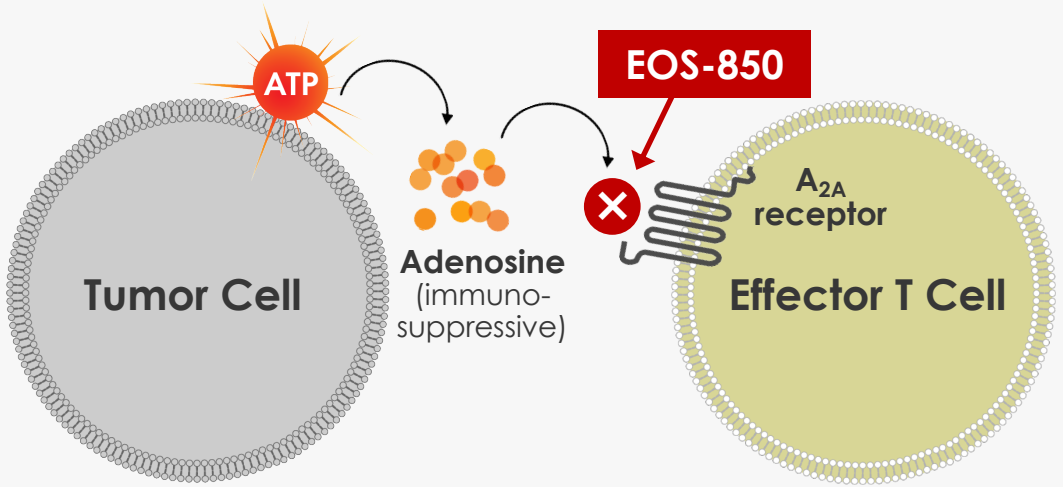
IO-001 study: First in human study with EOS100850 (EOS-850), a novel potent $A_{2A}R$ antagonist, shows excellent tolerance and clinical benefit in immune resistant advanced cancers. AACR Abstract #: 10228

DRUG MECHANISM OF ACTION:

Blocking the immunosuppressive Adenosine Pathway



EOS-850 is a highly selective and potent A_{2A} receptor antagonist that:

- **remains active** even at the high adenosine concentration found in tumors due to a long residence time
- **does not cross the blood-brain barrier**

Study Design

EOS-850 Monotherapy Dose Escalation

20 mg QD → 40 mg QD → 40 mg BiD → 80 mg BiD → 160 mg BiD

- 3 + 3 design
- DLT 28 days = 1 cycle
- Pre- & On-treatment biopsy for all

Key inclusion criteria

- Age ≥ 18 years
- Confirmed metastatic solid tumor
- Failure of standard of care
- ECOG PS0 or 1
- Measurable disease per RECIST v1.1

Key exclusion criteria

- Prior anti-cancer therapy within 4 weeks
- Known active CNS metastases, severe CV disease
- Prior significant toxicity with immunotherapy

Key Study Objectives

Primary

- To define the MTD/RP2D of EOS-850
- Safety and tolerability of EOS-850

Secondary

- Pharmacokinetic & Pharmacodynamic assessment of EOS-850 monotherapy
- Antitumor activity of EOS-850

Baseline Characteristics

Characteristic	Value (N=21)
Median age (range)	60 (39-75)
Male sex, n(%)	14 (66%)
Primary Diagnosis, n(%)	
mCRPC	5 (24%)
Colorectal	4 (19%)
Head & Neck	3 (14%)
other n=1 each*	9 (43%)
Number of prior therapies	
Median (range)	3 (1-10)
Prior immunotherapy, n (%)	4 (19%)

* Bladder, Breast, Endometrium, Lung, Melanoma, Ovarian, Pancreas, Prostate cancer (small cell), Sarcoma

mCRPC: metastatic castrate-resistant prostate cancer

EOS-850 was well tolerated across all doses tested

- **21 patients** were enrolled at 5 dose levels and completed the DLT evaluation
- **No DLTs** observed and **no grade 3/4 drug-related TEAE**
- **5 patients remain on treatment;** the remaining patients discontinued due to disease progression

Treatment-Emergent Adverse Events (n=21)	Drug-Related	Any Attribution
	Number of Patients (%)	
Any Grade	15 (71.4%)	21 (100.0%)
Grade 1-2	15 (71.4%)	21 (100.0%)
Grade 3-4	0 (0.0%)	8 (38.1%)
Grade 5	0 (0.0%)	0 (0.0%)
Led to discontinuation	0 (0.0%)	2 (9.5%)

Drug Related TEAEs (Grade 1-2), n=21	Number of Patients (%)
Fatigue	6 (28.6%)
Alanine aminotransferase increased	4 (19.0%)
Decreased appetite	4 (19.0%)
Aspartate aminotransferase increased	3 (14.3%)
Diarrhoea	3 (14.3%)
Gamma-glutamyltransferase increased	2 (9.5%)
Blood alkaline phosphatase increased	1 (4.8%)
Hyperbilirubinaemia	1 (4.8%)
Constipation	1 (4.8%)
Myalgia	1 (4.8%)
Dizziness	1 (4.8%)
Eosinophilia	1 (4.8%)
Interstitial Pneumonitis	1 (4.8%)
Flushing	1 (4.8%)

(Cut-off 15 Jan 2020)

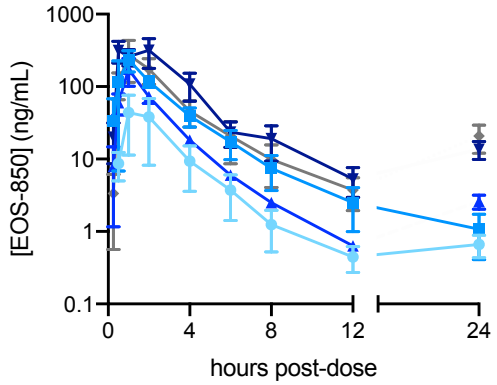
Good Pharmacokinetics and Prolonged Pharmacodynamics of EOS-850 Support Selection of 80mg BID as the RP2D

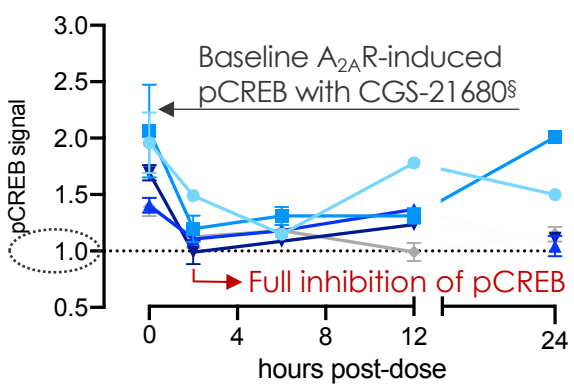
Do Not Post

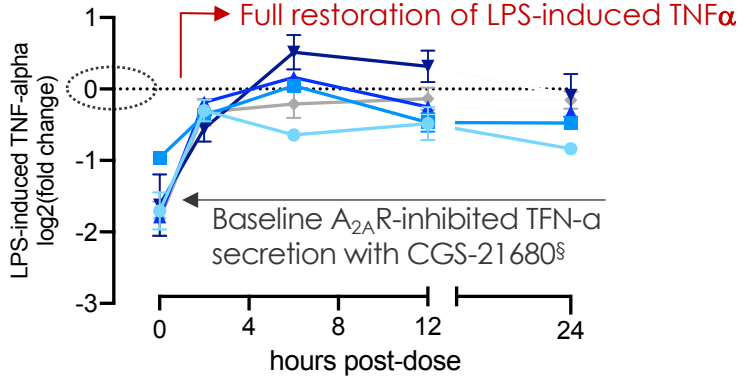
PK | PD

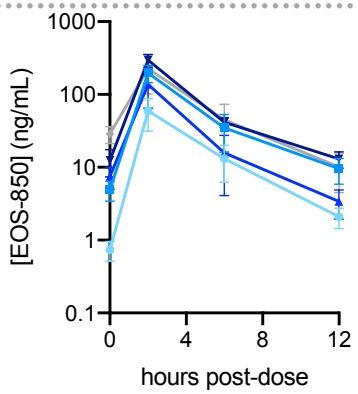
Cycle 1 Day 1

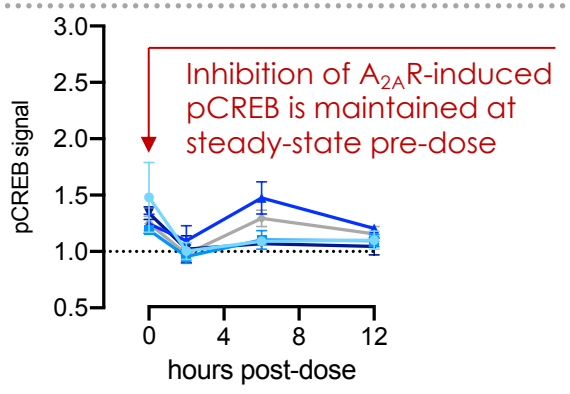
Cycle 2 Day 1

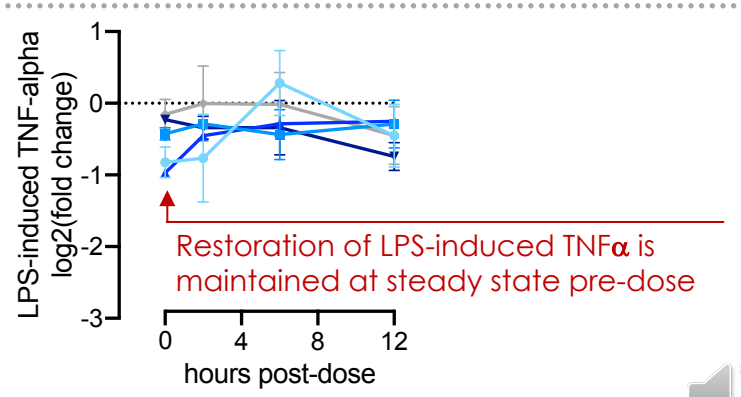












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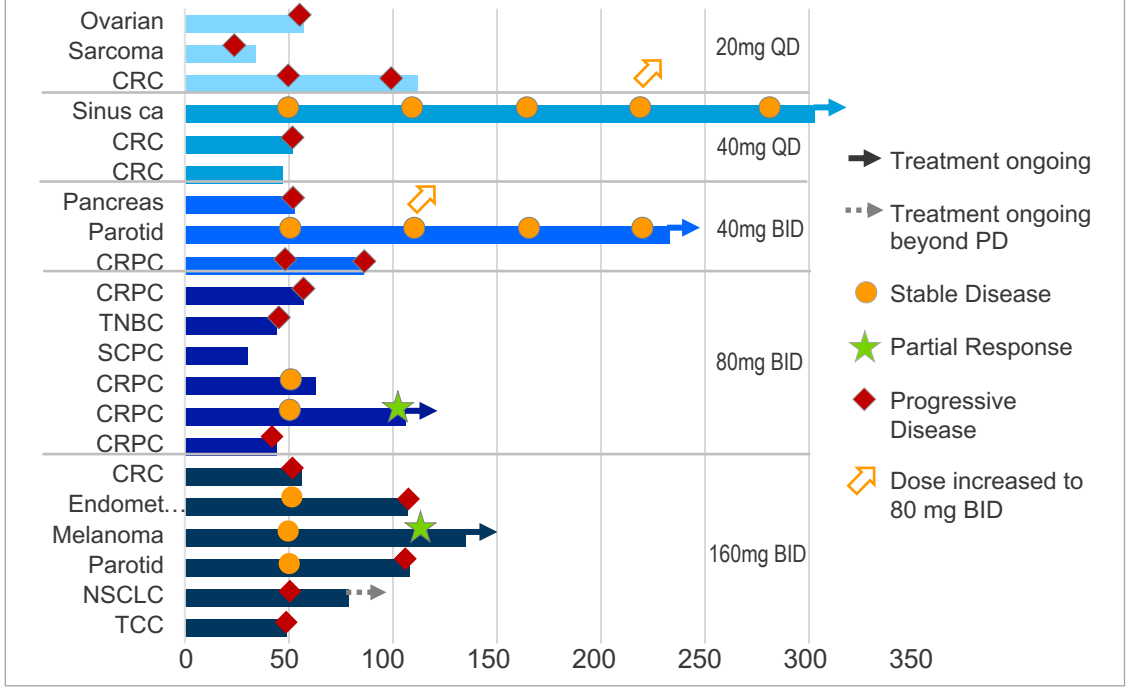
20 mg QD, n=3 | 40 mg QD, n=3 | 40 mg BID, n=3 | 80 mg BID, n=6 | 160 mg BID, n=6

* Whole blood assays; § CGS-21680: $A_{2A}R$ agonist

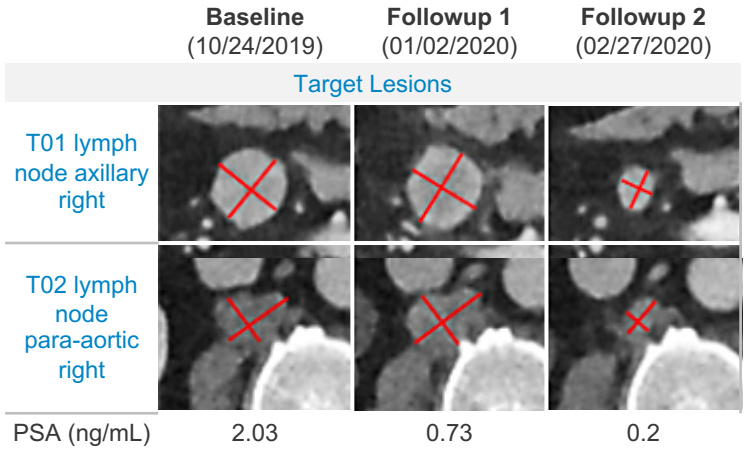
EOS-850 Demonstrates Monotherapy Clinical Benefit in heavily pretreated patients across multiple indications.

Do Not Post

Best Response	QD doses (n=6), n (%)	BID doses (n=15), n (%)	Total (n=21), n (%)
Complete Response	0%	0%	0%
Partial Response	0%	2 (13%)	2 (9.5%)
Stable Disease	1 (16.5%)	4 (27%)	5 (24%)
Progressive Disease	4 (67%)	8 (53%)	12 (57%)
Not Assessed	1 (16.5%)	1 (7%)	2 (9.5%)

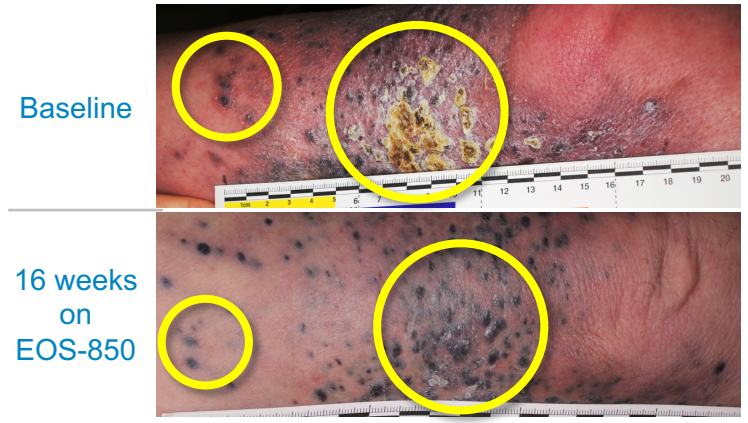


Partial response in a 67-year-old Male with Castrate-Resistant Prostate Cancer



- Documented Progression after all SOC hormonal therapy and 2 prior lines of chemotherapy
- Received EOS-850 80 mg BID
- Partial response at 16 weeks with 41% reduction in size of all target lesions per RECIST associated with decreased PSA.
- Therapy ongoing at 16 Weeks

Partial response in a 67-year-old Male with BRAF Wild-Type Cutaneous Melanoma



- 2 prior lines of immunotherapy, Pembrolizumab followed by Ipilimumab, with documented PD
- Received EOS-850 160 mg BID
- Grade 1 Pneumonitis at 8 weeks
- Partial response per RECIST at 16 weeks with 44% reduction in size of target lesion on the arm and reduced pain and lymphedema.
- Therapy ongoing at 19 Weeks

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CRC: Colorectal Cancer, CRPC: castrate-resistant prostate cancer, SCPC: prostate cancer with small cell histology, TNBC: triple-negative breast cancer, Endom: endometrial cancer, NSCLC: non-small cell lung cancer, TCC: transitional cell cancer of the bladder

EOS-850 Demonstrates Safe Profile with Good Target Coverage and Initial Clinical Benefit in Multiple Indications

80 mg BID selected as the Recommended Phase 2 Dose

- **Safe and tolerated** at all dose levels with no DLT observed
- **Sustained inhibition of $A_{2A}R$** and prolonged pharmacodynamic (PD) activity with BID dosing
- **PK**: Good dose-proportionality through 80 mg BID
- Preliminary evidence of clinical benefit in 7 patients with **2 ongoing partial responses in a checkpoint inhibitor-refractory melanoma patient and a patient with metastatic prostate cancer**

Further evaluation is ongoing in selected indications:

- **Monotherapy expansion**
- **Combination with pembrolizumab or chemotherapy**

Presenter: Jean-Pascal Machiels (Coordinating Investigator)

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Info: Joanne Lager, iTeos Therapeutics Inc., Cambridge, MA, USA | joanne.lager@iteostherapeutics.com