Modra Pharmaceuticals

transforming taxane therapy

March 2021

Non-confidential introduction to Modra

Modra is a Dutch Oncology-Focused Biotech

- Headquartered in Amsterdam, the Netherlands
- Founded in 2010 out of the National Cancer Institute (NKI)
- Developing better tolerated, boosted oral taxanes, with two clinical assets
  - ModraDoc006/r ready to initiate pivotal study in metastatic castrate resistant prostate cancer within 12 months, with follow in breast cancer (main focus of this presentation)
  - ModraPac005/r completed initial phase I
  - Potential for development of additional oral taxanes using Modra platform
- Goal to replace IV taxanes, some of the most broadly used anticancer therapies
- Principal venture investments from Aglaia Oncology Ventures and Waterman Ventures

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Modra is Developing Next-Generation Boosted Oral Taxanes to Transform Taxane Therapy

Compelling benefits over IV while addressing challenges of other oral taxanes

- Eliminated severe neutropenia, neuropathy, and reduced alopecia
- Low grade GI toxicities broadly comparable to IV
- Taken at home once-a-week, no hospital infusions

Low development/regulatory risk

- Completed phase II studies in prostate and breast cancer
- Manufacturing process already scaled to 50% commercial
- Supportive market research

Large therapeutic and commercial impact in prostate and breast cancer

- Replace IV taxanes in large 'installed' patient bases
- Extend the 'oral envelope'
- Attractive all-oral combinations
- Opportunity to overcome taxane resistance

Multiple value generators

- Attractive standalone oncology therapeutic
- Monotherapy franchise extension in prostate, breast cancer
- Positive differentiator for existing therapies when used in unique all-oral combinations

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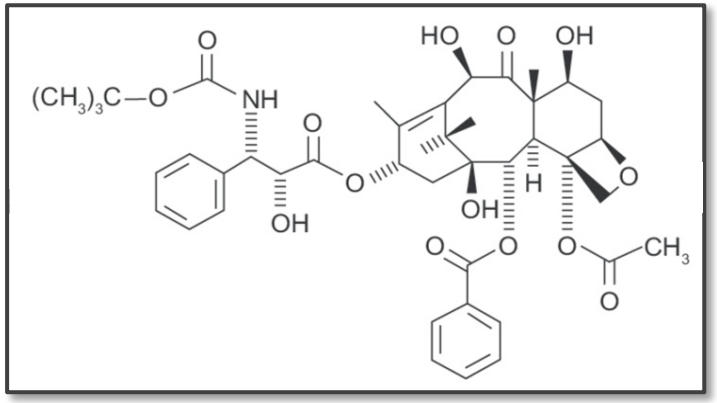
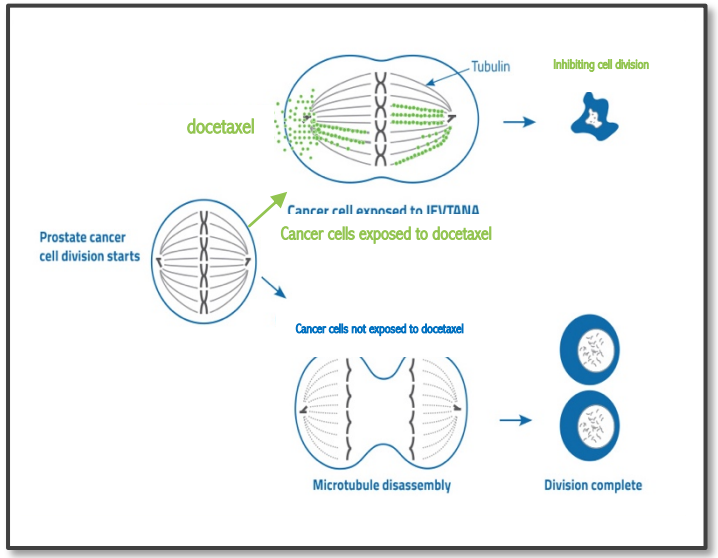
Docetaxel is a Part of the Taxane Class of Anti-Cancer Therapies

An established and well understood chemotherapy used in many solid tumors





Molecular Target	Reversibly binds tubulin, used in construction of cell cytoskeletons
Mechanism of Action	Cytotoxic - inhibits cell division by inhibition of mitotic spindle assembly
Regulatory Status	▪ First approved in US in 1995 ▪ Approved indications: NSCLC, HRPC (CRPC), breast cancer, gastric adenocarcinoma, SCCHN
Administration	Usually once every 3 weeks, in hospital, via an IV infusion
Commercial	Peak sales ±$3B (2010)

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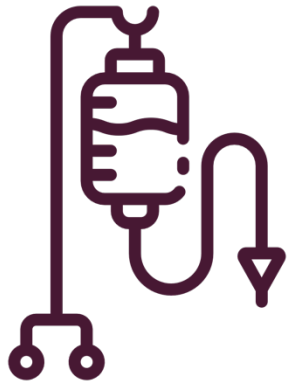
Traditional Docetaxel Therapy Has Three Major Limitations

Expensive and burdensome infusion administration

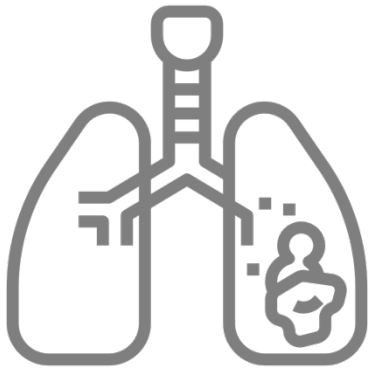


Costs to both patients and healthcare systems

Serious toxicities

Dose reductions, premature cessation of treatment

Tumors develop resistance to therapy



Tumors start to grow again

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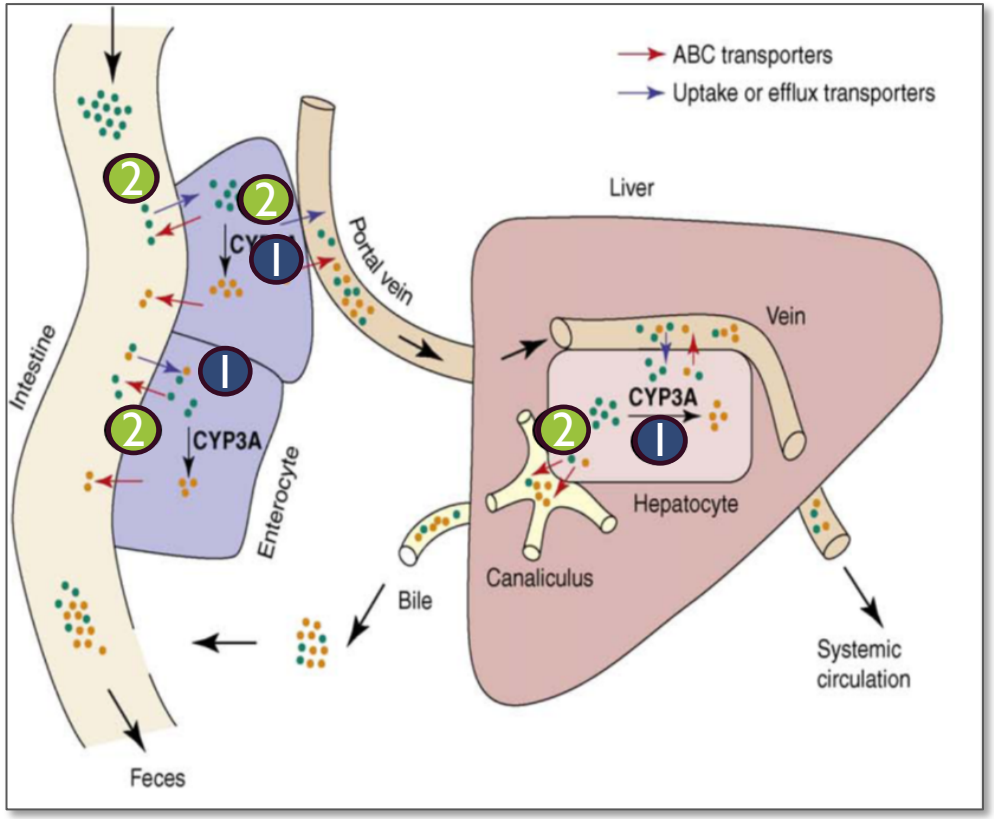
Implementing a Successful Oral Taxane is a Challenge

- **Pharmaceutical properties are far from ideal**
  - Poor water solubility
  - Toxic excipients in IV formulation
- **Biological properties create barriers to achieving sufficient therapeutic exposure**
  - Intestinal & hepatic enzymes (CYP3A) (1)
  - Efflux transporter P-glycoprotein (P-gp) (2)



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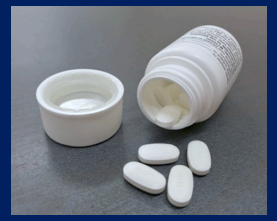
ModraDoc006/r Addresses These Challenges and Limitations

First major innovation in docetaxel therapy in 25 years

ModraDoc006/r

oral docetaxel tablet



- Toxic excipients eliminated
- One day/week dosing
- Low pill burden & manageable tablet size
- Differentiated PK

ritonavir - booster

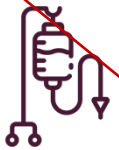
- Boosts ModraDoc006 bioavailability to ensure therapeutic exposure levels
- Inhibits P-gp and CYP3A4
- Concept, used widely in HIV/HCV, now applied to oncology
- Multiple beneficial impacts on oral docetaxel

Oral at home delivery

Best-in-class tox
- Neutropenia
- Neuropathy
- Alopecia

Reverse resistance

Expensive and unpleasant infusion administration



Serious toxicities

Tumors develop resistance to therapy

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Preclinical Data Supports Modra Concept and Provides Potential for Significant Upside

Proof of concept established

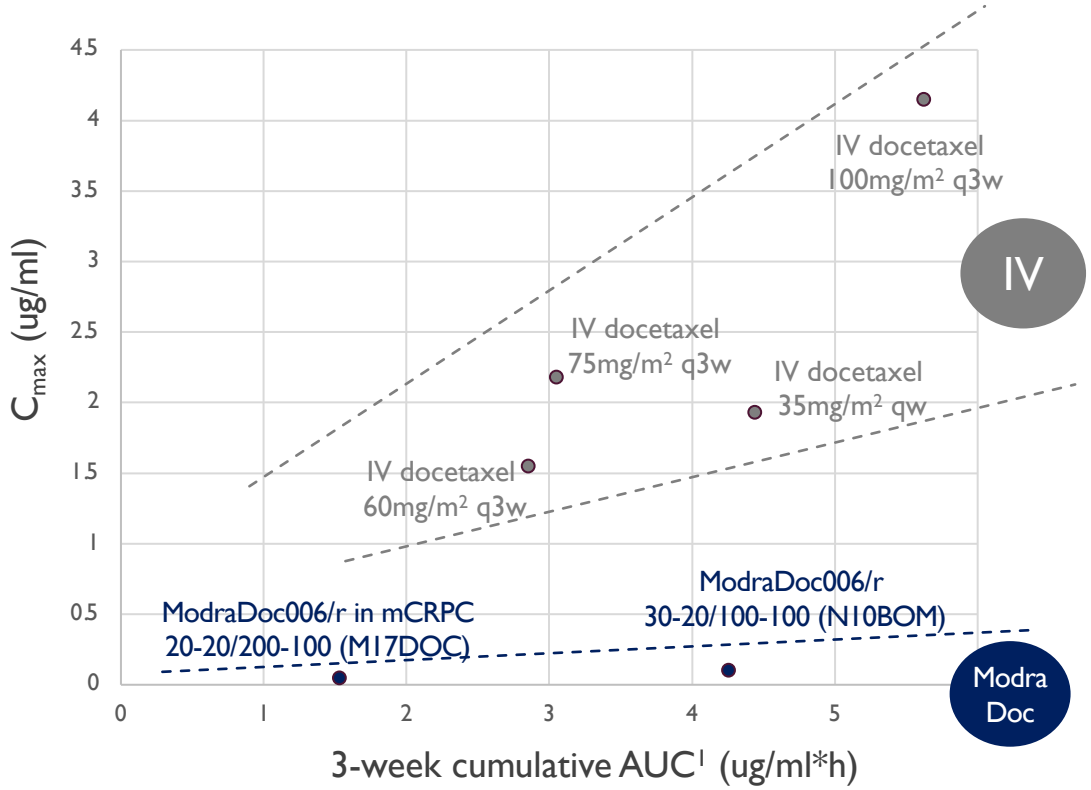
- Role of CYP3A4 in reducing docetaxel exposure in multiple models
- Ability of ritonavir to increase docetaxel systemic exposure by inhibiting CYP3A4

Potential upsides in terms of efficacy

- Addition of ritonavir to docetaxel also increases docetaxel concentrations intratumorally
- Potential to increase antitumor activity shown in prostate and breast cancer animal models
- Promising data to reverse resistance to docetaxel in in-vitro prostate cancer models

ModraDoc006/r Changes PK Relationships v IV docetaxel

Clinical studies show vastly reduced C_{max} for any given AUC



Similar exposure levels → drives efficacy

Lower C_{max} at any given exposure level → a key driver in reducing some toxicities

1. AUCs for weekly regimens were multiplied by 3 to achieve 3 weekly AUC estimates (for rationale, see Baker)
Source: for ModraDoc006/r - Modra clinical studies; for IV - Baker et al, CCR 2004

ModraDoc006/r dosing nomenclature: X-Y/A-B
ModraDoc006 – X= morning, Y = evening; ritonavir – A = morning; B = evening
All in mg, fixed dose, BIDW

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Substantial Improvement in Side Effects vs IV Docetaxel

Including neutropenia & neuropathy, typical dose-limiting toxicities

Key toxicities All grades	M18MDP Phase IIb (ongoing)[1]		TAX327 Phase III
	ModraDoc006/r 20-20/ 200-100	IV 75mg/m²	IV 75mg/m²
n	*14*	*36*	*332*
Typical DLTS			
Neutropenia	0%	28%	41%
Neuropathy	0%	14%	30%
Infections	0%	6%	32%
Diarrhea	29%	19%	32%
Nausea	29%	14%	41%
Fatigue/ asthenia	14%	20%	53%
Mucositis	0%	6%	20%
Nail tox	14%	8%	30%
Alopecia	36%	47%	65%

Grade 3-4	M18MDP **Phase IIb (ongoing)**[1]		TAX327 **Phase III**
	ModraDoc006/r 20-20/ 200-100	IV 75mg/m²	IV 75mg/m²
n	*14*	*36*	*332*
Neutropenia	0%	22%	32%
Neuropathy	0%	0%	2%
Infections	0%	6%	6%
Diarrhea	0%	0%	2%
Nausea	0%	0%	3%
Fatigue/ asthenia	0%	0%	5%
Mucositis	0%	0%	1%
Nail tox	0%	0%	0%

Reductions in neutropenia, neuropathy, and alopecia fully consistent with prior studies

1. Preliminary data as of Jan 2021

Source: ongoing data from M18MDP, Taxotere® label for TAX327 data

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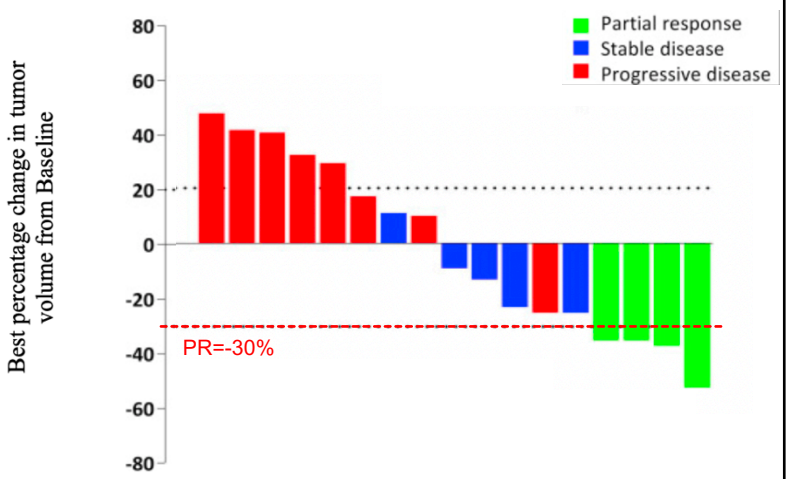
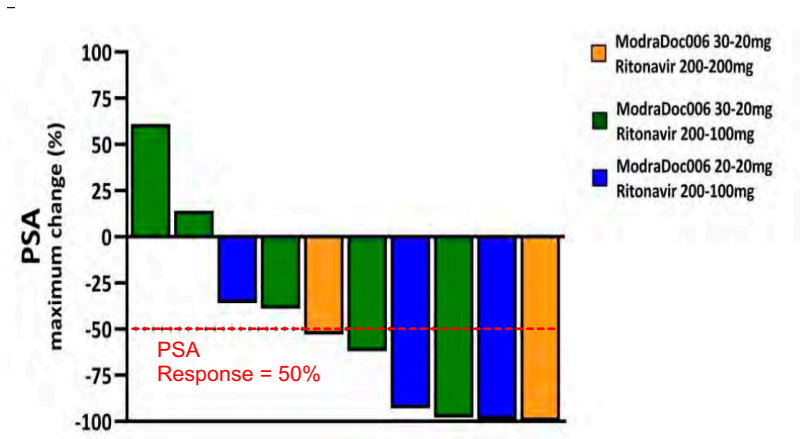
Consistent Indications of Activity for ModraDoc006/r Across Multiple Early-Stage Clinical Studies

Phase I (solid tumors, dose-finding) (N10BOM)



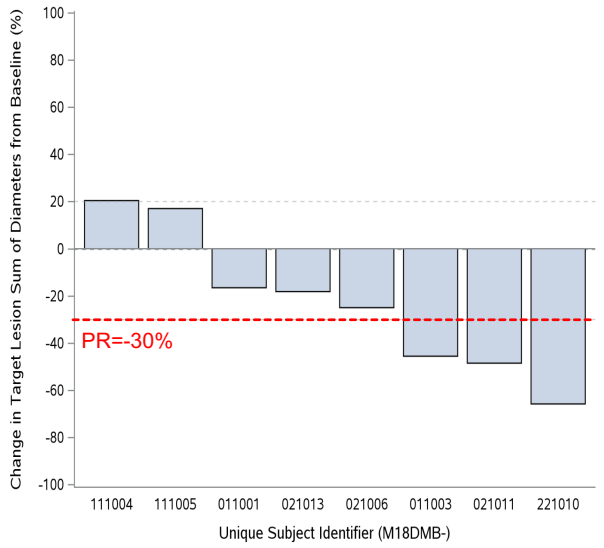
- 3 confirmed partial responses (+1 unconfirmed)
- 5 patients with stable disease
- Out of 28 heavily pretreated patients

Phase 1b (mCRPC, dose finding) (M17DOC)



- 6/10 PSA responses in evaluable patients
- 2/5 PRs in patients with measurable disease

Phase IIa (HER2- mBC) (M18DMB)



- 3 partial responses
- 3 stable disease (including 2 >20% tumor shrinkage)
- Out of 8 evaluable patients

Source: N10BOM: investigator's brochure; M17DOC & M18DMB – clinical study reports

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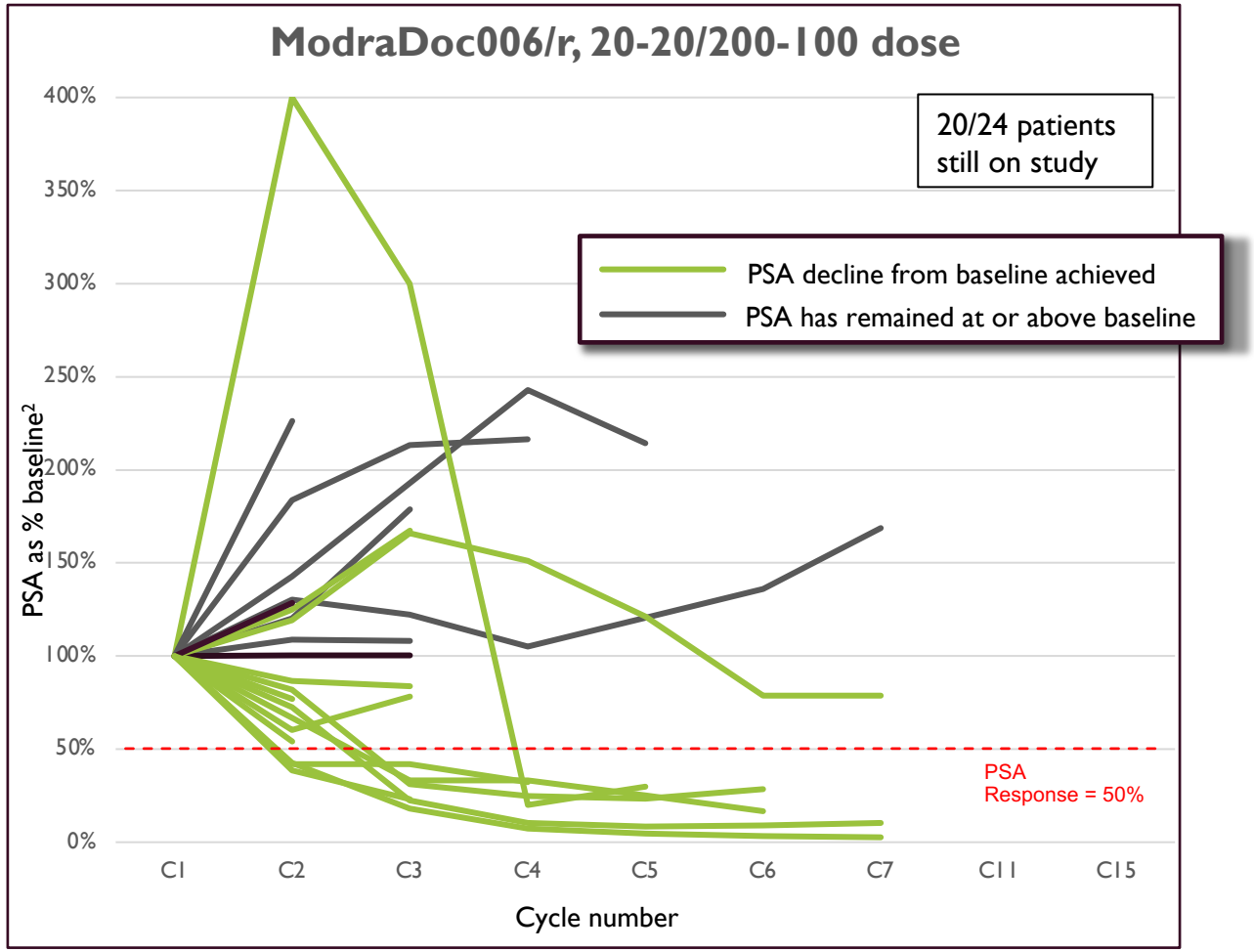
Emerging Results from Phase IIb Study Also Support Promising Activity in mCRPC at 20-20/200-100 Dose[1]

Based on preliminary PSA response data from M18MDP, presented at ASCO-GU 2021



1. Preliminary as of January 2021
2. For patients with missing data, average of prior and subsequent measurement taken ((2 patients in IV, 1 patient in ModraDoc006/r arms).

Source: ongoing data from M18MDP study

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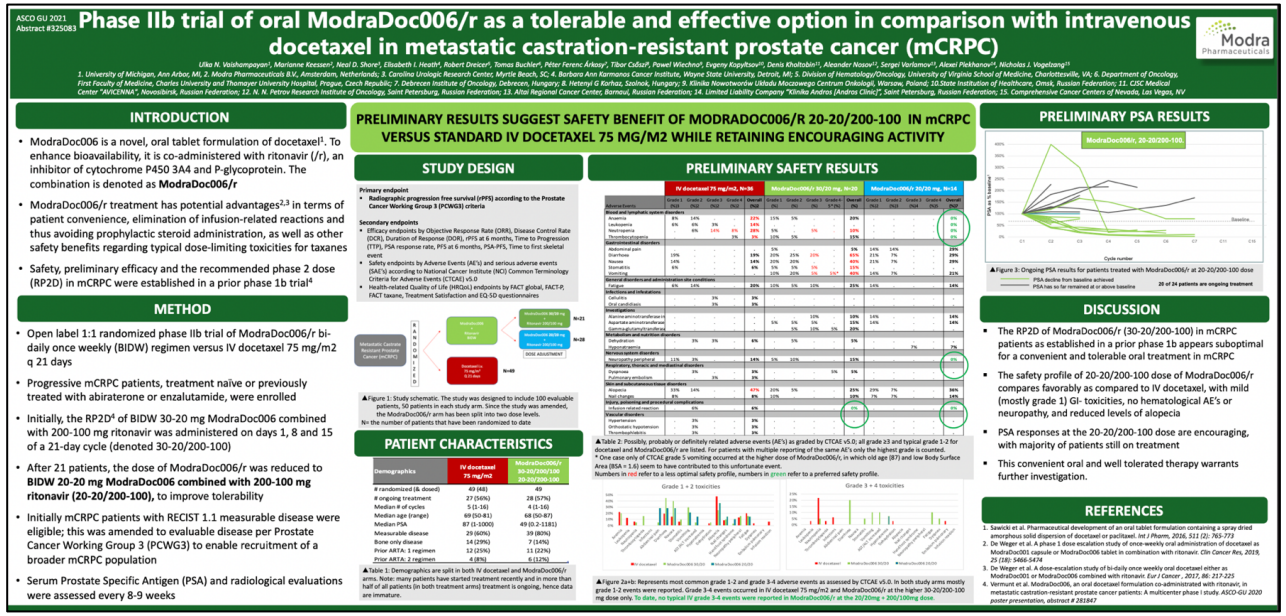
Preliminary Data from Phase IIb Study in mCRPC Presented at ASCO-GU 2021

Selected as part of "Best of ASCO GU 2021"



ASCO GU 2021 Abstract #325083

Phase IIb trial of oral ModraDoc006/r as a tolerable and effective option in comparison with intravenous docetaxel in metastatic castration-resistant prostate cancer (mCRPC)

Modra Pharmaceuticals

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INTRODUCTION

- ModraDoc006 is a novel, oral tablet formulation of docetaxel[1]. To enhance bioavailability, it is co-administered with ritonavir (/r), an inhibitor of cytochrome P450 3A4 and P-glycoprotein. The combination is denoted as **ModraDoc006/r**
- ModraDoc006/r treatment has potential advantages[2,3] in terms of patient convenience, elimination of infusion-related reactions and thus avoiding prophylactic steroid administration, as well as other safety benefits regarding typical dose-limiting toxicities for taxanes
- Safety, preliminary efficacy and the recommended phase 2 dose (RP2D) in mCRPC were established in a prior phase 1b trial[4]

METHOD

- Open label 1:1 randomized phase IIb trial of ModraDoc006/r bi-daily once weekly (BIDW) regimen versus IV docetaxel 75 mg/m2 q 21 days
- Progressive mCRPC patients, treatment naïve or previously treated with abiraterone or enzalutamide, were enrolled
- Initially, the RP2D[4] of BIDW 30-20 mg ModraDoc006 combined with 200-100 mg ritonavir was administered on days 1, 8 and 15 of a 21-day cycle (denoted 30-20/200-100)
- After 21 patients, the dose of ModraDoc006/r was reduced to **BIDW 20-20 mg ModraDoc006 combined with 200-100 mg ritonavir (20-20/200-100),** to improve tolerability
- Initially mCRPC patients with RECIST 1.1 measurable disease were eligible; this was amended to evaluable disease per Prostate Cancer Working Group 3 (PCWG3) to enable recruitment of a broader mCRPC population
- Serum Prostate Specific Antigen (PSA) and radiological evaluations were assessed every 8-9 weeks

PRELIMINARY RESULTS SUGGEST SAFETY BENEFIT OF MODRADOC006/R 20-20/200-100 IN MCRPC VERSUS STANDARD IV DOCETAXEL 75 MG/M2 WHILE RETAINING ENCOURAGING ACTIVITY

STUDY DESIGN

Primary endpoint
- Radiographic progression free survival (rPFS) according to the Prostate Cancer Working Group 3 (PCWG3) criteria

Secondary endpoints
- Efficacy endpoints by Objective Response Rate (ORR), Disease Control Rate (DCR), Duration of Response (DOR), rPFS at 6 months, Time to Progression (TTP), PSA response rate, PFS at 6 months, PSA-PFS, Time to first skeletal event
- Safety endpoints by Adverse Events (AE's) and serious adverse events (SAE's) according to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v5.0
- Health-related Quality of Life (HRQoL) endpoints by FACT global, FACT-P, FACT taxane, Treatment Satisfaction and EQ-5D questionnaires

▲Figure 1: Study schematic. The study was designed to include 100 evaluable patients, 50 patients in each study arm. Since the study was amended, the ModraDoc006/r arm has been split into two dose levels.
N= the number of patients that have been randomized to date

PATIENT CHARACTERISTICS

Demographics	IV docetaxel 75 mg/m2	ModraDoc006/r 30-20/200/100 20-20/200-100
# randomized (& dosed)	40 (40)	49
# ongoing treatment	27 (56%)	28 (57%)
Median # of cycles	5 (1-16)	4 (1-16)
Median age (range)	69 (50-81)	68 (50-87)
Median PSA	87 (1-1000)	49 (0.2-1181)
Measurable disease	29 (60%)	39 (80%)
Bone only disease	14 (29%)	7 (14%)
Prior ARTA: 1 regimen	12 (25%)	11 (22%)
Prior ARTA: 2 regimens	4 (8%)	6 (12%)

▲Table 1: Demographics are split in both IV docetaxel and ModraDoc006/r arms. Note: many patients have started treatment recently and in more than half of all patients (in both treatment arms) treatment is ongoing, hence data are immature.

PRELIMINARY SAFETY RESULTS

▲Table 2: Possibly, probably or definitely related adverse events (AE's) as graded by CTCAE v5.0; all grade ≥3 and typical grade 1-2 for docetaxel and ModraDoc006/r are listed. For patients with multiple reporting of the same AE's only the highest grade is counted.
* One case only of CTCAE grade 5 vomiting occurred at the higher dose of ModraDoc006/r, in which old age (87) and low Body Surface Area (BSA = 1.6) seem to have contributed to this unfortunate event.
Numbers in red refer to a less optimal safety profile, numbers in green refer to a preferred safety profile.

▲Figure 2a+b: Represents most common grade 1-2 and grade 3-4 adverse events as assessed by CTCAE v5.0. In both study arms mostly grade 1-2 events were reported. Grade 3-4 events occurred in IV docetaxel 75 mg/m2 and ModraDoc006/r at the higher 30-20/200-100 mg dose only. To date, no typical IV grade 3-4 events were reported in ModraDoc006/r at the 20/20mg + 200/100mg dose.

PRELIMINARY PSA RESULTS

▲Figure 3: Ongoing PSA results for patients treated with ModraDoc006/r at 20-20/200-100 dose
PSA decline from baseline achieved
PSA has so far remained at or above baseline
20 of 24 patients are ongoing treatment

DISCUSSION

- The RP2D of ModraDoc006/r (30-20/200-100) in mCRPC patients as established in a prior phase 1b appears suboptimal for a convenient and tolerable oral treatment in mCRPC
- The safety profile of 20-20/200-100 dose of ModraDoc006/r compares favorably as compared to IV docetaxel, with mild (mostly grade 1) GI- toxicities, no hematological AE's or neuropathy, and reduced levels of alopecia
- PSA responses at the 20-20/200-100 dose are encouraging, with majority of patients still on treatment
- This convenient oral and well tolerated therapy warrants further investigation.

REFERENCES

1. Sawicki et al. Pharmaceutical development of an oral tablet formulation containing a spray dried amorphous solid dispersion of docetaxel or paclitaxel. *Int J Pharm, 2016, 511 (2): 765-773*
2. De Weger et al. A phase 1 dose escalation study of once-weekly oral administration of docetaxel as ModraDoc001 capsule or ModraDoc006 tablet in combination with ritonavir. *Clin Cancer Res, 2019, 25 (18): 5466-5474*
3. De Weger et al. A dose-escalation study of bi-daily once weekly oral docetaxel either as ModraDoc001 or ModraDoc006 combined with ritonavir. *Eur J Cancer , 2017, 86: 217-225*
4. Vermunt et al. ModraDoc006, an oral docetaxel formulation co-administrated with ritonavir, in metastatic castration-resistant prostate cancer patients: A multicenter phase I study. *ASCO-GU 2020 poster presentation, abstract # 281847*

"The initial data suggest a remarkably favorable toxicity profile, without signs of cytopenia or neuropathy in patients treated with ModraDoc006/r at the weekly dose of 20 mg twice in a day. **The risk of infection and anemia are critical hurdles in the use of IV docetaxel in mCRPC and limit its usage** despite its established position as standard of care in this patient population. **This speaks to the importance of providing an alternative therapeutic such as ModraDoc006/r** to address the unmet need still present in standard treatment of this disease and to improve outcomes in mCRPC,"

Ulka Vaishampayan, MD, Professor of Internal Medicine, Division of Hematology/ Oncology at the University of Michigan

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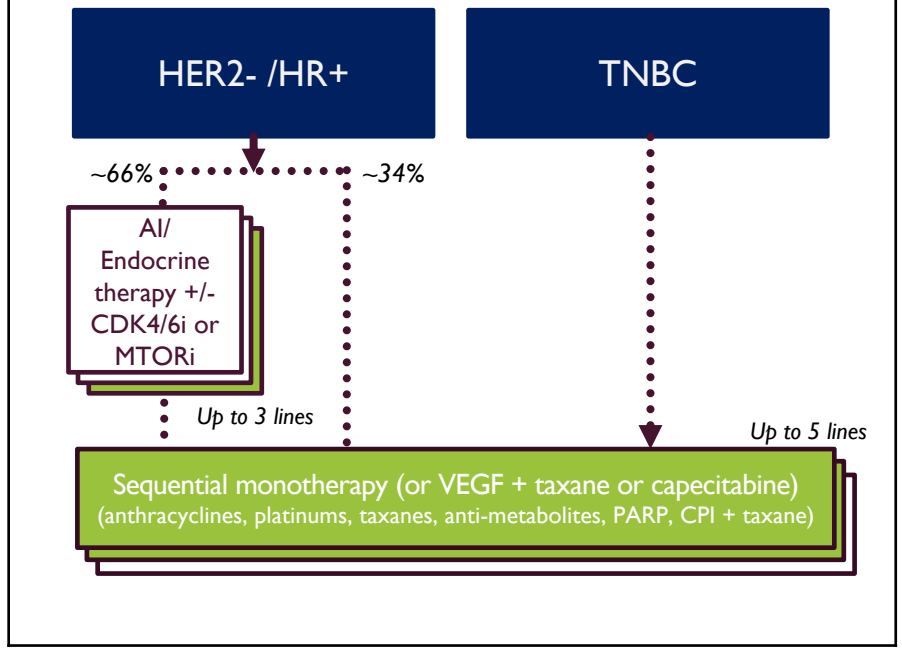
Development Focus – Prioritized Tumor Types Focus on Delivering Impact & Value

Castrate Resistant Prostate Cancer

nmCRPC	mCRPC	Post-DTX
Apalutamide 2018	Docetaxel 2004	Cabazitaxel 2010
Enzalutamide 2018	Sipuleucel-T 2010	Abiraterone 2011
Darolutamide 2019	Abiraterone 2012	Enzalutamide 2012
	Enzalutamide 2014	Alpharadin 2013
	Olaparib (BRCA/ATM) 2020	
	Pembrozulimab (+MSI high)	

Locally Advanced/Metastatic HER2- Breast Cancer



- Stable, large populations of (docetaxel) taxane usage
- Prior treatments all oral → extend "**oral envelope**"
- Opportunities for monotherapy and all-oral combinations

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ModraDoc006/r has an Attractive Target Product Profile for its Lead Indication

Primary Indication & Population	Patients with mCRPC, suitable for treatment with a taxane after prior treatment with an ARTA
Treatment Duration	~30 weeks
Route of Administration	Oral
Dosage Form	ModraDoc006 tablets (10mg) co-administered with ritonavir tablets (100mg)
Administration Schedule	BIDW, fasted: ▪ Morning: 20mg ModraDoc006/r plus 200mg ritonavir ▪ Evening: 20mg ModraDoc006/r plus 100mg ritonavir
Efficacy	(At least) equivalent to IV docetaxel
Side Effects	▪ Eliminated/reduced severe neutropenia, neuropathy ▪ Reduced alopecia ▪ Equivalent GI tox to IV docetaxel

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Competitive Overview: Modra has Unique Opportunity to Capitalize on Recent Developments in the Oral Taxane Space

Which remains highly attractive despite clinical setbacks of competitors

- Our perspective, supported by feedback from KOLs, is that taxanes will remain a mainstay in the sequence of therapy in both prostate and HER2- breast cancer (as well as several other tumor types)
- Given therapeutic overlaps, an approved oral docetaxel therapeutic stands to replace both IV docetaxel and parts of IV paclitaxel market
- Recent setbacks for other oral taxane programs are unfortunate for patients…
- …however, improved much safety characteristics (especially neutropenia), as well as development/regulatory pathway for ModraDoc006/r, will enable Modra to address and/or avoid issues encountered by other programs
- Market valued the two late-stage phase III individual oral taxane products (prior to setbacks) was at $700-1000+M → significant value creation potential for Modra

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Looking at Industry Benchmarks, ModraDoc006/r well Positioned to Achieve Attractive Premium Pricing

IV → Oral

5-FU (IV) → Xeloda® (capecitabine)

Xeloda® advantages
- Oral pro-drug of IV 5-FU
- Convenience, improved safety

Branded IV 5-FU price/week: ~$470[a]
Xeloda® price/week: ~$1870[a]

Xeloda® peak sales: $1.6B+[b]

Novel Branded Taxanes

Abraxane® (nab-paclitaxel)
- Advantages – safety & efficacy
- Indications: breast, NSCLC, panc.
- Price/week: ~$2400[a]
- Peak sales: ~$1B+[c]

Jevtana® (cabazitaxel) in mCRPC
- Advantages – activity in doc-resistant tumors
- Indications: prostate
- Price/week: ~$3500[a]
- Peak sales: $0.4B+[d]

Novel Prostate Cancer Therapies

Zytiga® (oral abiraterone)
- Price/week: ~$2600[a]
- Peak sales >$2.7B[e]

Xtandi® (oral enzalutamide)
- Price/week: ~$2700[a]
- Peak sales: $2.6B[f]

a. US prices: from drugs.com, wellsrx.com, based on typical monotherapy schedules
b. Fiercebiotech, Sept 16 2013 – 2012 figures
c. BioWorld Jan 2017 – 2016 figures
d. Globenewswire, Feb 8, 2017 – 2016 figures
e. Fiercepharma, jan 31. 2019 first 9 months 2018 figures
f. Fiercepharma, Jul 16, 2018, 2017 figures

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Peak Commercial Potential of over EUR 1B in N.America & Europe

With substantial additional potential upside in Asia, other tumor types

Peak sales estimate, EURm	N.America	Europe
Prostate	400	250
HER2- breast	250	200

Source: Venture Valuation Assessment

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Process Development & Manufacturing Substantially Derisked

- ModraDoc006
  - Docetaxel API purchased from third party CMO
  - Tablets historically manufactured at 6000 tablet batch clinical scale
  - Commercial-scale process development on track
    - Process development currently at 40-50% commercial scale (100K tablets)
    - Plan to use validation batches as supply for pivotal studies
  - Attractive COGS at current scale, to be further reduced at commercial scale
- Ritonavir
  - Currently use Norvir® tablets – but potential to use generic tablets

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Strong Drivers of both Narrow & Broad Exclusivity

ModraDoc006/r specific

Issued patents thru 2028/29
- Formulation & combination with ritonavir

Patent applications thru 2038
- Filed December 2018

Data exclusivity & patent-term extensions

Oral taxane/ritonavir combinations

Issued patents
- Cover broad set of taxanes for formulation and combination
- Including paclitaxel, cabazitaxel and functional derivatives

Ab initio development
- Differential PK profiles/impact of booster

IV taxane/ritonavir combinations

All generic components

Ab initio development
- Differential PK profiles/impact of booster

Safety disadvantages

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Key Members of Modra Team

Name	Role	Background
Colin Freund	CEO	▪ 18+ years oncology biotech experience ▪ QUE Oncology, Transgene, GPC Biotech, BCG
Eric van der Putten	Director	▪ 30+ years clinical research experience in oncology ▪ Partner, Aglaia Oncology Funds
Marianne Keessen	Director, Project Management	▪ 15+ years oncology nursing ▪ Project management at Netherlands Cancer Institute
Chris Huiskamp	CFO	▪ 20+ years international finance and operations experience ▪ 5+ years in clinical research ▪ Medpace, Assign, Sourcia
Prof. dr. Jan Schellens, MD	Chief Medical Officer (& Founder)	▪ Former head of Clinical Pharmacology at the Netherlands Cancer Institute ▪ 20+ years experience in oncology drug research
Prof. dr. Jos Beijnen	Chief Technology Officer (& Founder)	▪ Head of hospital pharmacy at the Netherlands Cancer Institute ▪ 20+ years experience in drug formulation
Laurens van Pinxteren	Head of CMC	▪ 18+ years pharma and biotech experience, primarily in manufacturing ▪ InteRNA, Mallinckrodt, The Medicines Company
Alan Barge, MD	Medical Advisor and Chairman of the Board	▪ Former Head of Oncology at Astra Zeneca ▪ 25+ years experience in oncology drug development