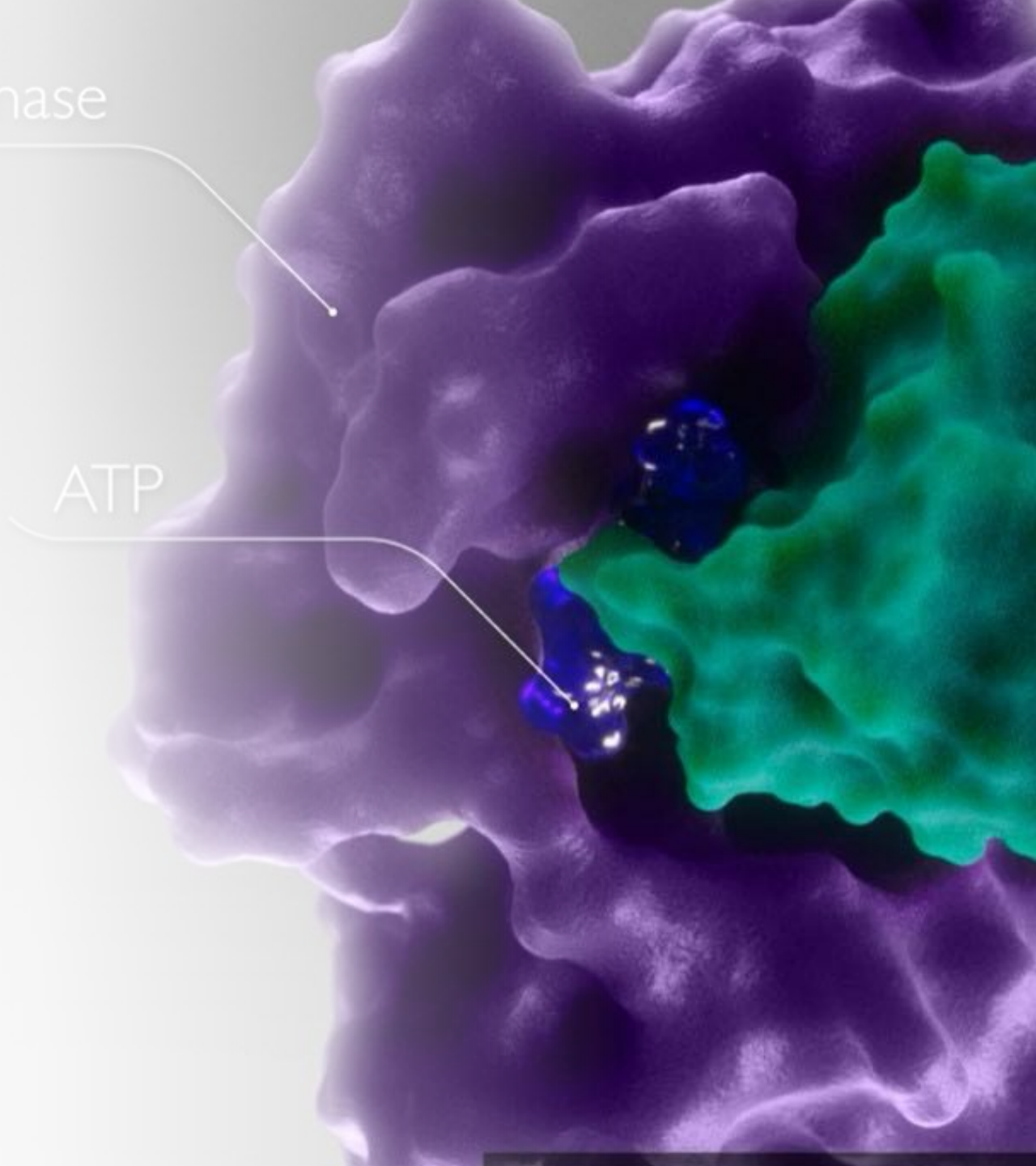
DO-2:
Next generation MET inhibitor

For improved treatment of lung cancer patients

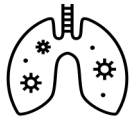


Deuter Oncology

Who we are

- Founded in Q4 ‘20 in Belgium
  - Dr Perera originated the initial idea for the use of deuteration as a means to modulate the metabolic properties of the parent drug
- Seed and Series A investments of ~€8M + non dilutive ~€0.5
- Investors include Newton Biocapital (lead investor), Noshaq & InVestsud
- Significant know-how on high-efficiency deuteration
- Exclusive global licence from Johnson and Johnson

Our value proposition



Potential ‘Best-in-class’ targeted MET kinase inhibitor with better safety profile to maintain or extend clinical benefit and allow combination therapy with a range of SOC.

DO-2 Phase 1 (started in 2023) is boding well to determine optimal dose. Convincing signs of clinical benefit; well tolerated with no incidences of drug related peripheral edema or liver enzyme elevations seen with competitors; no DLT observed.

CMC under control; kg batch in place; scale up is validated; 24 month stability data

IP exclusivity until 2035 – ww rights under parent patent
Novel applications relating to composition of matter and dosing regimen in preparation

Seasoned team to make this happen

Timothy Perera, PhD.
Founder/CEO

30 y Pharma Experience

OCTIMET CSO/CEO
Global Discovery Leader Lung Disease Area at J&J.
Discovery leader/project champion for 4 clinical stage agents including approved FGFR inhibitor Balversa (erdafitinib)

Els Hubloux
Chief Financial Officer

25 y Life Sciences Experience

Corporate and Venture Capital experience including Pronota, Capricorn Venture Partners, QBIC Venture Partners, Newton Biocapital Venture Partners. Executive roles included CFO, VC fund partner positions.
Experienced board member held various board positions in medtech and biotech companies.

Prof Jaap Verweij
Chief Medical officer

35 y Clinical Development

Prof Emeritus Erasmus Medical Oncology
Managing Director at The Cancer Drug Development Forum (CDDF)

Florence Wastelin M.Sc. MBA.
Clinical Operations

20 y at GSK Biologicals

Leading teams across global projects and leading Clinical Operations department for the development of immunotherapeutics against cancer.

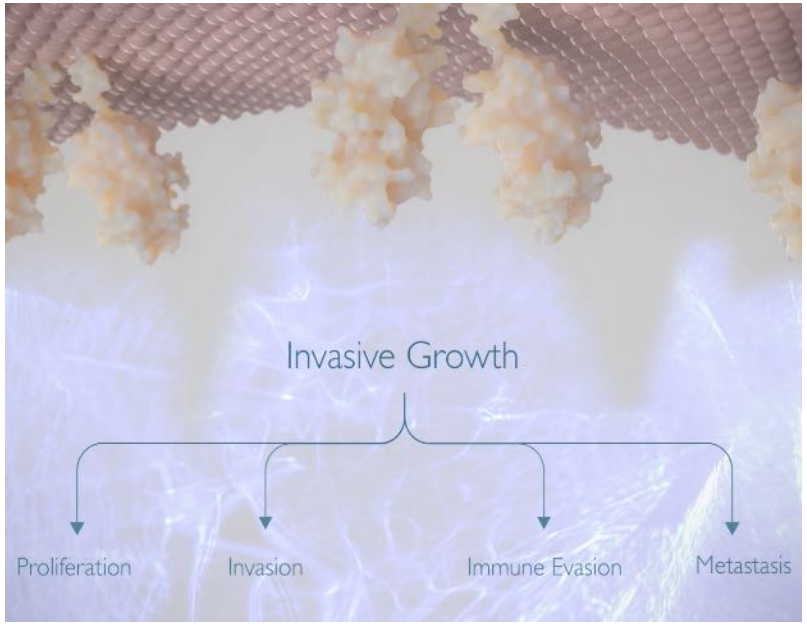
Hilde Windels MBA.
Corporate Development

25 y Biotech Experience

Including Devgen, Biocartis and med. and small size biotech companies. Executive roles included CFO, co-CEO and CEO positions.
Board member in 4 public and 1 private company.

Additional support from external partners in targeted outsourced activities.

MET, a clinically validated drug target



Oncogenic driver when wild type receptor is overexpressed due to
- MET amplification
- MET mutation (ex 14 skipping)

~2 to 5 % of advanced NSCLC

- MET is expressed in normal tissues including vascular endothelial cells
- MET dysregulation is associated with a poor prognosis in a range of cancers
- Clinical activity proven for class
  - Only in 2nd line (in EU) patients with non-small cell lung cancer (NSCLC) harbouring exon14 skipping (METex14) mutations.

Capmatinib	Novartis	Approved
Tepotinib	Merck	Approved
Savolitinib	AstraZeneca	Approved

- Yet, significant toxicities are seen
  - high daily doses (500-800mg) frequently leading to dose interruptions and reductions.
  - impacting Quality of Life and clinical benefit.

Peripheral edema and liver toxicity are frequently observed with approved agents

Figure - available from: Thoracic Cancer

1 Number of patients : 313 (cohorts A+C) from registration trial VISION (JAMA Oncol. 2023;9(9):1260-1266,doi:10.1001/jamaoncol.2023.1962)
2 Number of patients : 364 (all cohorts) from registration trial GEOMETRY (N Engl J Med 2020;383:944-957, DOI: 10.1056/NEJMoa2002787)
3 https://ec.europa.eu/health/documents/community-register/2022/20220216154592/anx_154592_en.pdf
4 https://www.accessdata.fda.gov/drugsatfda_docs/nda/2021/214096Orig1s000MultidisciplineR.pdf
5 https://ec.europa.eu/health/documents/community-register/2022/20220620155859/anx_155859_en.pdf
6 https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/213591Orig1s000MultidisciplineR.pdf

Peripheral edema

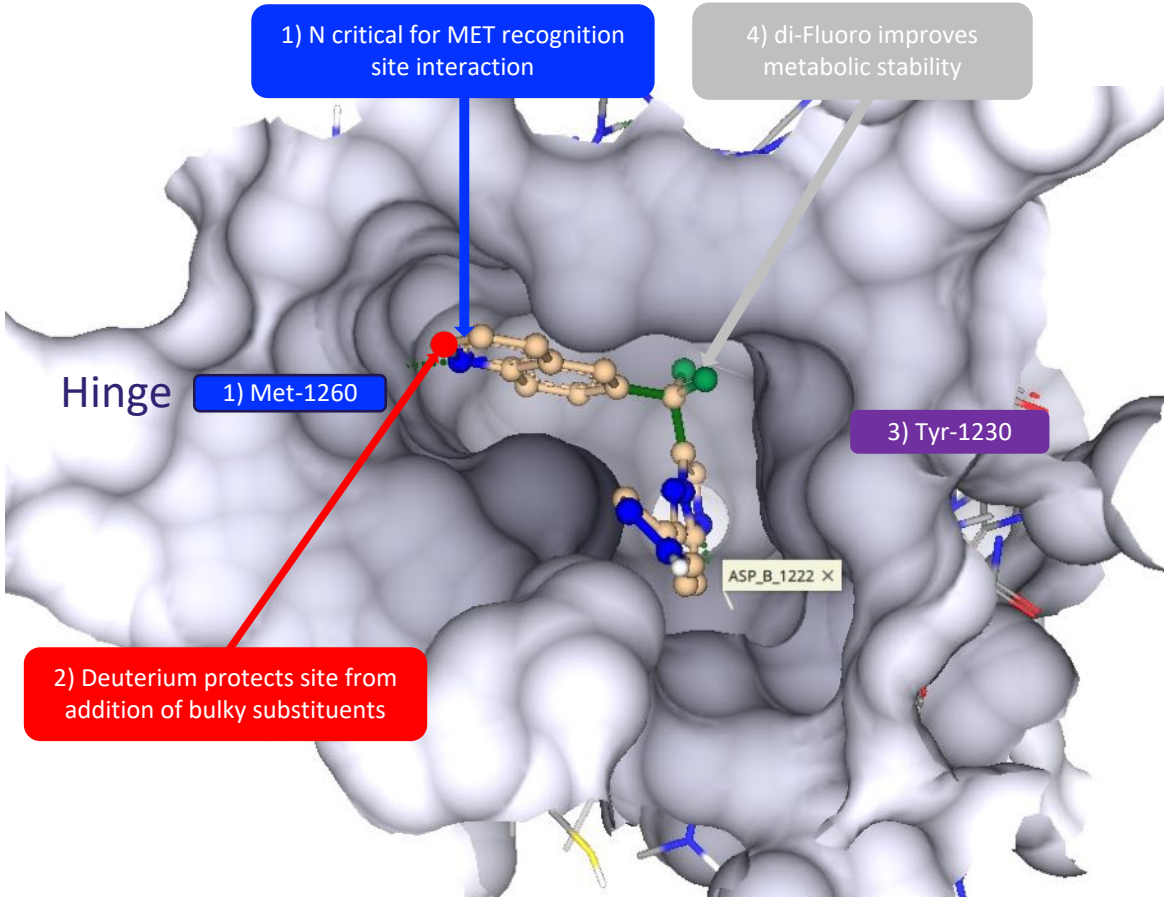
- 67% of tepotinib[1] and 51% of capmatinib[2] treated patients endure some degree of edema
- Median time to onset of edema 9 weeks[3]
- Peripheral edema; observed in the pre-clinical tox study[4] with tepotinib.
- NOT observed with DO-2

Liver enzyme elevations

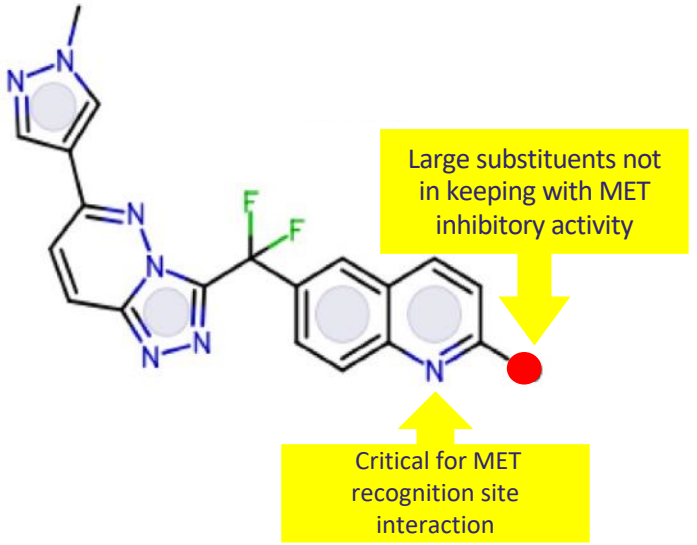
- seen in 48% of tepotinib[3] and 46% of capamatinib[2] treated patients
- Liver toxicity; observed in the pre-clinical tox study[4] with tepotinib and capmatinib[6].
- NOT observed with DO-2

- Tox profile of approved agents comparable to SOC (Chemo/Immunotherapy)
- Not reimbursed in many countries… Belgium, France

DO-2 designed to fit into the ATP binding pocket of the MET kinase

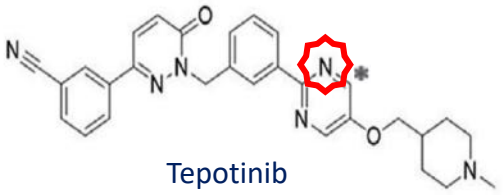


Surface of the ATP binding pocket of MET kinase

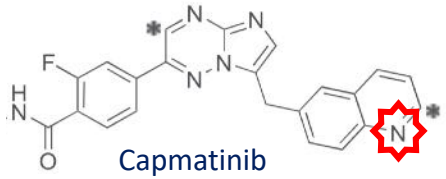


1) Critical recognition site at Met-1160 that is bound by the N of the quinoline
2) Position adjacent to critical N is liable to oxidation by Aldehyde oxidase. Bulky substitutions at this site are not tolerated. Deuterium protects metabolism at this site.
3) Parallel alignment of Tyr 1230 and DO-2 leads to strong interaction resulting in selectivity and a slow off rate
4) di-fluoro substituents significantly improves metabolic stability

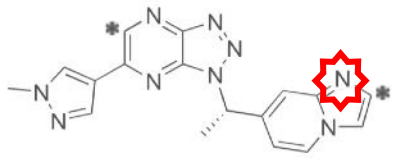
Metabolism of chemical scaffold of selective Type 1B MET kinase inhibitors…



Tepotinib
Approved



Capmatinib
Approved



Savolitinib
Approved

JNJ-38877605 (DO-0)
Terminated

Nitrogen (✡) => critical for binding to MET

Aldehyde Oxidase 1 replaces the Hydrogen* by a bulky Oxygen which prevents binding to intended target

- Reducing exposure to active parent drug
- Requiring higher daily doses

Most abundant circulating metabolite(s) of parent drug with no/negligible pharmacological activity for:

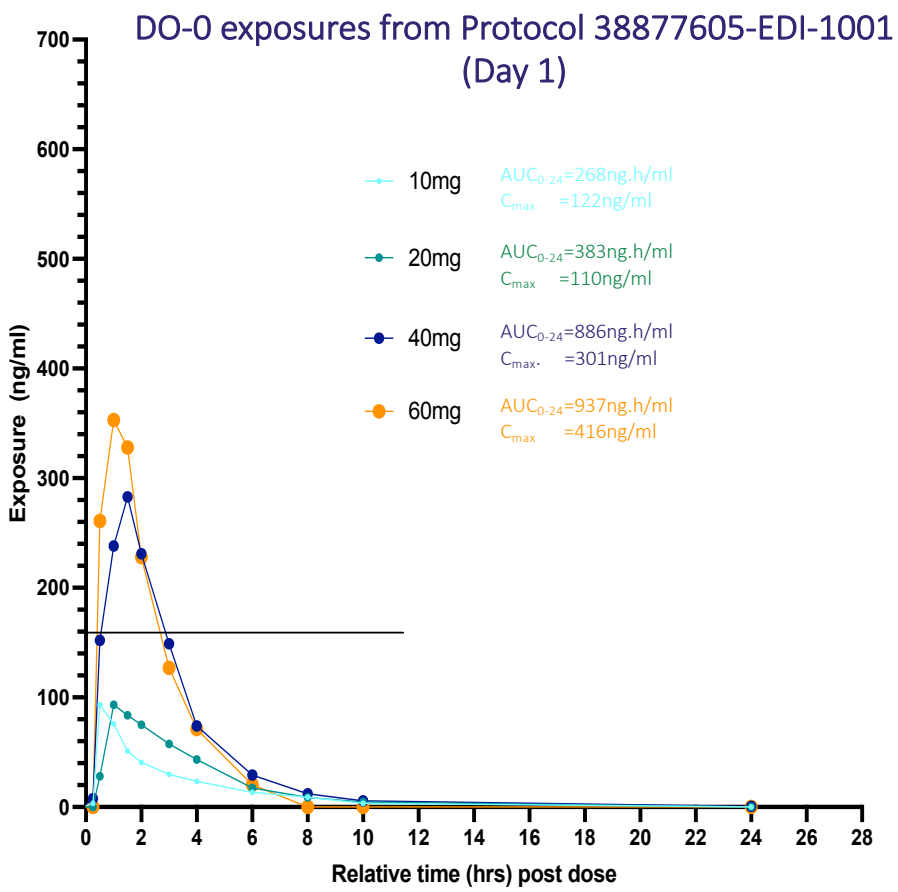
- Capmatinib[1.] = 50% inactive metabolite(s)
- Tepotinib[2.] = 65% inactive metabolite(s)
- Savolitinib[3.] = 88% inactive metabolite(s)
- DO-2 = 10% inactive metabolite

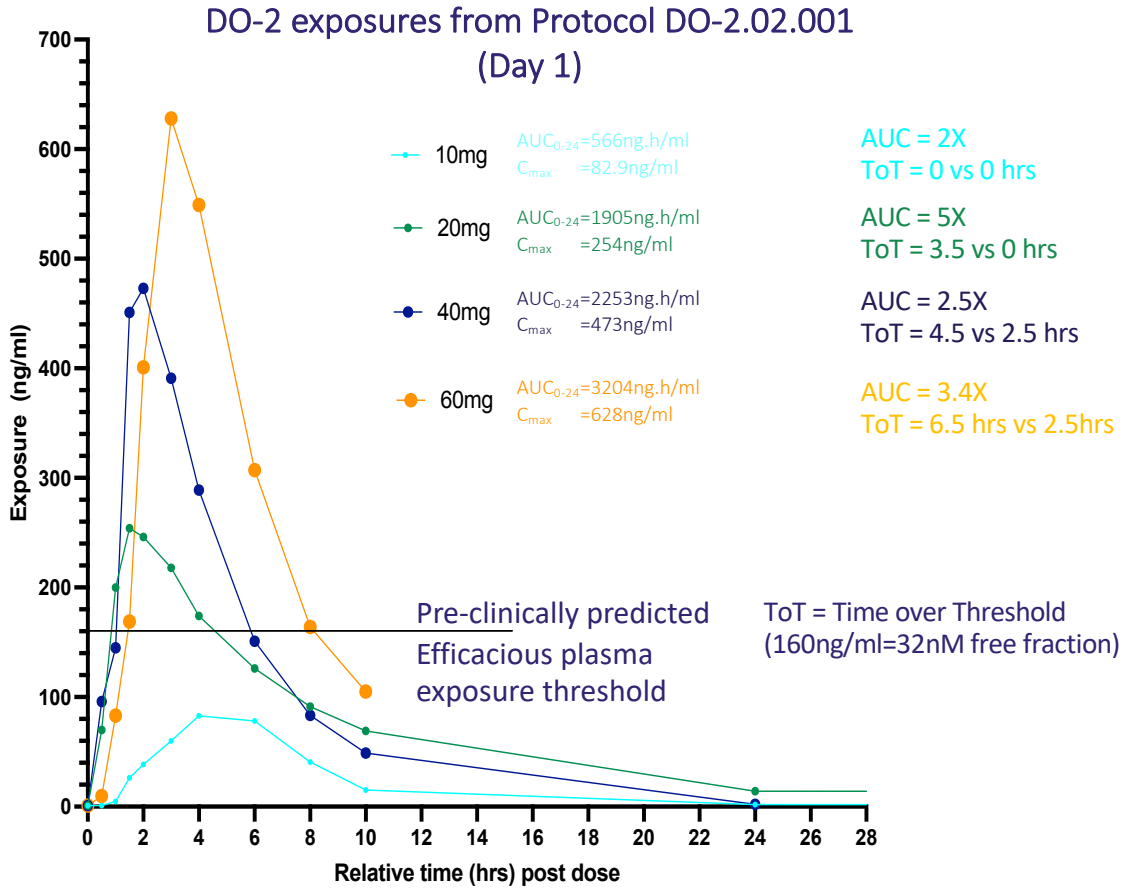
→ ….lead to adverse events

1) Glaenzel et al, Drug Metab Dispos 48:873–885, October 2020 : 2) Xiong et al CPT Pharmacometrics Syst. Pharmacol. 2021;10:428 : 3) Miah et al, Clin Pharmacol Drug Dev. 2023 Apr;12(4):424-435

Hypothesis validation: Significantly improve active (parent) drug exposures in the clinic

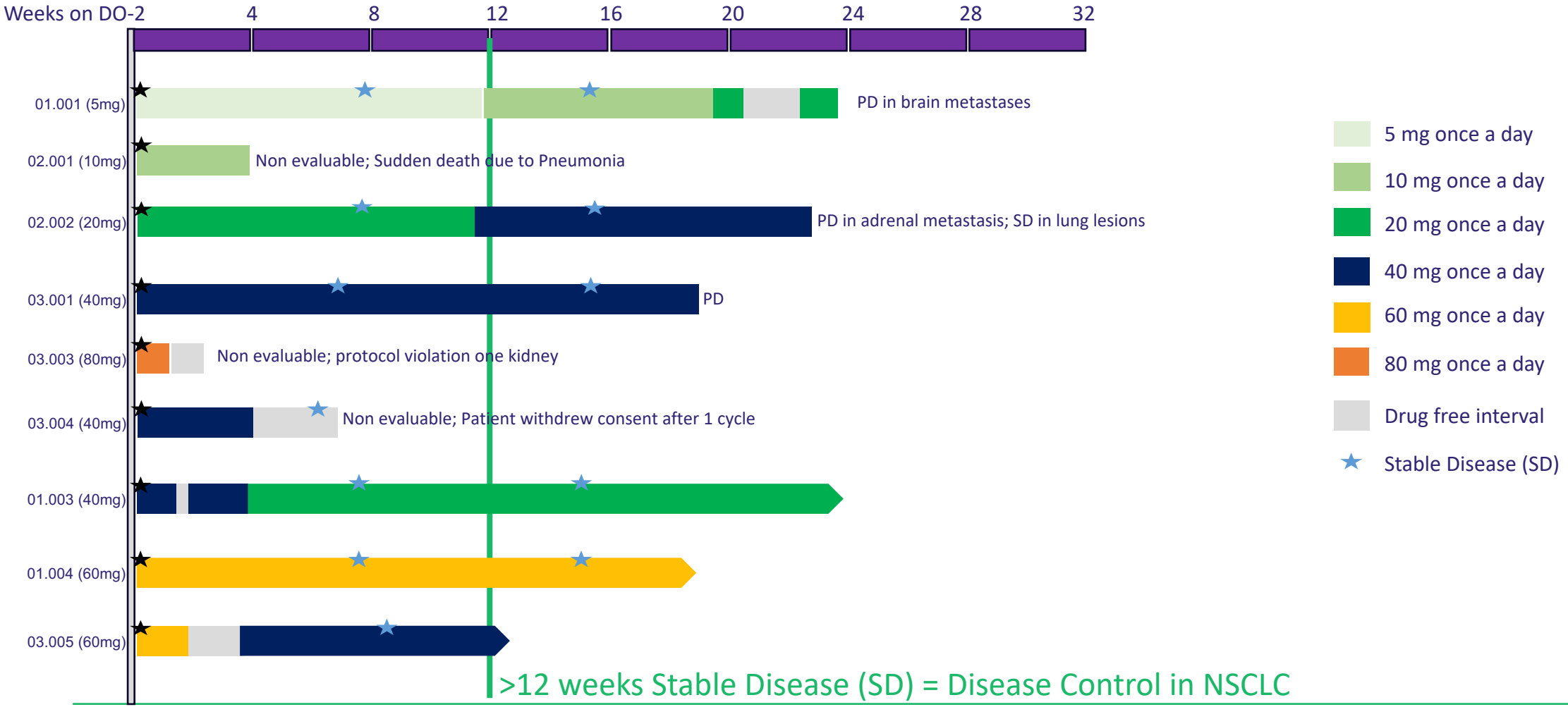
Clinical exposures of deuterated version (DO-2) are ~2.5 to 5-fold higher than with the non-deuterated version (DO-0). DO-2 maintains efficacious levels (ToT) for longer, achieving target inhibition levels.





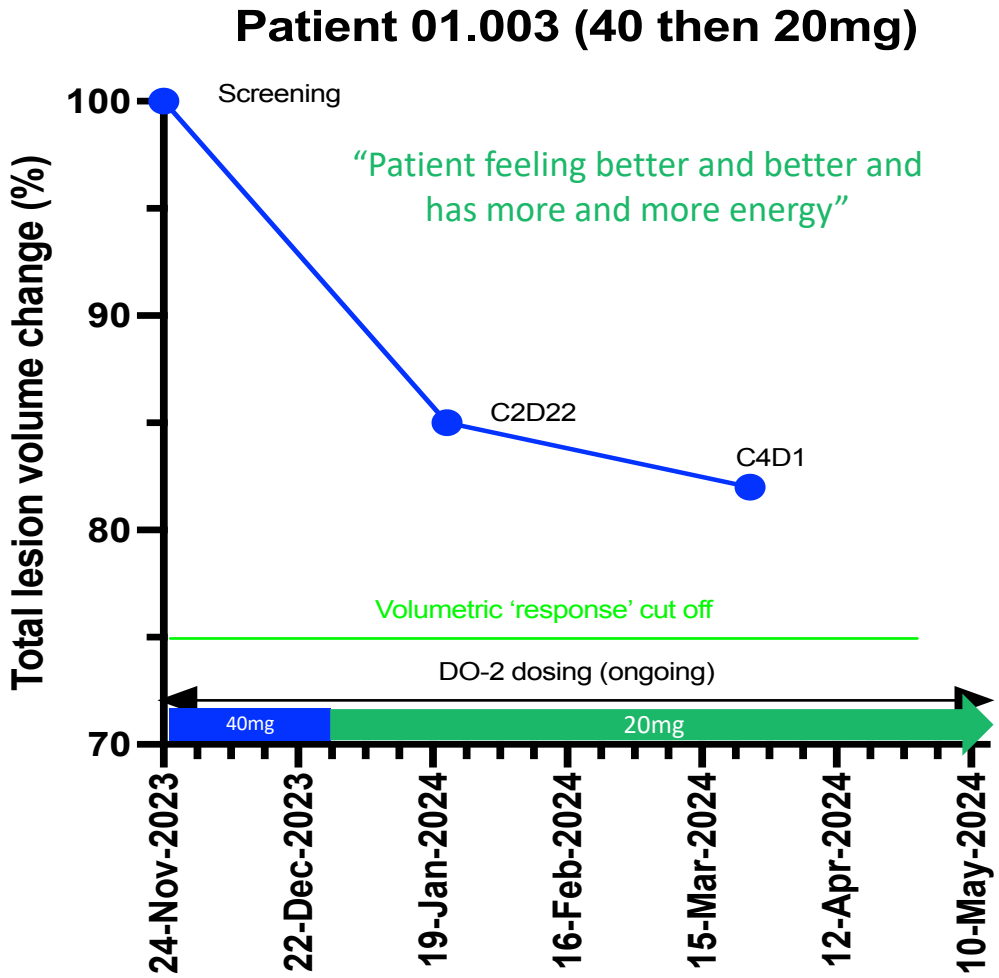
Prolonged stable disease in majority of patients

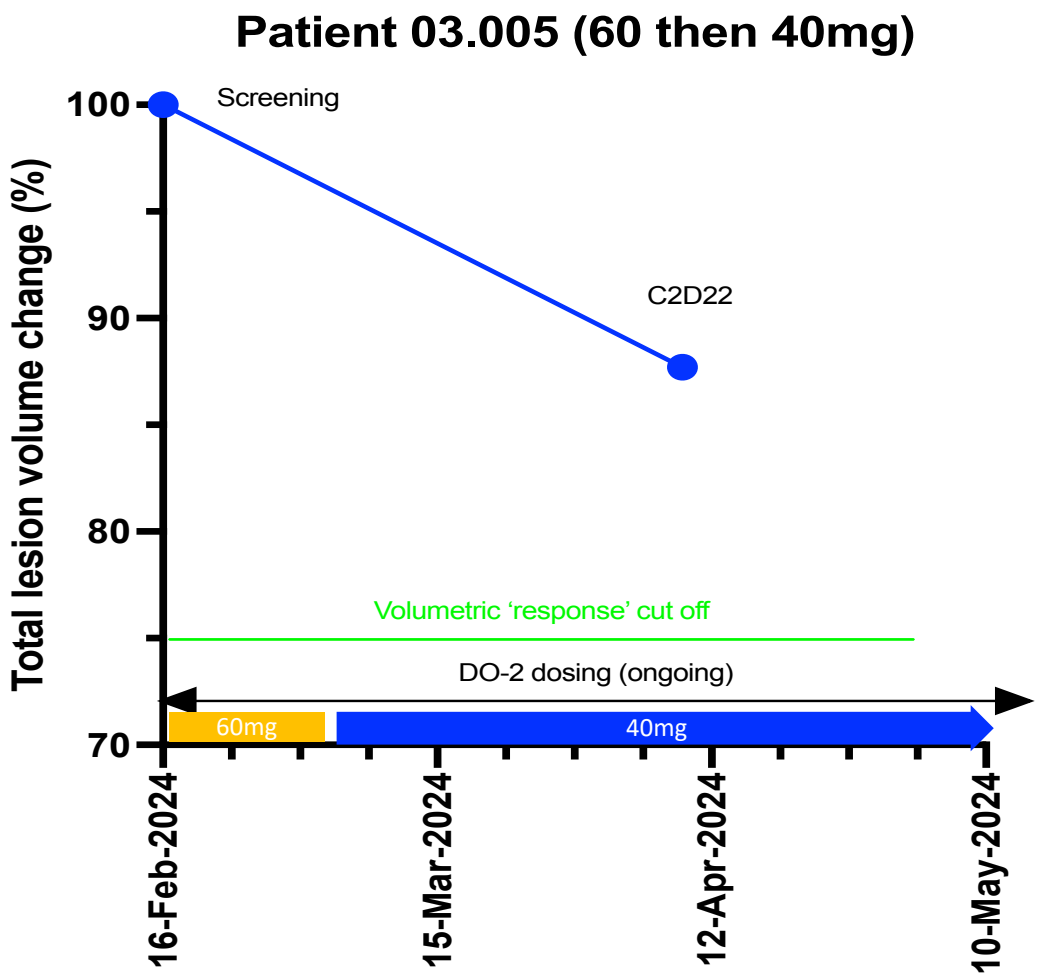
100% Disease control rate (6/6 evaluable patients)



>12 weeks Stable Disease (SD) = Disease Control in NSCLC

Significant clinical benefit reported for severtal patients Correlating with volume reductions seen with 3D analyses

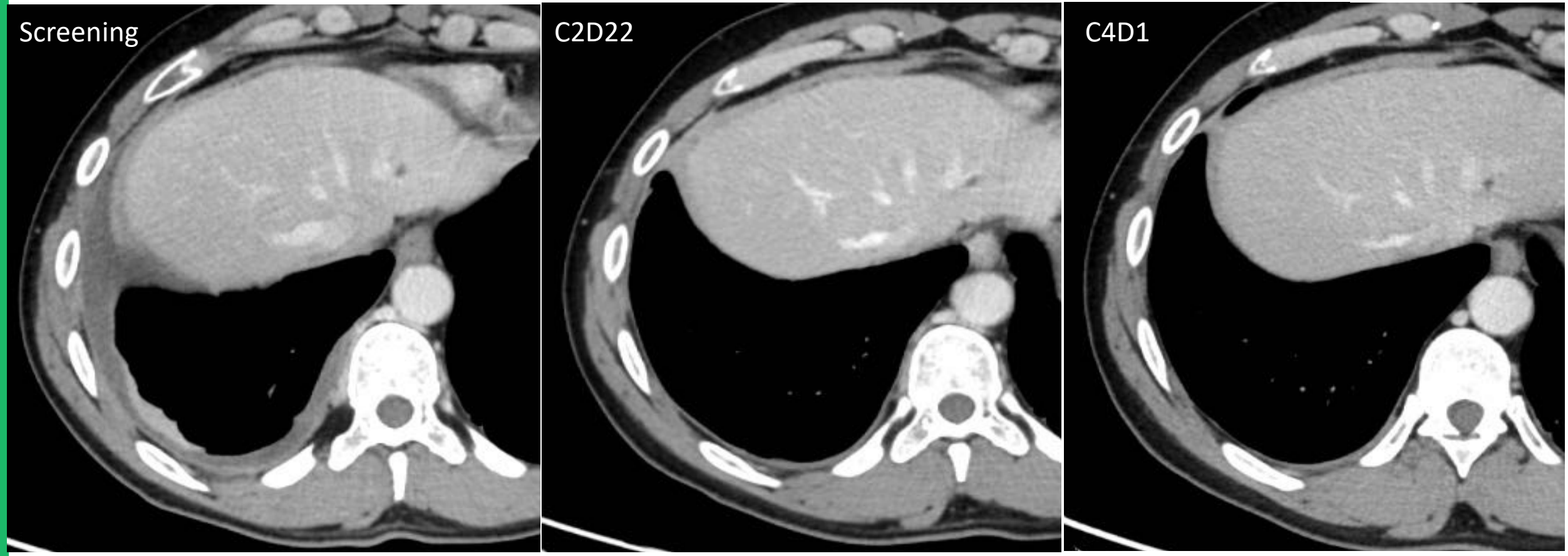




Complete resolution of pleural effusion

Patient 01-004

"Reduction in chest pain reported at day 8; complete absence of chest pain; after 2 cycles; pleural fluid reported to be absent after 3 cycles.

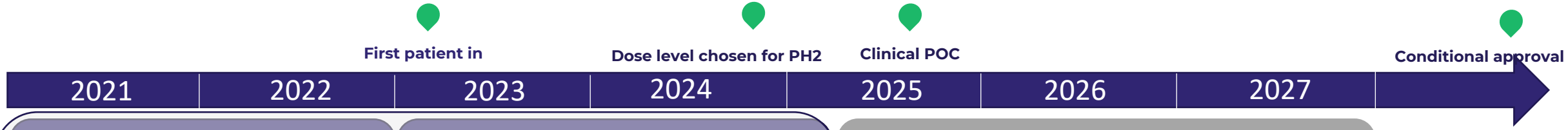


"The extent of the right pleural effusion **at C2D22 is completely resorbed**. There are only some residual pleural and intrafissural thickening/atelectasis, which are **virtually resolved at C4D1**".

Large market potential

- Current MET inhibitors only approved in the METex14 skip mutation positive setting (~3% of NSCLC)
  - Representing a potential market of >$1B (Novartis projected peak sales of $1.5B)
- Much larger currently ‘unmet medical needs’ await a well tolerated MET inhibitor
  - Monotherapy in MET mutant settings
    - MET amplified NSCLC, gastric cancer, ovarian cancer
    - MET amplification/fusions in glioblastomas
    - MET amplification in gastroesophageal cancers
  - Combination settings
    - Intrinsic/acquired resistance to immune checkpoint inhibitors in a range of cancers
    - Acquired resistance to EGFR, kras, Alk, Ros… inhibitors in NSCLC
    - Acquired resistance to EGFR inhibitors in colon and head & neck cancers…

Development plan (overview)



Strong pre-clinical data package. CMC done

Enabling studies finalised
- Improvement over competitive drugs
- Superiority of DO-2 over capmatinib at lower doses

Phase 1 study
(to determine RP2D in MET Amp >10 fold or Exon14 skip)

Current status (N= 9)
Close to final dose selection
Clinical benefit observed

Ongoing (N=16)
Finalise dose selection
Mini expansion cohort in selected setting
(Eg 1st line ex14 skip patients)

Phase 2
MET exon 14 skip
Flemming 2 stage design at RP2D

1st line ex 14 skip patients
- Stage 1 (N = 26)
  - ≤ 10 ORR's then stop for futility
  - ≥ 11 ORR's, then continue to recruit to 55
  - ≥ 16 ORR's, then GO to randomized registration intent study (180 patients)
- Stage 2 (N=29)
  - ≤28 ORR's then P > 0.05 consider safety data
  - ≥29 ORR's then GO to randomized registration intent study (180 patients)

Current funding €8M

Series B €11M

Take home messages

- Improvement over competitive drugs already demonstrated in pre-clinical studies with convincing data.
  - Superiority of DO-2 over main competitors at much lower doses.
  - Large therapeutic window
- Phase 1 study boding well for validation of improved safety at efficacious dose levels
  - No peripheral edema or liver enzyme elevations.
  - No other adverse events of note
  - PK/PD results promising - DO-2 exposure predicted to be fully efficacious aleady achieved
  - Early signs of clinical benefit observed
    - weight gain, alleviation of pain, reduction and total clearance of pleural effusion, tumor shrinkage.
- Compound and drug prodcut manufacture optimized with long shelf life.
- Significant, rapidly growing market with sub-optimal competitive agents, yet with blockbuster potential.

Looking for €11M Series B investment to generate Phase 2 efficacy data

Thank you for your attention

Dr Timothy Perera

tperera@deuteroncology.com

www.deuteroncology.com