TurckBio
Bringing Science to Market

RADIOPHARMACEUTICALS – THERAGNOSTIC PAIRINGS

- July 26, 2022

SUCCESS AND FAILURE

Zevalin
Bexxar

> $20 mUSD

Xofigo $415 mUSD
Lutathera > $400 mUSD
Pluvicto > $500 mUSD?

TurckBio
Bringing Science to Market

HOW CAN RPS BECOME BLOCKBUSTERS?

> 1,000 mUSD ?

Zevalin	> $20 mUSD
Bexxar	

Xofigo	$415 mUSD
Lutathera	> $400 mUSD
Pluvicto	> $500 mUSD?

TurckBio
Bringing Science to Market

LEVERAGE POINTS

Case in point: PSMA-617

Case in point: Lutathera

Case in point: Iomab-B

- Targets not druggable by ADCs and other agents
  - Low level of target expression
  - Non internalizing non-oncogenic targets
  - Small targeting moieties
  - Chemo resistance
- Leverage unique safety / efficacy profile
- Abscopal effect / synergy

TurckBio
Bringing Science to Market

WHERE RPS ARE TODAY CLINICALLY

- Single agent
- Last or late line
- Palliative
- Conventional alternatives limiting commercial success

TurckBio
Bringing Science to Market

WHERE WE NEED TO GO

- Early lines of therapy (1L, 2L)
  - Combinations with conventional drugs
  - Maintenance, Adjuvant
  - MRD positivity
- "Cures" or long term CRs
- Leverage specific advantages of Radiopharmaceutical

TurckBio
Bringing Science to Market

HOW RADIOPHARMACEUTICALS CAN WIN BIG

Potential upfront settings

Part of combination therapies

- Replace chemo
- Replace EBRT
- Leverage potential synergies
  - PD-(L)1, PARP etc.
  - Leverage abscopal effect
- Additive effect with different safety profile

MRD paradigm: adjuvant / maintenance

- "Surgical kill" (a-emitters)

TurckBio
Bringing Science to Market

A SIMPLE TRUTH

Case in point:
Zevalin vs
Rituximab

When directly competing with conventional therapies, radiopharmaceuticals will lose

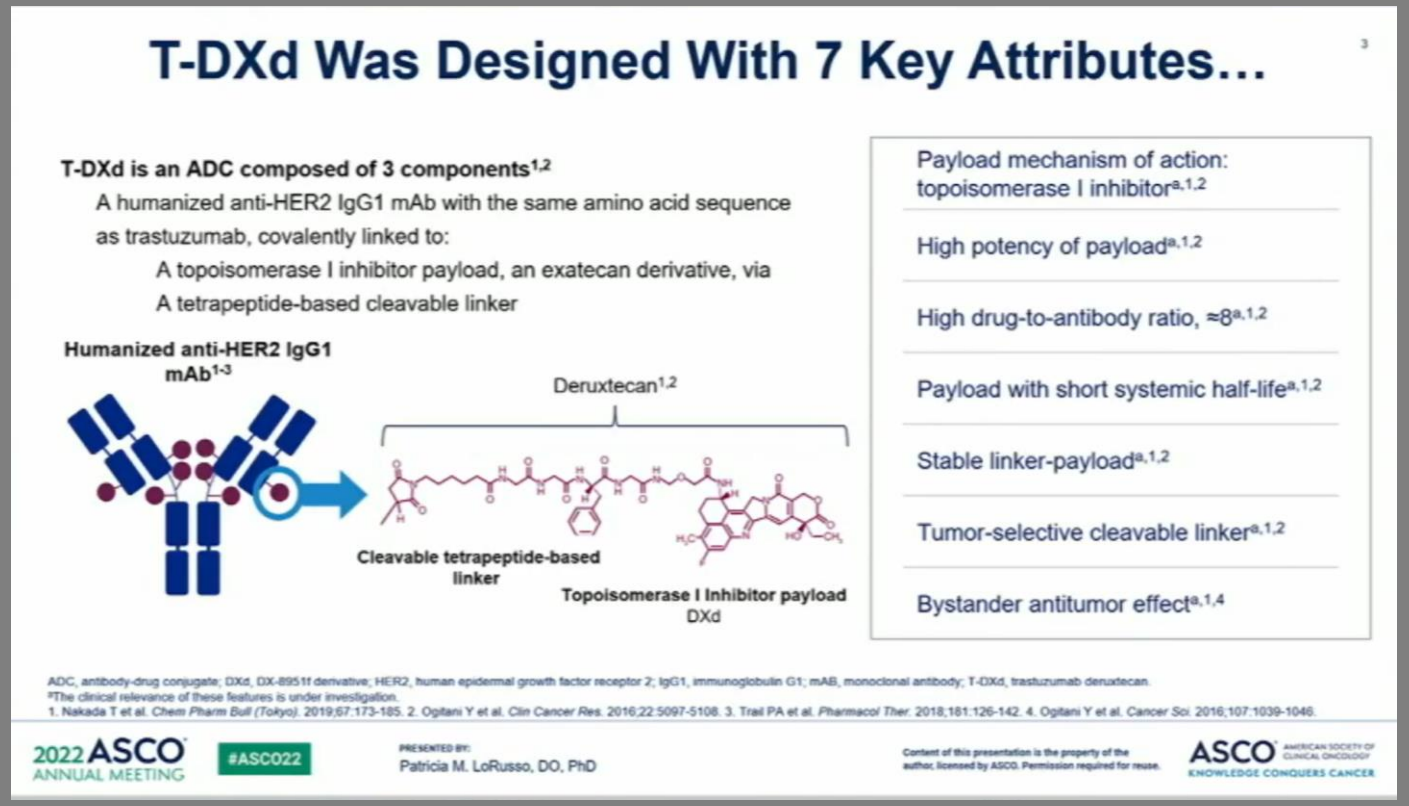
- Radiopharmaceuticals need to be clearly superior to conventional therapy
  - Efficacy
  - Safety

TurckBio
Bringing Science to Market

A WARNING: ADCS MAKING PROGRESS

- T-DXd's (Enhertu) profile is like a RPs'
- ADCs remain key competitors
- Their safety profile mimics that of the payload

➢ Tolerability is a positive differentiator for RPs



TurckBio
Bringing Science to Market

ALPHA VS BETA

Criteria:

• Target expression level	Low: α
• Cross-fire	long range: β
• Abscopal effect	β
• Radiation resistance	α
• MRD setting	α
• Community use	α, (β)

TurckBio
Bringing Science to Market

CAN TRACERS SUPPORT BROADER USE…

- … as RPs are used more upfront and in larger indications?
- … and in cancers that may have many actionable mutations?

➢ Yes, but…

TurckBio
Bringing Science to Market

IMAGING TRACERS - CLINICALLY COMPELLING

- Dosimetry – "image twin"
- Target expression - patient selection
- Cancer heterogeneity
- Early response marker
- Tracking: AI opportunity

TurckBio
Bringing Science to Market

IMAGING TRACERS - CLINICALLY COMPELLING

- Dosimetry – "image twin"
- Target expression - patient selection
- Cancer heterogeneity
- Early response marker
- Tracking: AI opportunity

TurckBio
Bringing Science to Market

POURING WATER IN YOUR WINE…

- Only few tracers have potential relevance beyond being a companion
  - PSMA is the exception!
- PET tracers are not great for screening
  - High “hit ratio” needed (say 1 : <3)
- PET companion tracers are not necessarily an advantage if they are required to use the therapeutic
  - Access
  - Stakeholder economics

TurckBio
Bringing Science to Market

COMPANION TRACER FOR PATIENT SELECTION?

- Standard approaches to analyze target expression
  - Biopsy, CTC, ctDNA, ctRNA
  - IHC, PCR, NGS etc.

- Many options
- Established as companion tests for conventional therapies
- Broad set of data often available

TurckBio
Bringing Science to Market

COMPANION TRACER STRATEGIES

- Leverage in vitro tests combined with imaging, where appropriate
  - Pre-select patients with existing data on mutations
- Create treatment algorithms driven by tracers
  - Move beyond excluding low expressers
- Dosimetry based individual dosing as a post approval option, if possible
- AI-driven response predictions
  - Combine imaging and clinical data

Case in point: Lutathera

TurckBio
Bringing Science to Market

TRACER-DRIVEN ALGORITHMS

Case in point: Keytruda vs Lutathera

Ideally, companion tracers should drive comprehensive treatment choices rather than just excluding a subset of patients

- E.g. PD-(L)1 – TPS > 1%, NSCLC
  - High expression level – single agent therapy
  - Low expression level CPI + chemo
- Adaptive: Quick, well-defined early response, if not combination

TurckBio
Bringing Science to Market

COMPANION TRACERS NEED TO DRIVE VALUE

Case in point: Lutathera

Case in point: PSMA

- How competitive is the therapeutic?
- Is the data generated unique and useful?
- Do data gate a specific treatment, or have broader use?
- Do they change patient management and improve outcomes?
- Is it the best option?
- Is it cost-effective?

TurckBio
Bringing Science to Market

WHERE DOES THIS LEAVE US?

Companion tracers need to create unique clinical value to support a product

- Think about companion diagnostics more broadly
  - Avoid companion tracer requirement unless there is a compelling use case
  - Leverage existing in-vitro data
  - Consider in vitro-tests combined with PET tracers in particular for screening
- Expand the tracer use case beyond binary patient selection
- Leverage tracers to drive a comprehensive treatment algorithm

Be bold - think long-term CR and cure!

TurckBio
Bringing Science to Market

COMMENTS - QUESTIONS?

roland.turck@turckbio.com

TurckBio
Bringing Science to Market