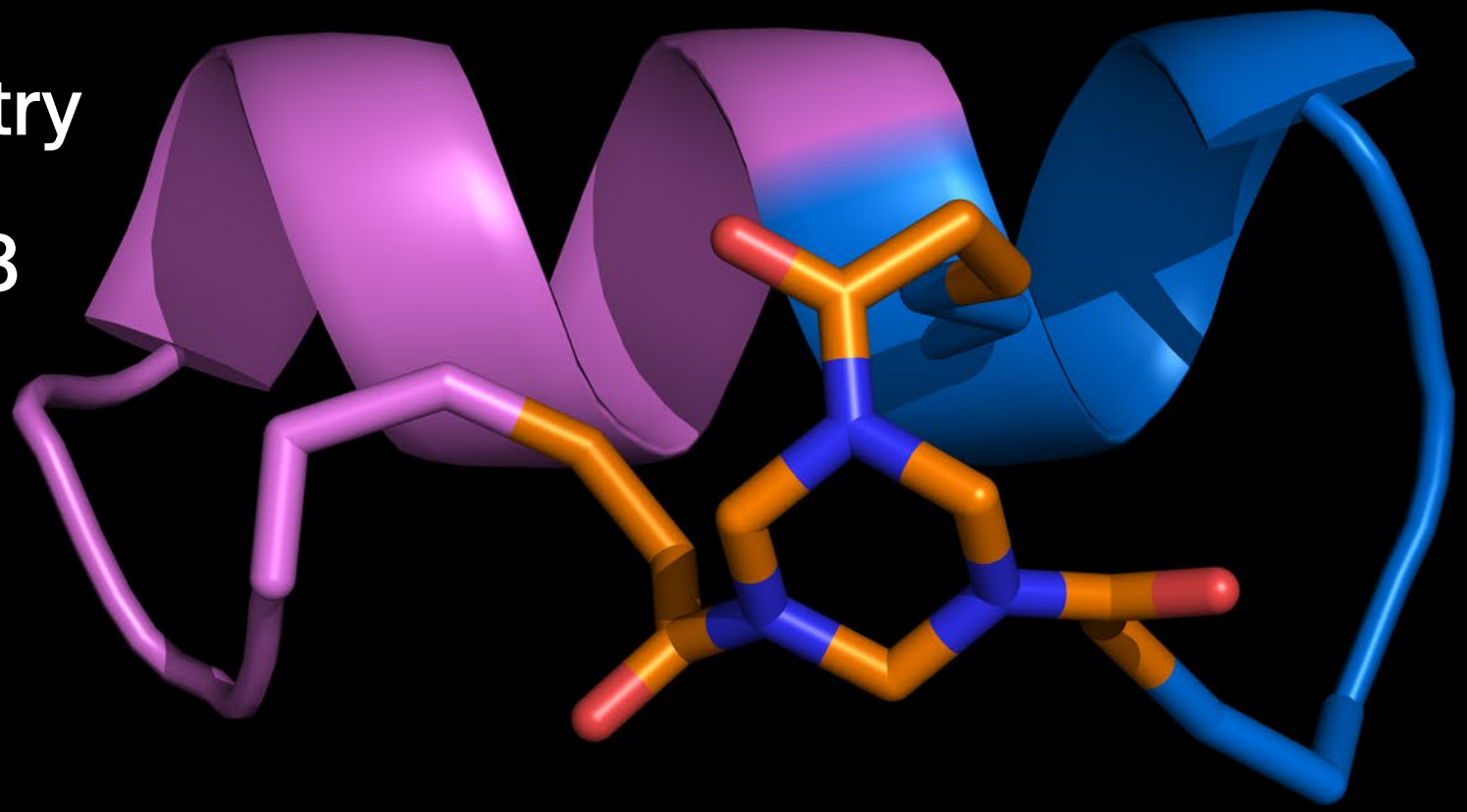
Expanding the Potential of ADCs: Bicyclic Peptide (Bicycle®) Toxin Conjugates May Offer Advancements Over Traditional ADCs

Mark Frigerio, VP Chemistry

World ADC, Europe - 2023



Bicycle®

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This presentation may contain forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements may be identified by words such as "aims," "anticipates," "believes," "could," "estimates," "expects," "forecasts", "goal," "intends," "may" "plans," "possible," "potential," "seeks," "will," and variations of these words or similar expressions that are intended to identify forward-looking statements. All statements other than statements of historical facts contained in this presentation are forward-looking statements, including statements regarding: our future plans, prospects, trends or strategies and other business matters; our current and prospective product candidates, planned clinical trials and preclinical activities, and the timing and success of our development of our anticipated product candidates.

Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our preclinical and clinical results, our plans to initiate clinical trials and the designs of the planned trials and other future conditions, and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, the risk that any one or more of our product candidates will not be successfully developed or commercialized, the risk of cessation or delay of any ongoing or planned clinical trials, the risk that we may not realize the intended benefits of our technology, including that we may not identify and develop additional product candidates for our pipeline, the risk that we may not maintain our current collaborations or enter into new collaborations in the future, or that we may not realize the intended benefits of these collaborations, the risk that our product candidates or procedures in connection with the administration thereof will not have the safety or efficacy profile that we anticipate, the risk that prior results will not be replicated or will not continue in ongoing or future studies or trials, the risk that we will be unable to obtain and maintain regulatory approval for our product candidates, the risk that the size and potential of the market for our product candidates will not materialize as expected, risks associated with our dependence on third-parties, risks regarding the accuracy of our estimates of expenses, risks relating to our capital requirements and needs for additional financing, and risks relating to our ability to obtain and maintain intellectual property protection for our product candidates. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in our Annual Report on Form 10-K, filed with the Securities and Exchange Commission on February 28, 2023, as well as in other filings we may make with the SEC in the future, as well as discussions of potential risks, uncertainties and other important factors in our subsequent filings with the Securities and Exchange Commission. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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Bicycle Therapeutics

Founded by Sir Gregory Winter & Prof. Christian Heinis

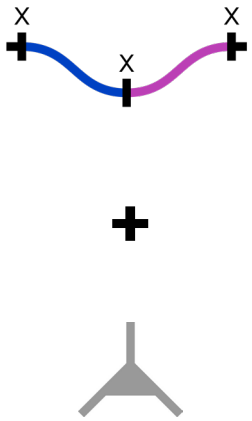
UK & US based (Cambridge, UK; Boston, USA)

2018 Nobel Prize in Chemistry
"for the phage display of peptides and antibodies"

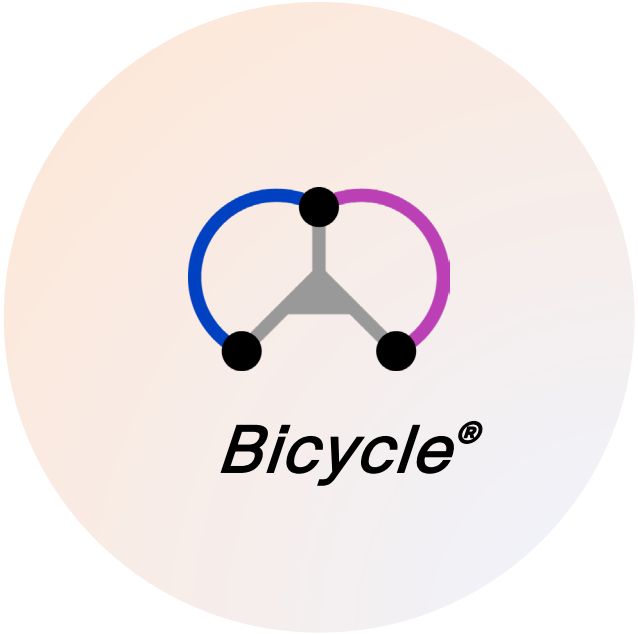
Target / Product	Partner / Sponsor	Indication	Modality	Preclinical	IND-enabling	Phase I	Phase II/ Expansion	Phase III
Internal Programs								
BT5528 (EphA2)		Oncology	Bicycle® Toxin Conjugate					
BT8009 (Nectin-4)		Oncology	Bicycle® Toxin Conjugate					
BT7480 (Nectin-4/CD137)		Immuno-oncology	Bicycle TICA™					
BT7455 (EphA2/CD137)		Immuno-oncology	Bicycle TICA™					
Partnered Programs								
THR-149 (Kallikrein inhibitor)	OXURION	Ophthalmology						
BT1718 (MT1-MMP)	CANCER RESEARCH UK	Oncology	Bicycle® Toxin Conjugate					
BT7401 (multivalent CD137 system agonist)	CANCER RESEARCH UK	Immuno-oncology						
Undisclosed	Genentech A Member of the Roche Group	Immuno-oncology						
Multiple targets	AstraZeneca	Cardiovascular, metabolic, respiratory						
Novel anti-infectives	Innovate UK	Anti-infectives						
Novel CNS targets	Dementia Discovery Fund IONIS	CNS						
Novel neuromuscular targets	IONIS	Neuromuscular						

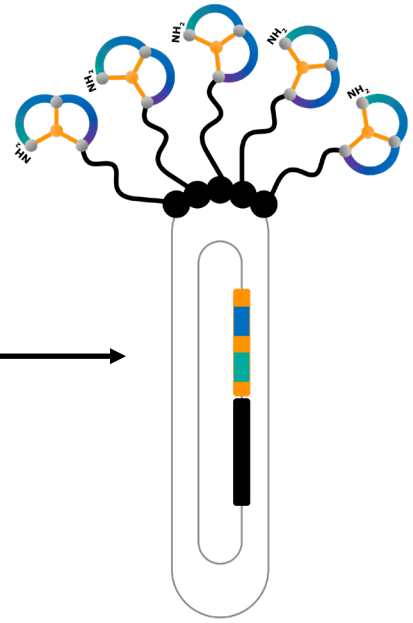
Bicycles are a new therapeutic modality – bicyclic peptides

Short linear peptide

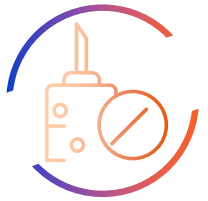


Scaffold
Chemical modification with scaffold





Diverse *Bicycle®* phage libraries (>10^{20})



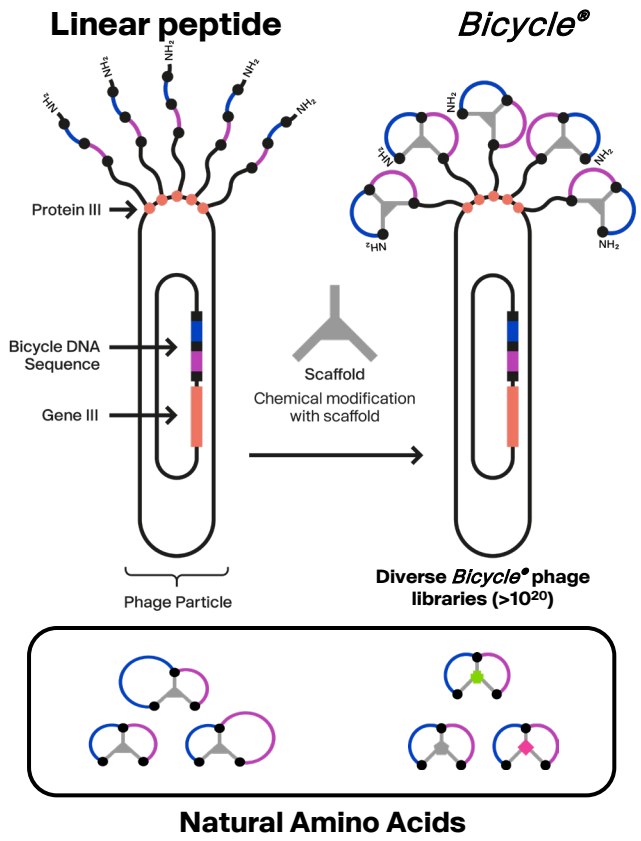
Powerful/versatile platform
- Immense combinatorial potential
- Combines advantages of both small molecules and antibodies

Multi-formats
- Monomeric Bicycles
- Bicycle Toxin Conjugates® (BTCs)
- Tumor-targeted immune cell agonists (*Bicycle* TICAs)

Robust patent protection

Bicycle® platform delivers a toolkit of building blocks to create novel medicines

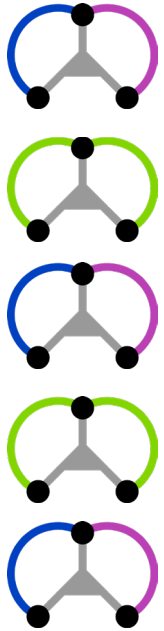
Bicycle® Phage Display - Discovery



Peptide & Medicinal Chemistry

Optimize *Bicycle*® *monomers*

Non-natural Amino Acids

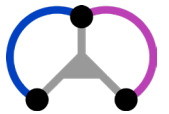


Tumor Targeting and Effector *Bicycles*

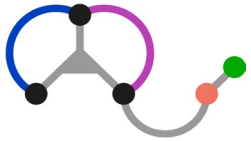
Build and Optimize Therapeutic *Bicycles*

Easy conjugation of Linkers and Payloads

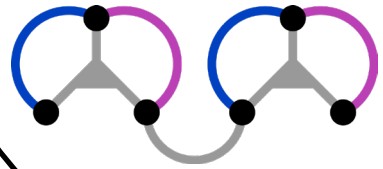
Potential *Bicycle*® Medicines



Monomeric *Bicycles*

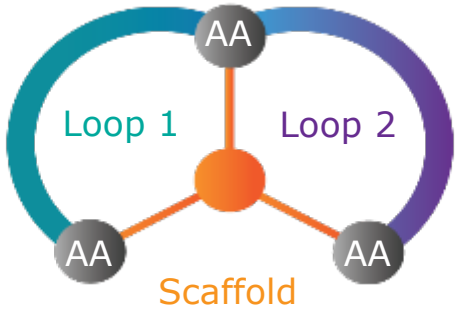


Targeted Drug Conjugates



Targeted/ Multi-specific *Bicycles*

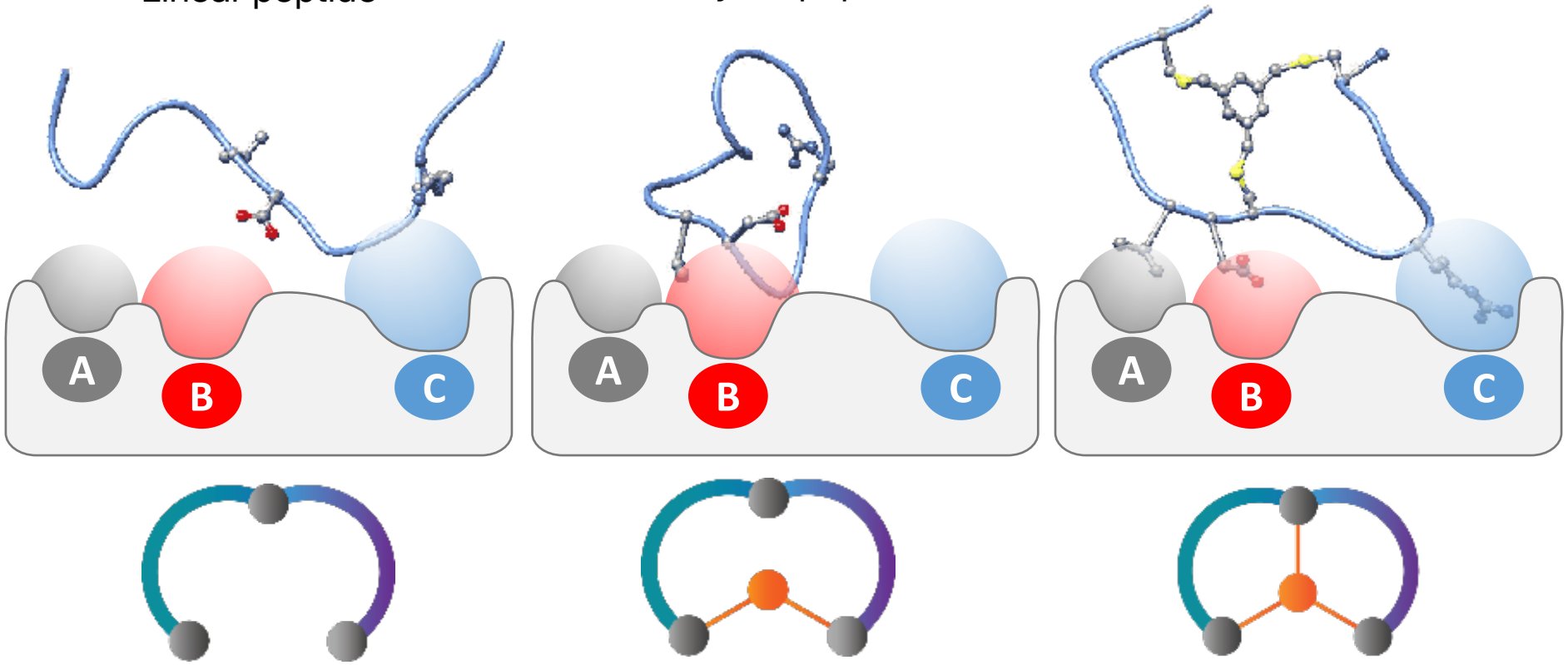
Structural constraints create *Bicycle®* advantage



Linear peptide

Cyclic peptide

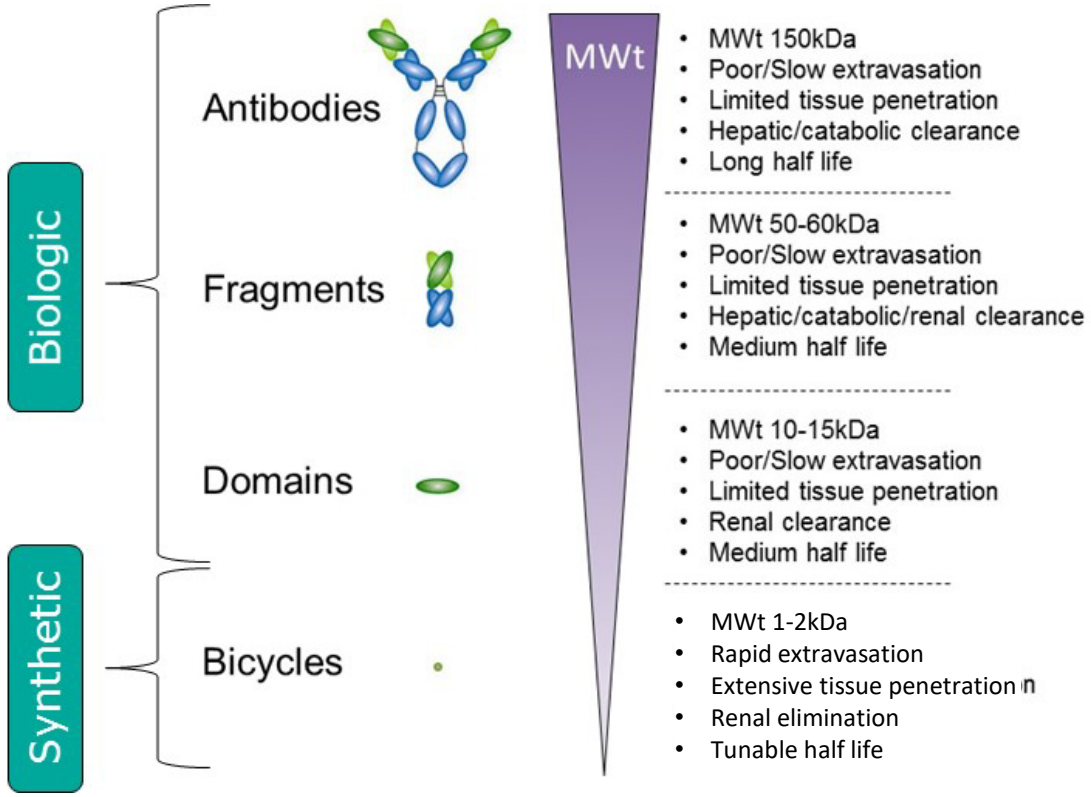
Constrained Bicycle



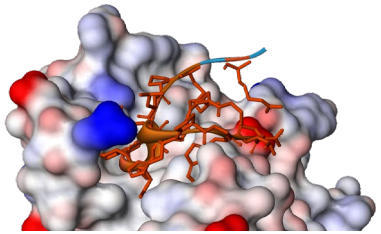
MT1-MMP affinity (FP competition)

BCY00009863 (MT1-MMP) K_i (nM)	BCY00009862 (MT1-MMP) K_i (nM)	BCY00009520 (MT1-MMP) K_i (nM)
>10000 (n=2)	115.1 ± 22.9 (n=2)	1.15 ± 0.07 (n=2)

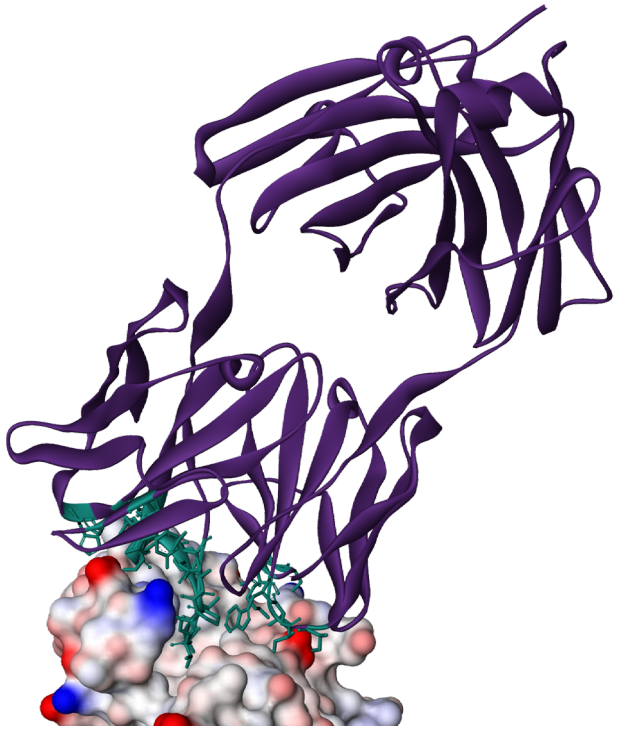
Bicycles are chemically efficient, precision guided and fit for purpose delivery vehicles



	Bicycles	Fab
Weight	2.3 kDa	48 kDa
Size	19 aa	445 aa
Binding residues	16 aa (85%)	24 aa (5%)

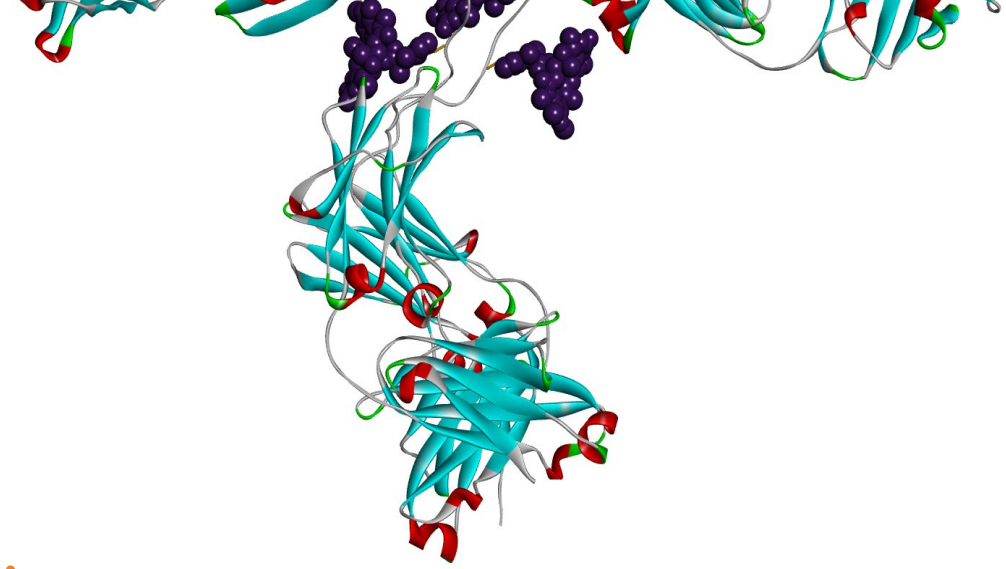


EphA2-binding
Bicycle®



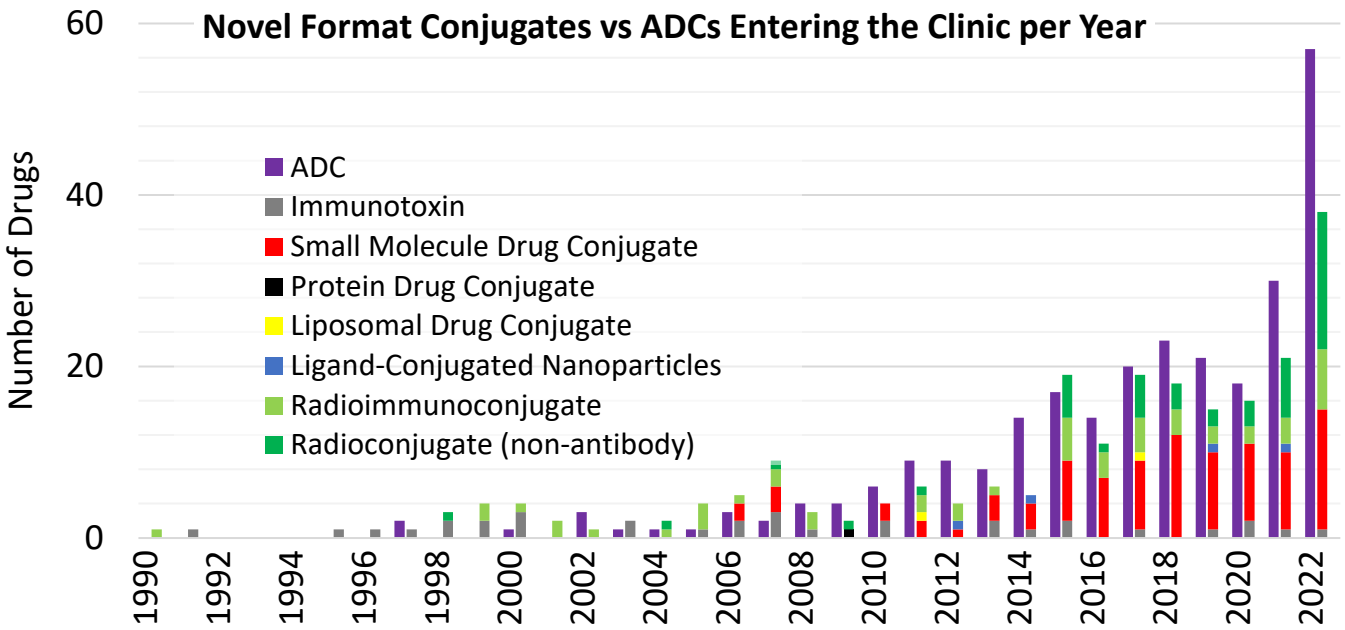
EphA2-binding
Fab

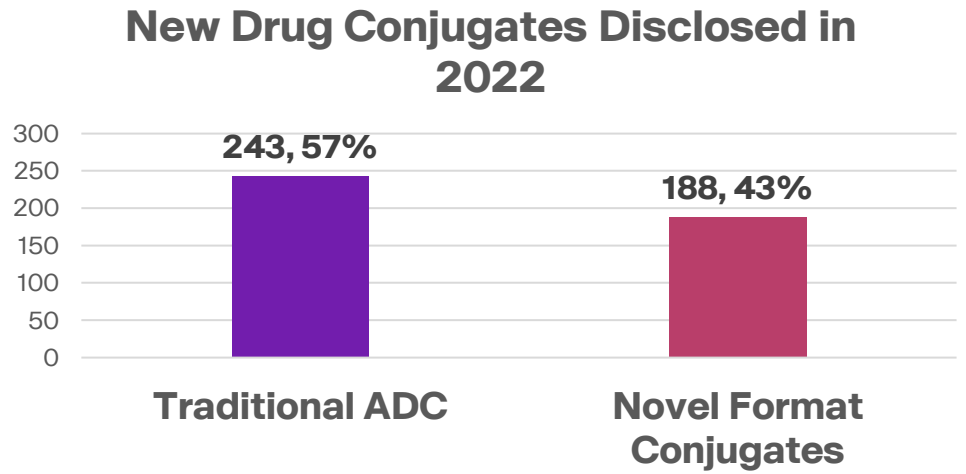
Bicycles are designed to combine the advantages of both small molecules and antibodies

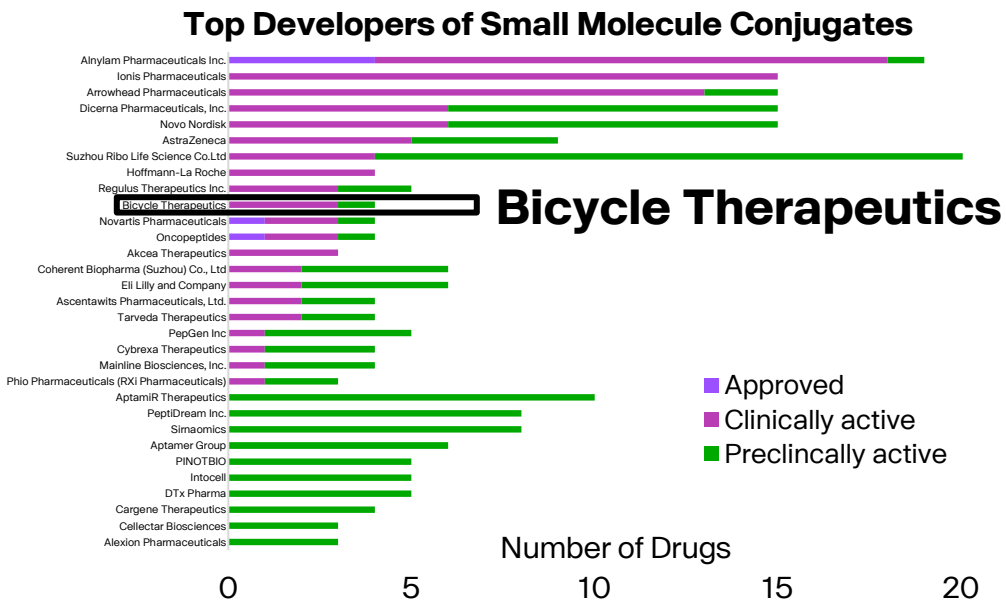


	Bicycle®	Small molecule	Antibody
Small size	**Yes – 1.5-2kDa**	Yes – <0.8kDa	No – >150kDA
Specificity	**High**	Low	Multiple
Chemical synthesis (NCEs)	**Yes**	Yes	No
Rapid tissue penetration	**Yes**	Yes	No
Complex protein targets druggable	**Yes**	Limited	Yes
Route of elimination	**Renal**	Liver	Liver

Novel Format conjugates growth and impact





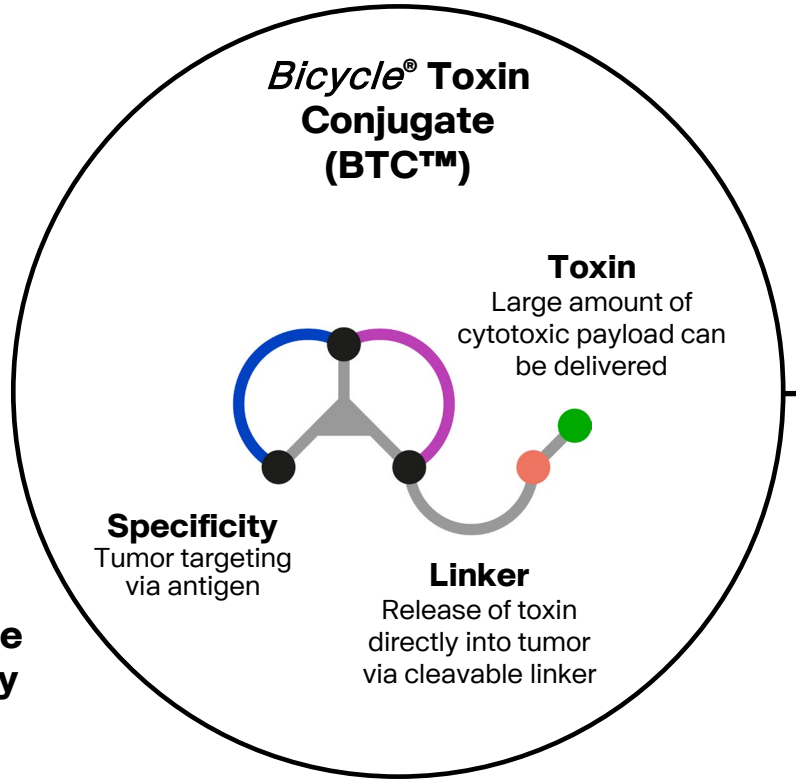


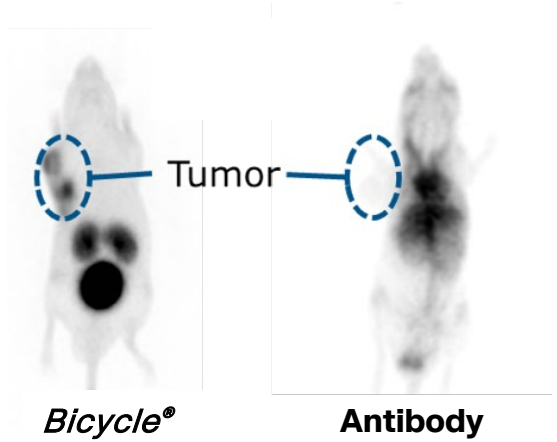
- **The wider conjugates landscape is continuing to expand, with novel formats at the front of this**

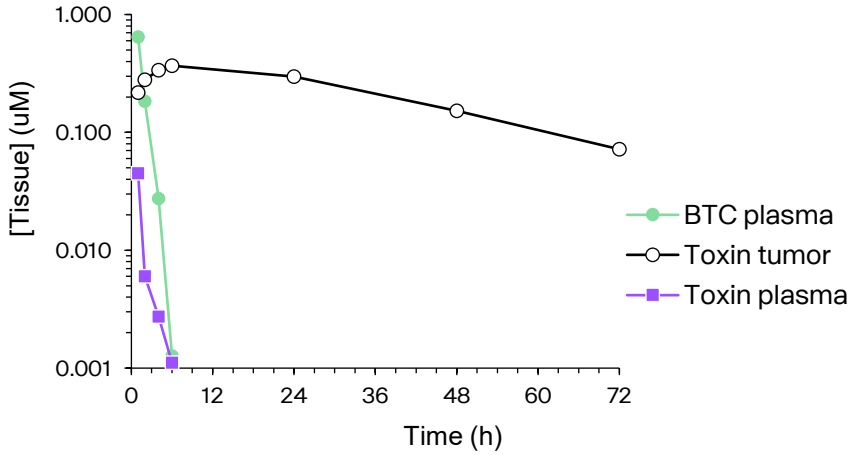
BTCs – preclinical data indicates higher potency and specificity with fewer side effects than ADCs

- **MW of 1.5-2kDa**
- **50-100x smaller than antibodies**

- **High selectivity**
- **Allows more potent toxin to be delivered directly to tumor**

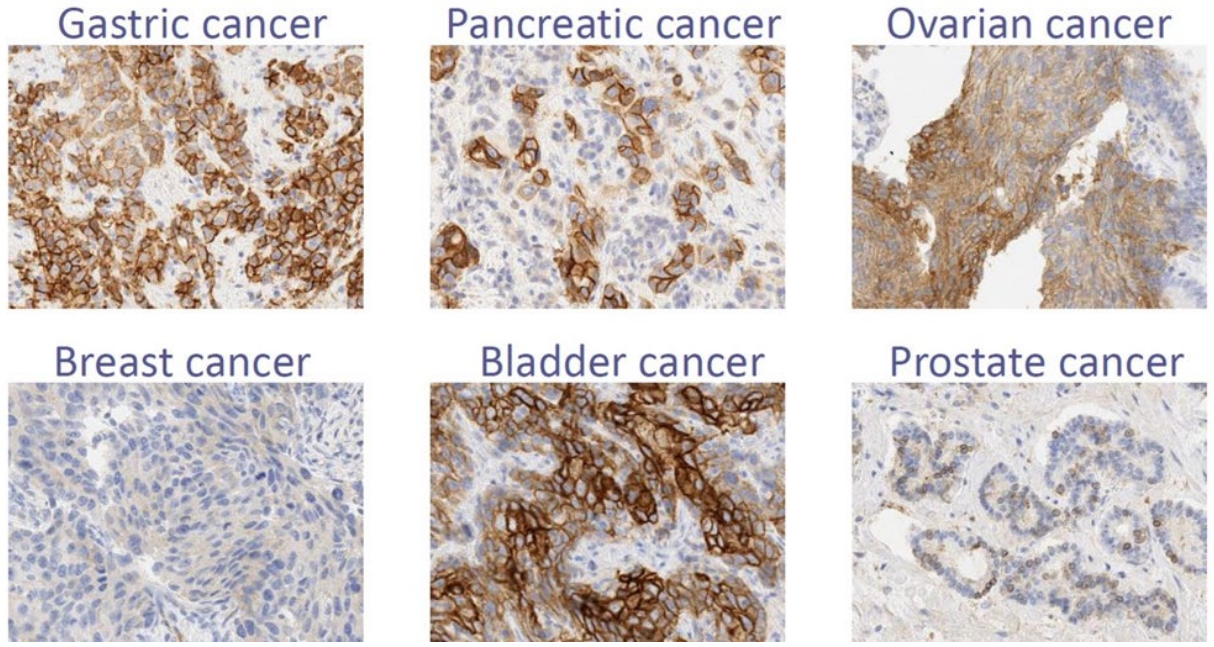






EphA2 is a high value target for the treatment of cancer

- EphA2, a member of Eph subfamily of receptor tyrosine kinases
- Regulates cell migration, adhesion, proliferation and differentiation
- Highly expressed in many human cancers and correlates with tumor progression
  - Ovarian
  - Urothelial
  - NSCLC
  - Head & Neck
  - Gastric
  - TNBC



*Kamoun, et al, Nanoliposomal Targeting of Ephrin Receptor A2 (EphA2): Clinical Translation, Merrimack Pharmaceuticals

Multiple approaches targeting EphA2-expressing tumors have failed

- MEDI-547 (MedImmune) ADC: halted following first dose-cohort coagulopathy[1]
- DS-8895a (Daiichi) antibody: limited efficacy in EphA2+ gastric and esophageal cancer, significant infusion reactions. Discontinued because of poor risk-benefit profile[2]
- MM-310 (Merrimack) antibody-targeted nanoliposome: terminated - “unable to reach optimal therapeutic index”[3]

Invest New Drugs (2013) 31:77–84
DOI 10.1007/s10637-012-9801-2

PHASE I STUDIES

Phase 1, open-label study of MEDI-547 in patients with relapsed or refractory solid tumors

Christina M. Annunziata · Elise C. Kohn · Patricia LoRusso · Nicole D. Houston · Robert L. Coleman · Manuela Buzoianu · Gabriel Robbie · Robert Lechleider

Investigational New Drugs
https://doi.org/10.1007/s10637-022-01237-3

PHASE I STUDIES

A phase 1 safety and bioimaging trial of antibody DS-8895a against EphA2 in patients with advanced or metastatic EphA2 positive cancers

Hui K. Gan[1,2,3] · Sagun Parakh[1,2,3] · F. T. Lee[1] · Niall C. Tebbutt[3] · Malaka Ameratunga[3] · Sze Ting Lee[1,2,4,5] · Graeme J. O'Keefe[1,4] · Sylvia J. Gong[1,4] · Christine Vanrenen[3] · Jaren Caine[3] · Mara Giovannetti[6] · Carmel Murone[1] · Fiona E. Scott[1,2] · Nancy Guo[1] · Ingrid J. G. Burvenich[1,2] · Cameron Paine[4] · Mary J. Macri[6] · Masakatsu Kotsuma[7] · Giorgio Senaldi[7] · Ralph Venhaus[6] · Andrew M. Scott[1,2,4,5]

Clinical Trial · J Immunother Cancer. 2019 Aug 14;7(1):219. doi: 10.1186/s40425-019-0679-9.

Safety, tolerability, pharmacokinetics, and pharmacodynamics of the afucosylated, humanized anti-EPHA2 antibody DS-8895a: a first-in-human phase I dose escalation and dose expansion study in patients with advanced solid tumors

Kohei Shitara [1], Taroh Satoh [2], Satoru Iwasa [3], Kensei Yamaguchi [4], Kei Muro [5], Yoshito Komatsu [6], Tomohiro Nishina [7], Taito Esaki [8], Jun Hasegawa [9], Yasuyuki Kakurai [9], Emi Kamiyama [9], Tomoko Nakata [9], Kota Nakamura [9], Hayato Sakaki [9], Ichinosuke Hyodo [10]

merrimack

Merrimack Discontinues Development of MM-310

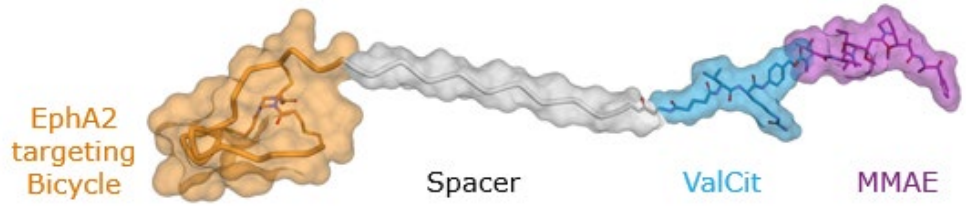
April 4, 2019

-- Safety update shows Phase 1 study unable to reach optimal therapeutic index for MM-310 due to continued observation of cumulative peripheral neuropathy --

-- Company expects to reduce workforce reflective of narrowed preclinical development pipeline; continues to prudently advance programs while completing the assessment of its strategic alternatives --

1. Annunziata et al, Invest New Drugs. 2013 Feb;31(1):77-84
2. Shitara et al, Journal for ImmunoTherapy of Cancer. 2019 7: 219-230 (Ph1 study); Gan et al, Invest New Drugs. 2022 40(4) 747-755
3. Merrimack Pharmaceuticals Inc., press release April 4, 2019

BT5528 is a first-in-class BTC-targeting EphA2



- BT5528 has potential to penetrate solid tumors; approximately 40X smaller than an ADC
- Toxin is released and retained in tumor cells, resulting in tumor cell death and bystander killing
- PK profile distinct from ADCs; renally eliminated, bypassing liver metabolism
- Recently completed dose escalation of Phase I clinical study

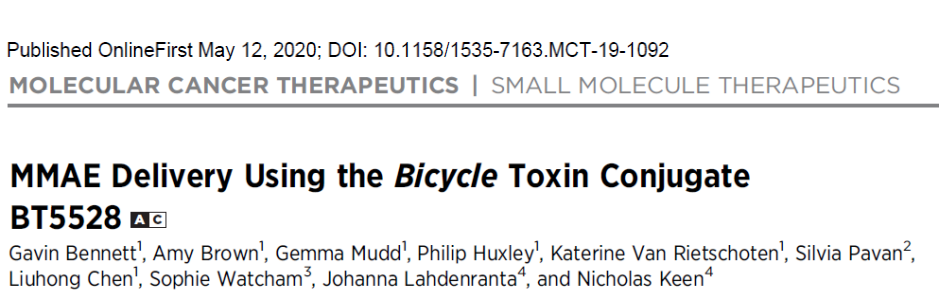

Journal of Medicinal Chemistry

pubs.acs.org/jmc Article

Identification and Optimization of EphA2-Selective Bicycles for the Delivery of Cytotoxic Payloads

Gemma E. Mudd,* Amy Brown, Liuhong Chen, Katerine van Rietschoten, Sophie Watcham, Daniel P. Teufel, Silvia Pavan, Rachid Lani, Philip Huxley, and Gavin S. Bennett

Cite This: https://dx.doi.org/10.1021/acs.jmedchem.9b02129 Read Online


Published OnlineFirst May 12, 2020; DOI: 10.1158/1535-7163.MCT-19-1092

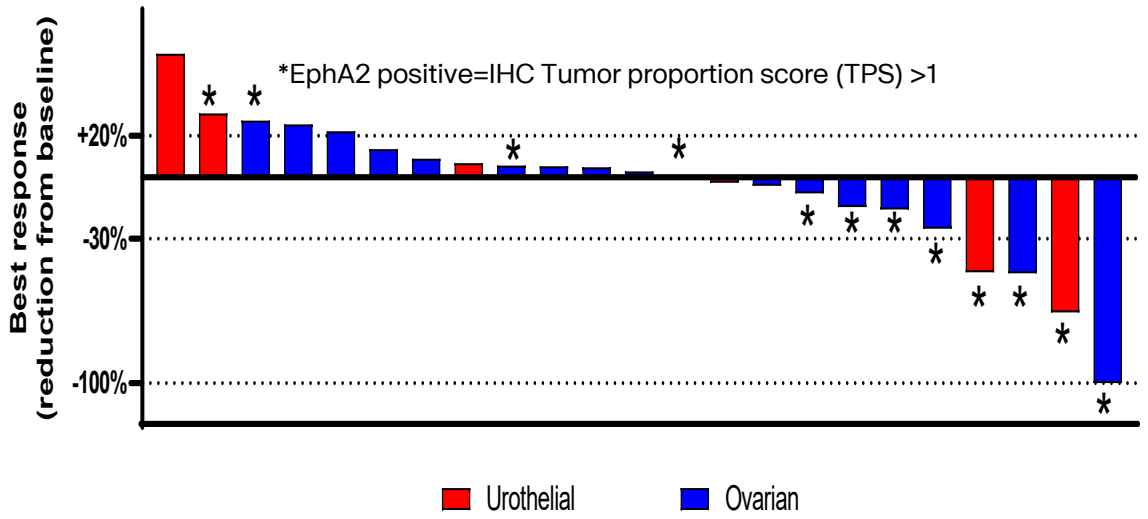
MOLECULAR CANCER THERAPEUTICS | SMALL MOLECULE THERAPEUTICS

MMAE Delivery Using the *Bicycle* Toxin Conjugate BT5528 AC

Gavin Bennett[1], Amy Brown[1], Gemma Mudd[1], Philip Huxley[1], Katerine Van Rietschoten[1], Silvia Pavan[2], Liuhong Chen[1], Sophie Watcham[3], Johanna Lahdenranta[4], and Nicholas Keen[4]

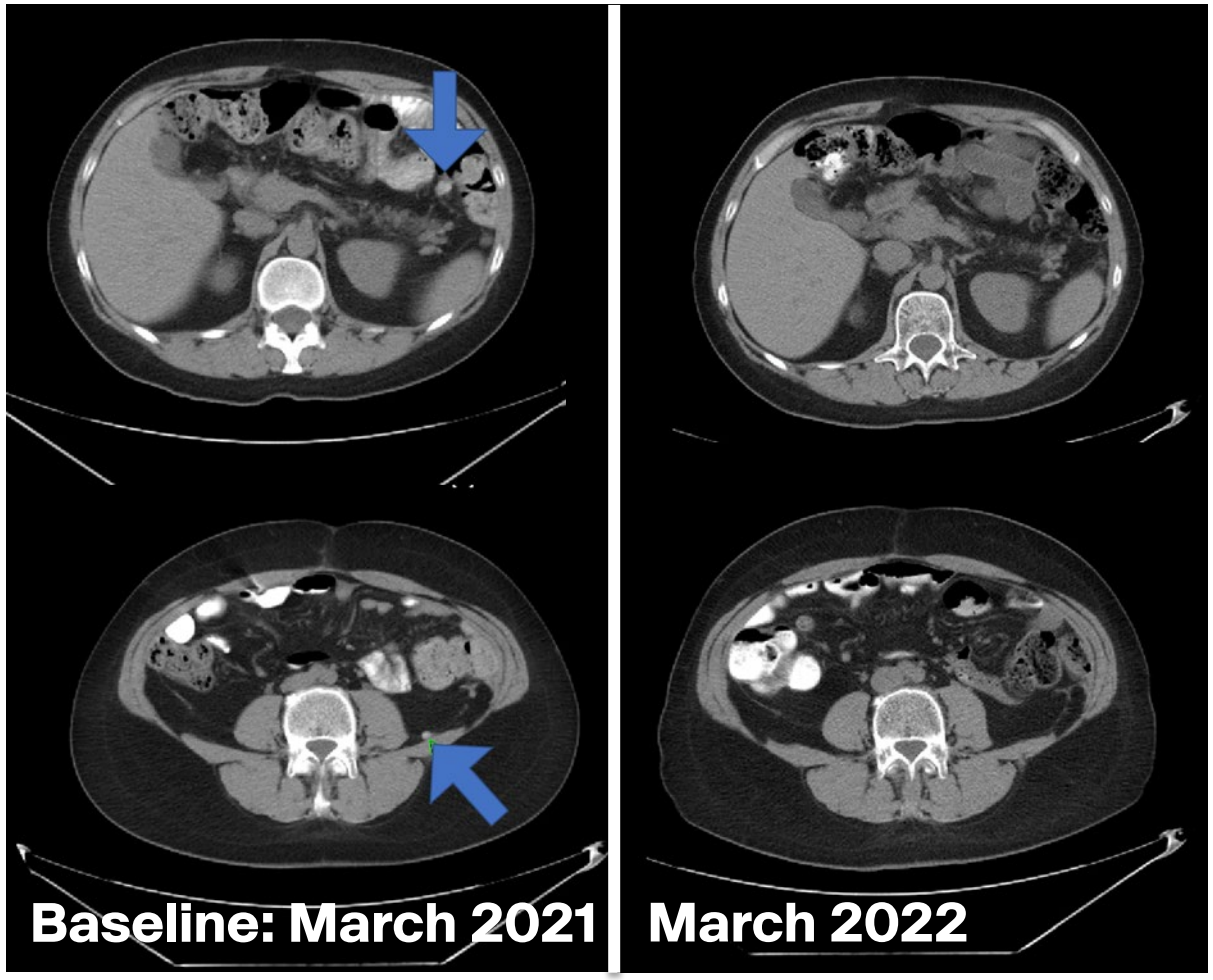
BT5528: Emerging relationship between EphA2 expression and response in ovarian and urothelial cancers

Best response by RECIST in response evaluable patients



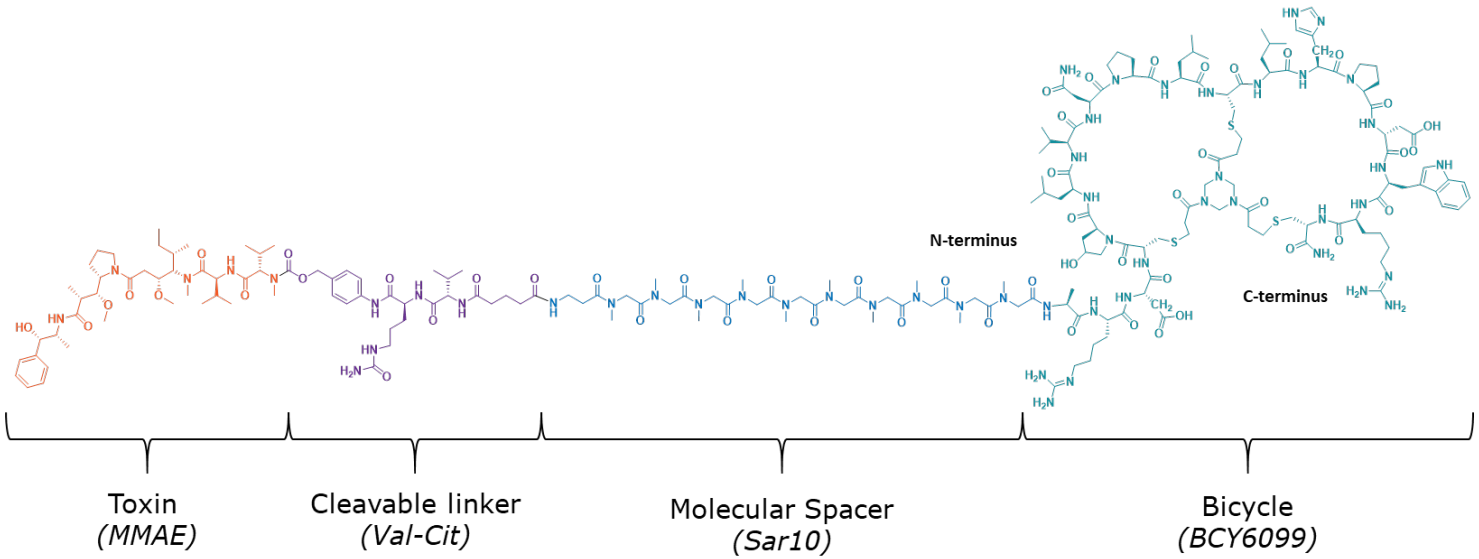
- Waterfall plot showing best response among urothelial and ovarian cancer patients in first in human study
- Immunohistochemistry data suggest EphA2 positive patients more likely to respond to BT5528
- Scan showing complete responder with ovarian cancer

CT scans-abdomen. First in human dose escalation trial.



Sept 22 Phase I update, all data as of Aug 22. For more information, please visit www.bicycletx.com

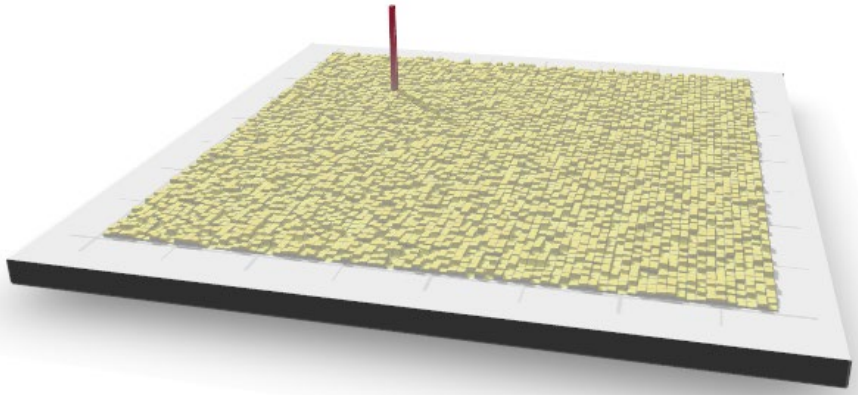
BT5528: structure and profile



High affinity binding to EphA2 protein across species and on cells. Species cross-reactivity, high selectivity.

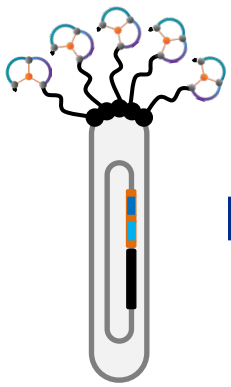
BT5528 affinity	Human	Mouse	Rat	NHP
FP comp (K_i, nM)	1.9 ± 0.9 n=29	5.2 ± 1.9 n=16	1.9 ± 1.3 n=10	
SPR (K_D, nM)	0.9 ± 0.4 n=2	2.0 ± 0.8 n=2	2.7 ± 0.4 n=2	1.0 n=1
Cell binding by HCS ($K_{b\,app}$, nM)	14.8 ± 10.5			

BT5528 only binds EphA2

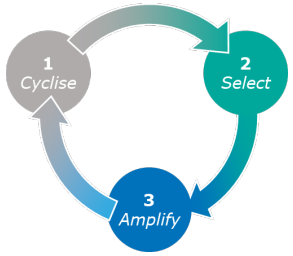


Membrane protein array: no binding of BT5528 @1µM to 5,527 other proteins

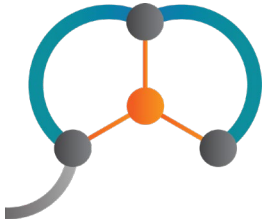
Chemical optimization of a high affinity EphA2 targeting *Bicycle*® with improved properties



2 scaffolds x 10 libraries,
➔ 8 peptide families

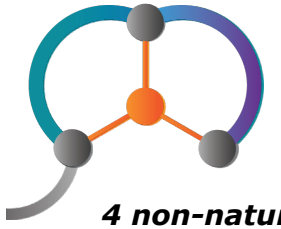


BCY6014

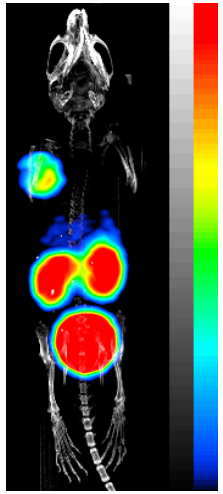


Chemistry Optimisation <40 analogs

BCY6099



4 non-natural amino acids



PET imaging of HT-1080 xenograft at 60 minutes

Modifications (*) to increase polarity, stability and/or potency

BCY6014 Ki = 16 nM – early *Bicycle*

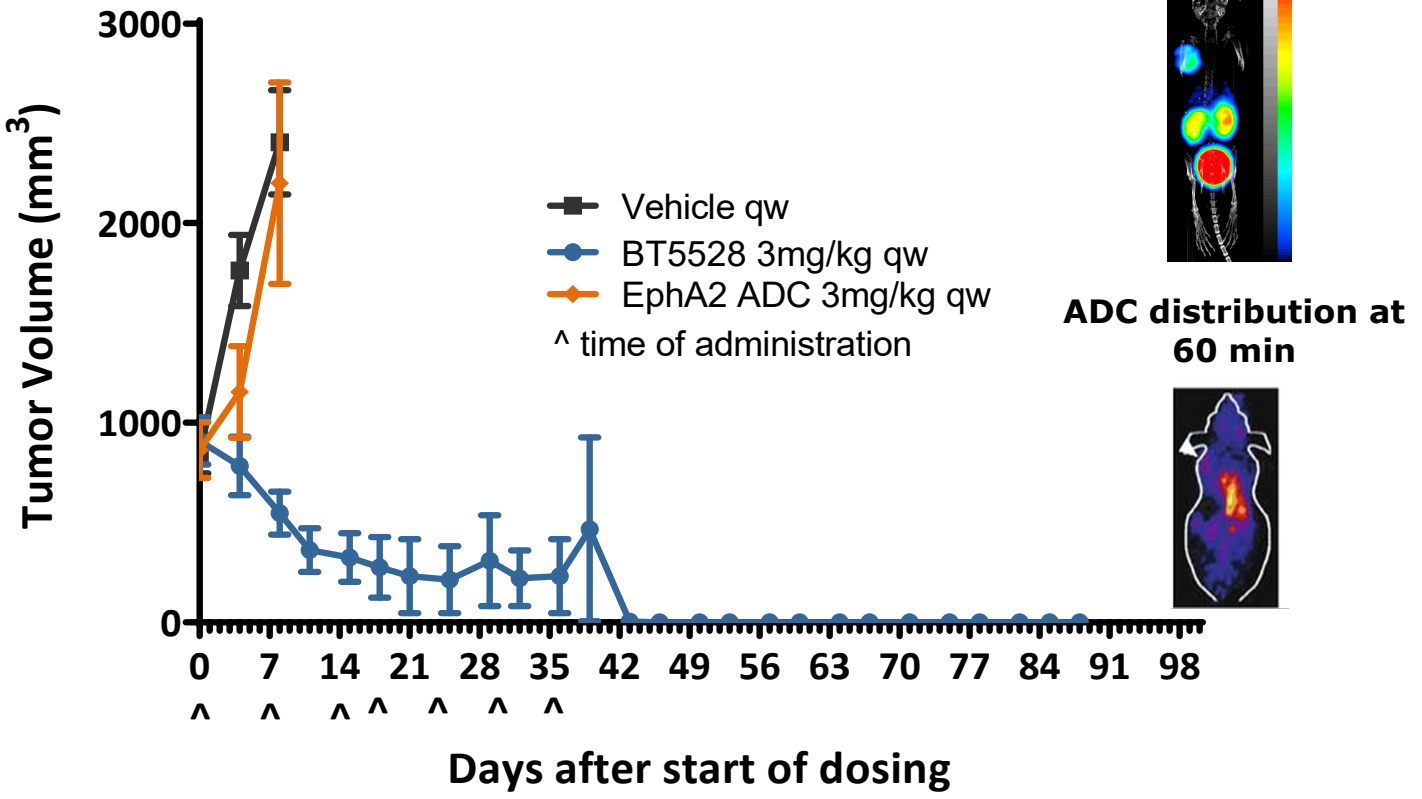
A	R	D	C	P	L	V	N	P	L	C	L	H	P	G	W	T	C	A

BCY6099 Ki = 3 nM – newly optimised *Bicycle*

A	hR	D	C	hyP	L	V	N	P	L	C	L	H	P	dD	W	hR	C	A
	*			*										*		*		

BT5528: activity in difficult-to-treat xenograft models

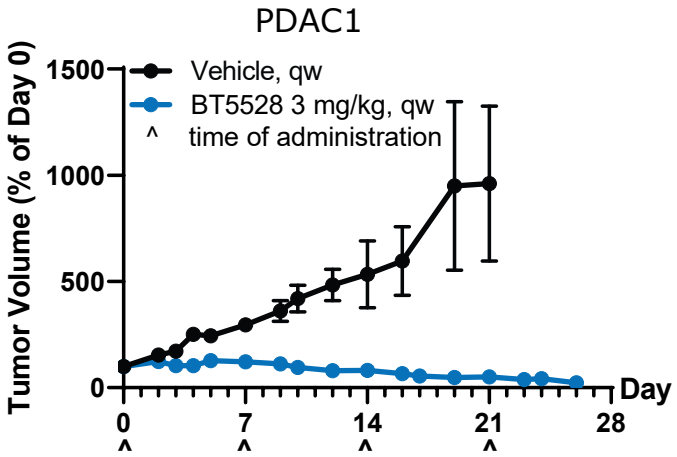
Superior activity to EphA2 ADC in large NSCLC xenograft models

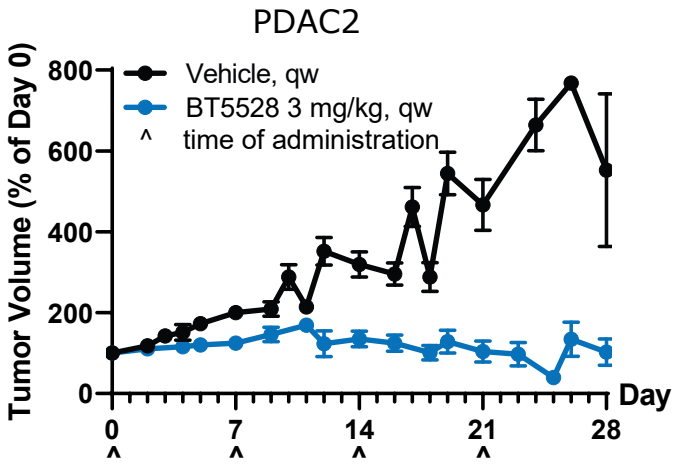


***Bicycle* distribution at 60 min**

ADC distribution at 60 min

Activity in pancreatic xenograft models





BT5528 offers a differentiated approach to EphA2

EphA2 has been viewed as a ”difficult” target

Clinical trial of EphA2-targeting ADC, MEDI-547, terminated after bleeding & liver effects seen at starting dose

BT5528 PK/PD profile offers pre-clinical anti-tumor activity without prolonged vascular exposure

Invest New Drugs (2013) 31:77–84
DOI 10.1007/s10637-012-9801-2

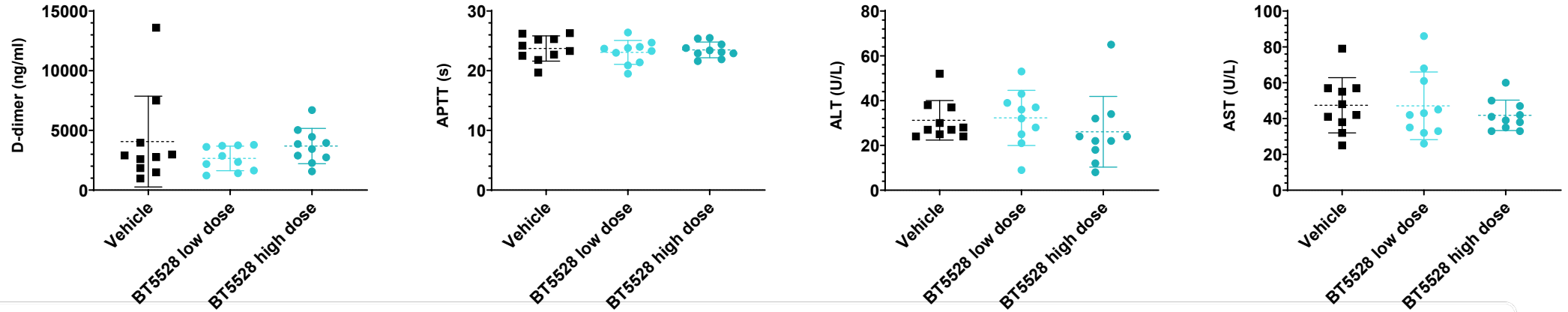
PHASE I STUDIES

Phase 1, open-label study of MEDI-547 in patients with relapsed or refractory solid tumors

Christina M. Annunziata · Elise C. Kohn · Patricia LoRusso · Nicole D. Houston · Robert L. Coleman · Manuela Buzoianu · Gabriel Robbie · Robert Lechleider

Treatment related adverse events	# events (% of patients) n of total
ALT increased	3 (50) 3/6
Haemorrhage	6 (83.3) 5/6

BT5528 toxicology study



- No signs of coagulopathy or bleeding in preclinical species
- No evidence of abnormal liver function
- Dosing to toxin equivalent doses >100x dose of MEDI-547 used in patients

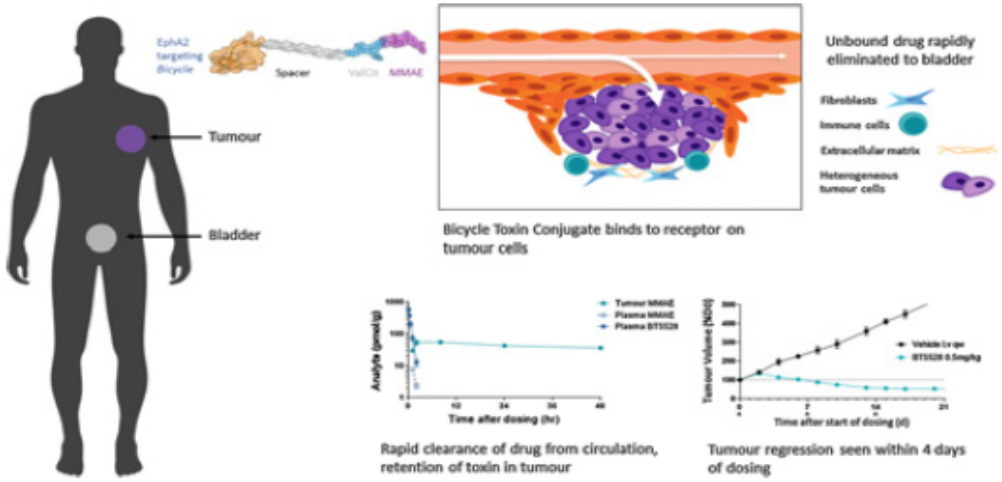
MMAE Delivery Using the *Bicycle* Toxin Conjugate BT5528 AC

Gavin Bennett[1], Amy Brown[1], Gemma Mudd[1], Philip Huxley[1], Katerine Van Rietschoten[1], Silvia Pavan[2], Liuhong Chen[1], Sophie Watcham[3], Johanna Lahdenranta[4], and Nicholas Keen[4]

ABSTRACT

The EphA2 receptor is found at high levels in tumors and low levels in normal tissue and high EphA2 expression in biopsies is a predictor of poor outcome in patients. Drug discovery groups have therefore sought to develop EphA2-based therapies using small molecule, peptide, and nanoparticle-based approaches (1–3). However, until now only EphA2-targeting antibody–drug conjugates (ADC) have entered clinical development. For example, MEDI-547 is an EphA2-targeting ADC that displayed encouraging antitumor activity in preclinical models and progressed to phase I clinical testing in man. Here we describe the development of BT5528, a bicyclic peptide ("*Bicycle*") conjugated to the auristatin derivative maleimidocaproyl-monomethyl auristatin E to generate the *Bicycle* toxin conjugate BT5528. The report compares and contrasts the Pharmacokinetics (PK) characteristics of antibody and *Bicycle*-based targeting systems and discusses how the PK and payload characteristics of different delivery systems impact the efficacy—toxicity trade off which is key to the development of successful cancer therapies. We show that BT5528 gives rise to rapid update into tumors and fast renal elimination followed by persistent toxin levels in tumors without prolonged exposure of parent drug in the vasculature. This fast in, fast out kinetics gave rise to more favorable toxicology findings in rats and monkeys than were observed with MEDI-547 in preclinical and clinical studies.

Graphical Abstract: http://mct.aacrjournals.org/content/molcanther/19/7/1385/F1.large.jpg.



BT5528: EphA2 targeted BTC™

Erythropoietin-producing hepatocellular A2 receptor: member of Eph subfamily of receptor tyrosine kinases

- Regulates cell migration, adhesion, proliferation and differentiation
- Overexpressed in human cancers and correlates with tumor progression
- Development of MEDI-547 (MedImmune) in ovarian cancer was halted following serious bleeding events in phase I

Internal	Target	Modality	Pre-clinical	IND-enabling	Phase I	Phase II
Bicycle	EphA2	*Bicycle*® Toxin Conjugate				

- BT5528-100: Phase I/II multi-center first-in-human study in patients with advanced solid tumors associated with EphA2 expression
- NCT04180371 Study ongoing
- Clinical update presented by Dr Meredith McKean at AACR-NCI-EORTC Triple Meeting Oct 7 2021
- Topline data from escalation phase released Sep 2022
  - BT5528 demonstrates anti-tumor activity in highly refractory ovarian and urothelial cancer patients
  - Emerging safety profile distinguishes it from other EphA2-targeted molecules
  - No coagulopathy or bleeding seen related to BT5528 dosing
- Dosing at recommended Phase II dose of 6.5 mg/m^2 q2w in expansion cohorts is ongoing
- Further BT5528 update in 2023

1. Annunziata, Christina M., et al. "Phase 1, open-label study of MEDI-547 in patients with relapsed or refractory solid tumors." *Investigational new drugs* 31.1 (2013): 77-84.

BT8009: Nectin-4 targeted BTC™

Nectin-4:

A cell adhesion molecule and one of four members of the nectin family

All nectins share the same overall structure defined by three extracellular immunoglobulin domains, a single transmembrane helix and an intracellular domain

- Overexpressed in human cancers and correlated with tumor progression
- Solid tumors with high levels of Nectin-4 expression are urothelial, TNBC, ovarian, head & neck and NSCLC

Internal	Target	Modality	Pre-clinical	IND-enabling	Phase I	Phase II
Bicycle	Nectin-4	*Bicycle*® Toxin Conjugate				

- BT8009-100: Phase I/II Study of the Safety, Pharmacokinetics, and Preliminary Clinical Activity of BT8009 in Patients With Nectin-4 Expressing Advanced Malignancies
- NCT04561362
- Study ongoing
- BT8009 Phase I trial results released at ASCO GU Feb 2023
- For more information, please visit www.bicycletx.com

Nectin-4 Bicycle® optimization from lead to BT8009

Parent *Bicycle*

Ac C P F G C M K N W S W P I W C

Amino Acids Important For Target Engagement

Poor solubility, short half-life. AAs required for binding identified

Ki (nM)	cLogP	$t_{1/2}$ (plasma)
18.4	-6.98	1.3h

Stabilised *Bicycle*

Ac C P F d C M hArg N W S W P I W C

Improve stability, hydrophilicity

Improvements made to half-life and hydrophilicity, whilst retaining binding AAs

Ki (nM)	cLogP	$t_{1/2}$ (plasma)
13	-6.74	>24h

Optimised *Bicycle*

Ac C P 1Nal d C M hArg D W S T P Hyp W C

+ affinity

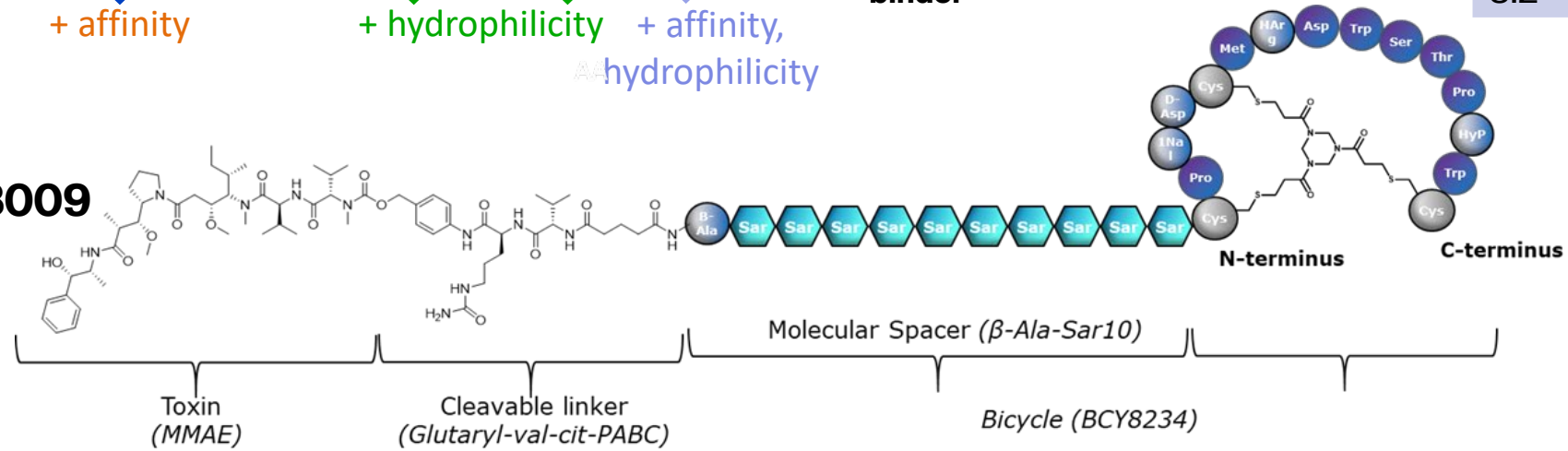
+ hydrophilicity

+ affinity, hydrophilicity

AAs further optimised to increase affinity, improve hydrophilicity. Selected as candidate peptide binder

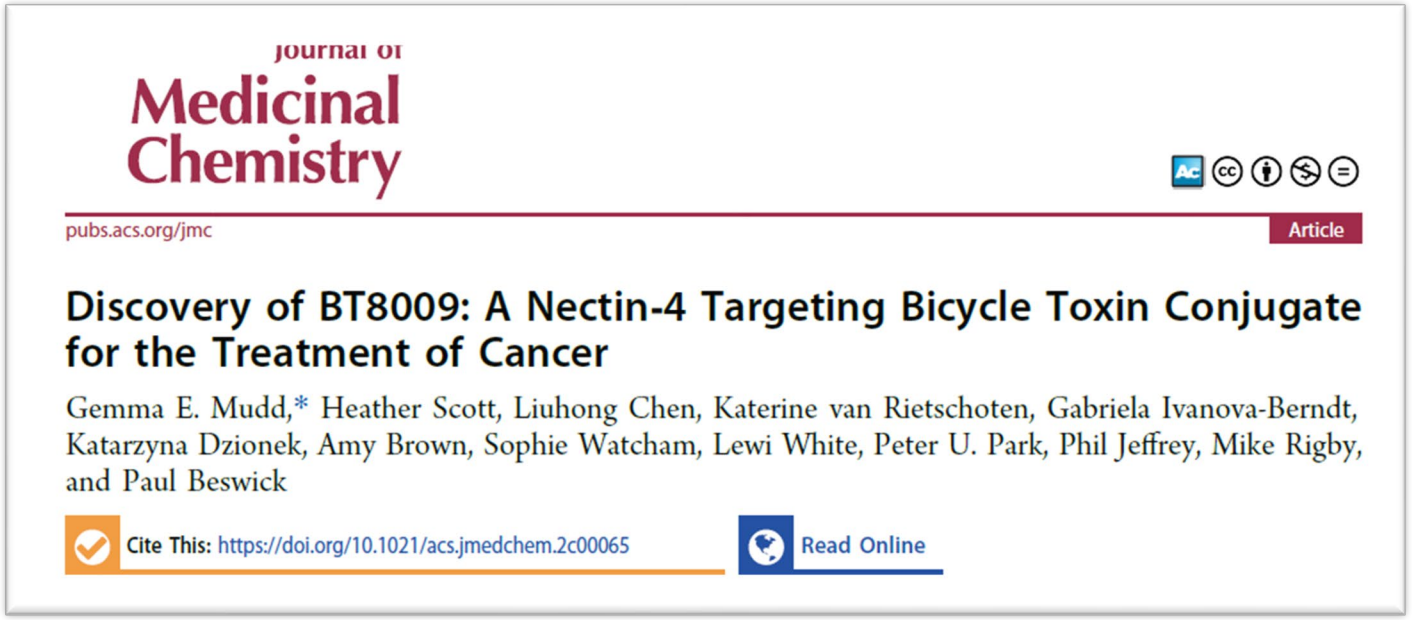
Ki (nM)	cLogP	$t_{1/2}$ (plasma)
3.2	-13.32	>24h

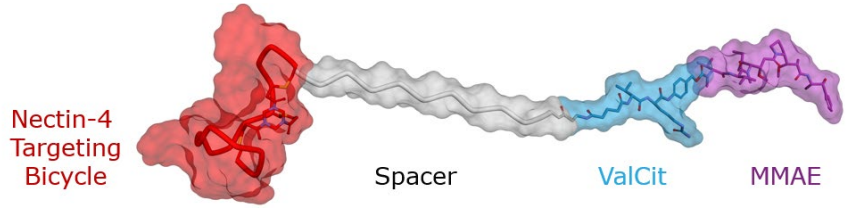
BT8009



MW=4173.8

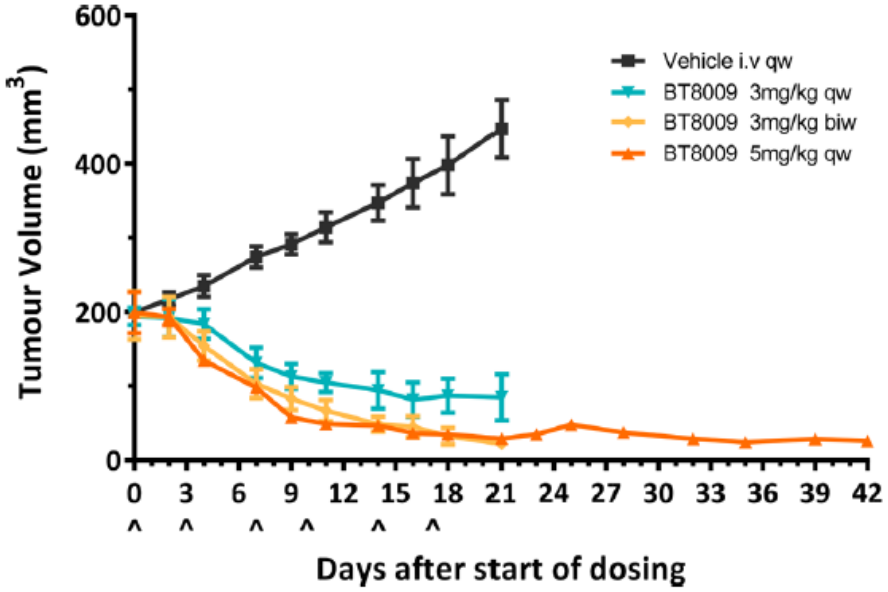
BT8009: Nectin-4 targeted BTC



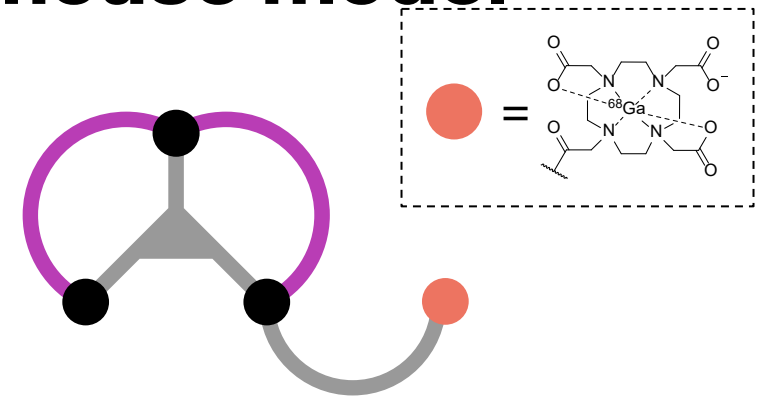


Human Nectin-4 KD (nM)	plasma protein binding (%)		In vitro plasma stability		mouse pharmacokinetics 3 mg/kg, IV (bolus)		
	Mouse	Human	mouse	human	$T_{1/2}$ (h)	Clp (mL/min/kg)	Vss (L/kg)
2.50	88.2	79.3	4.4	>57.8	1.0	3.5	0.25

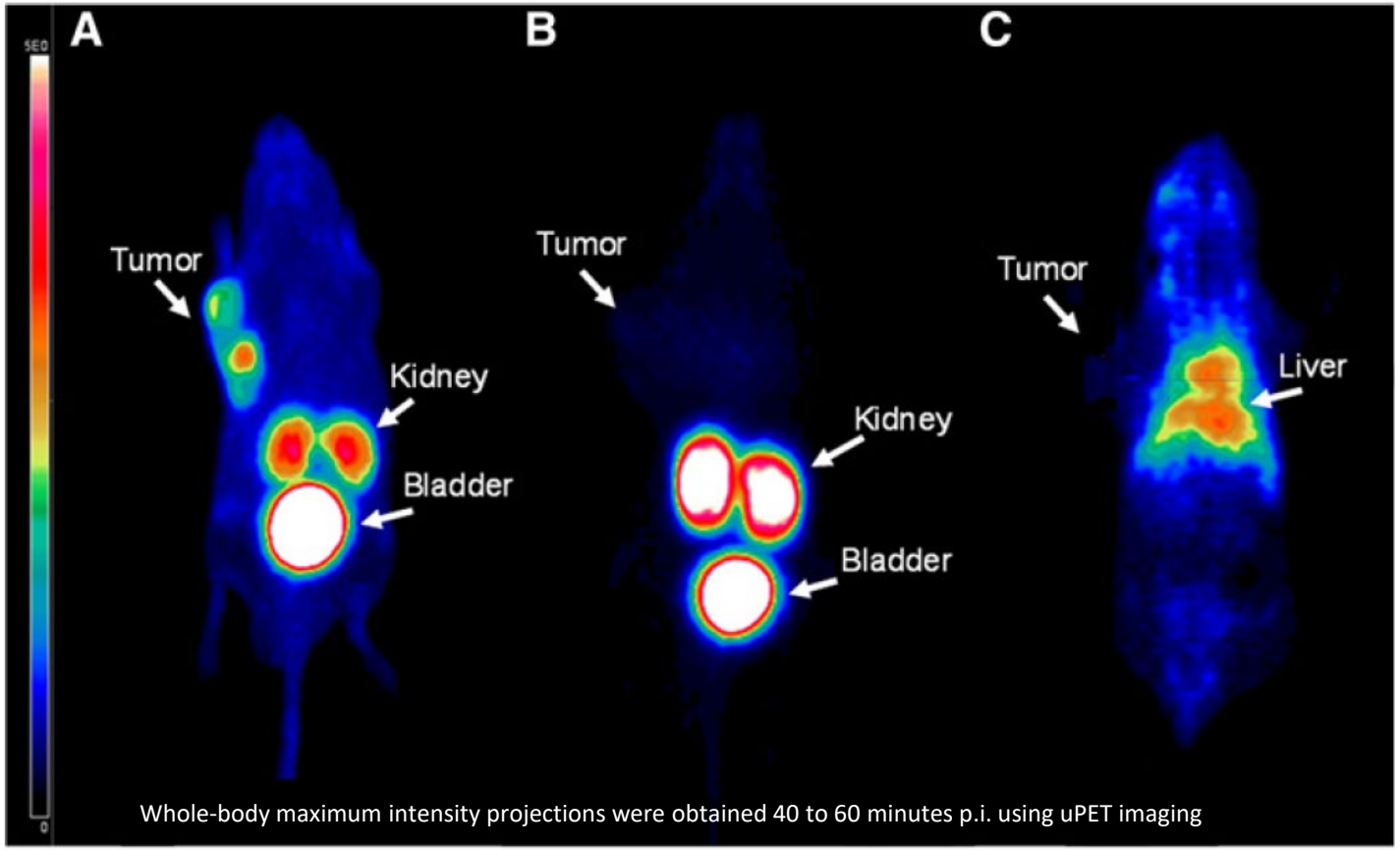
Activity in breast adenocarcinoma (MDA-MB468) CDX model



MT1-MMP targeting BRC shows far superior tumor uptake and contrast versus mAb in mouse model



MT1-MMP overexpressed in variety of cancers (non–small cell lung, gastric and breast)

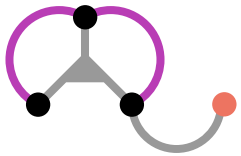


Convergence and Technologies

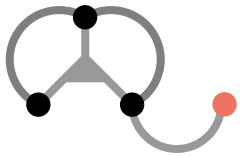
Cancer Research

Bicyclic Peptides as a New Modality for Imaging and Targeting of Proteins Overexpressed by Tumors

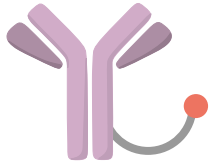
Matthias Eder[1,2], Silvia Pavan[3], Ulrike Bauder-Wüst[4], Katerine van Rietschoten[3], Ann-Christin Baranski[1,2], Helen Harrison[3], Spencer Campbell[3], Catherine L. Stace[3], Edward H. Walker[3], Liuhong Chen[3], Gavin Bennett[3], Gemma Mudd[3], Ursula Schierbaum[5], Karin Leotta[5], Uwe Haberkorn[5,6], Klaus Kopka[4], and Daniel P. Teufel[3]



MT1-MMP targeting BRC



Non-binding BRC



MT1-MMP targeting mAb conjugate

Bicycle® dkfz.

Potential of Bicycles as precision guided therapeutics

Bicycles rapidly penetrate tumour, eliminated through renal route

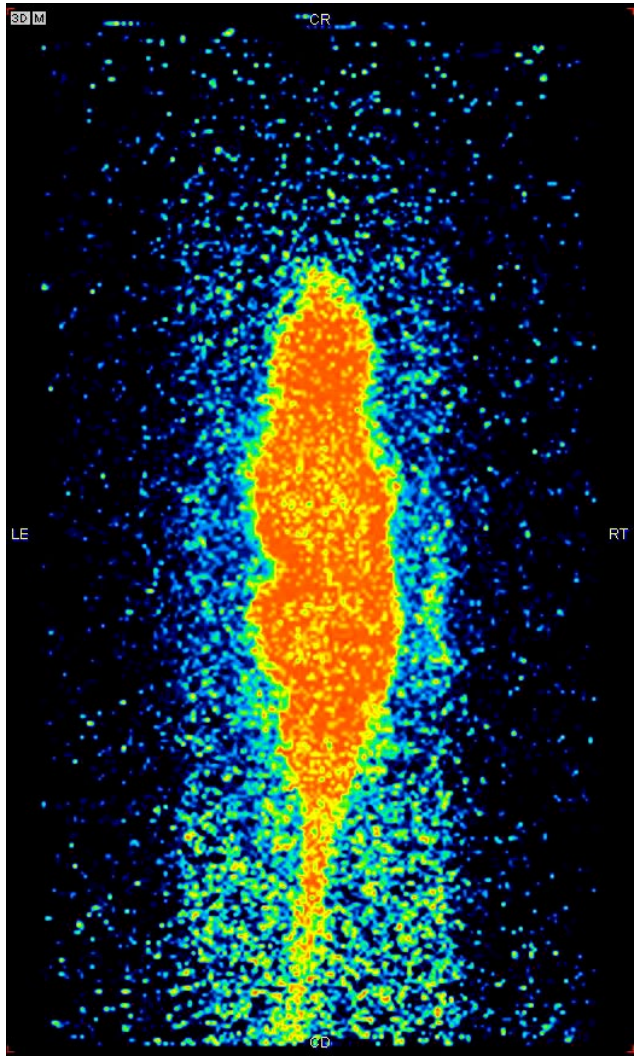
Short systemic exposure & tumour retention

Activity at site of action with reduced body burden

Can be used to deliver key pharmacological activity for solid tumours:

Cytotoxic payloads

Immune-oncology

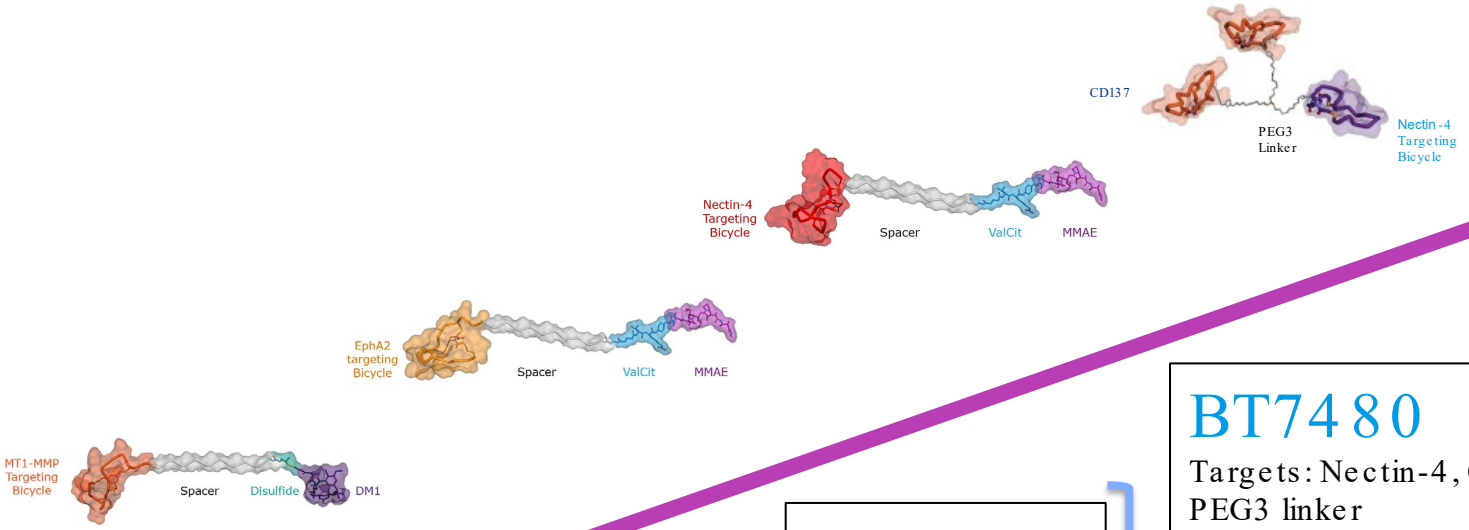


DKTK German Cancer Consortium

PET imaging of Bicycle-radioisotope conjugate, 0-60min post-injection

Imaging conducted in collaboration with
Prof. Dr. Matthias Eder
Dr. Ann-Christin Eder
Mohamed El Fakiri

Diversifying the *Bicycle*® platform



Targeted ASO/SiRNA delivery

BT1718
Target: MT1-MMP
DM1 payload
Disulfide linker

BT5528
Target: EphA2
MMAE payload
Val-Cit linker

BT8009
Target: Nectin-4
MMAE payload
Val-Cit linker

BT7480
Targets: Nectin-4, CD137
PEG3 linker

Validation

BT7455
Targets: EphA2, CD137
PEG3 linker
Next Bicycle TICA ™ scheduled for clinic

NK-TICA™

Validation

Next-gen BTCs
Different targets, linkers and payloads

Radiopharm

FIH 2018 2019 2020 2021 2023 and beyond

Summary

Bicycles offer a potential new modality for oncology therapeutics

- Antibody-like affinity and selectivity in a small molecule
- Chemically synthesized
- Rapid distribution to solid tumors, elimination via renal route

Bicycle TICAs show promise for targeted stimulation of immune cells in tumors

- BT7480 entered the clinic Q4 2021
- BT7455 (EphA2-CD137 Bicycle TICA™) in IND-enabling stage
- NK-TICA™ programs targeting natural killer (NK) cells identified and moving into lead optimization

Bicycle Toxin Conjugates® progressing in clinical studies

3 conjugates in clinical trials

- Clinical PK profile consistent with preclinical prediction
- Preliminary signs of anti-tumor activity seen
- Emerging safety profile supports potential of Bicycle platform

Thank you

Bicycle®

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