

## **Constrained peptides Unconstrained thinking**

**bicycle** therapeutics

July 2021

## **Forward-looking statements**

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 financial or business performance, conditions, plans, prospects, trends or strategies and other financial and business matters; our current and prospective product candidates, planned clinical trials and preclinical activities, current and prospective collaborations 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 forwardlooking statements. These risks and uncertainties include, but are not limited to, risks related to the ongoing COVID-19 pandemic, 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 (SEC) on March 11, 2021 as well as in other filings Bicycle 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.



We aim to redefine what's possible for people with cancer and other serious diseases by pioneering a new and differentiated class of innovative treatments

**Bicycles** are a novel Exploring by modality designed to address of novel therapeutic needs unmet by oncolor

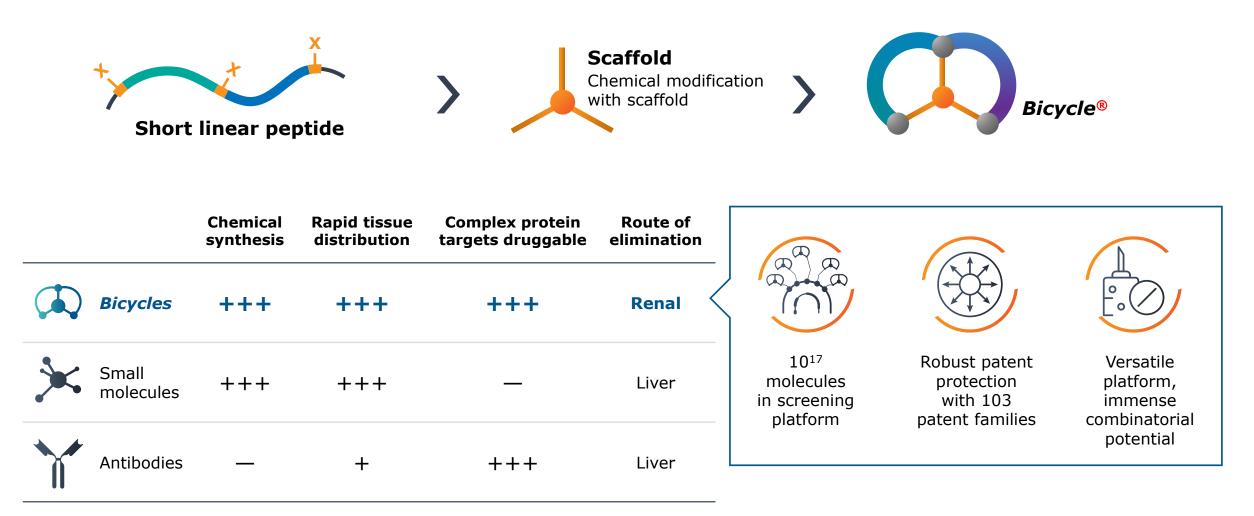
Exploring broad potential of novel technology in oncology & beyond through **partnerships**  4 assets in Phase I/II

trials, represent potential first-in-class / best-in-class medicines for oncology & ophthalmology\*



conventional approaches

# Bicycles are a new therapeutic modality wholly-owned by Bicycle Therapeutics





# Business strategy designed to explore full potential of *Bicycle*<sup>®</sup> technology



Oncology

*Bicycles* are perfect for solid tumors:

- Selective, controlled delivery to tumor
- Small size
- Drug targets intractable to other modalities
- Renal elimination



*Bicycle* Toxin Conjugates



Tumor Targeted immune cell agonists (TICAs)



## **Other serious diseases**

Exploring broad application of *Bicycles* beyond oncology through validating partnerships with leading therapeutic experts

AstraZeneca

Innovate UK

Dementia Discovery Fund

OXURION°





## **Robust proprietary and partnered pipeline**

Partner / Sponsor	Therapeutic Interest	Preclinical	IND- enabling	Phase I	Phase II
	Oncology				
	Oncology				
CANCER RESEARCH UK	Oncology				
	Oncology				
	Oncology				
CANCER RESEARCH UK	Oncology				
Genentech A Member of the Roche Group	Oncology				
O X U R I O N°	Ophthalmology				
AstraZeneca	Respiratory				
Innovate UK	Anti-infectives				
Dementia Discovery Fund	CNS				
IOŃIS™	Neuromuscular				
	CANCER RESEARCH WK CANCER CESEARCH CESEARCH CESEARCH CESEARCH CUR ION° AstraZeneca COXU R I O N° AstraZeneca Innovate UK	SponsorInterestSponsorInterestOncologyOncologyImport StreetOncologyImport StreetOncologyImport StreetOncologyImport StreetOncologyImport StreetOncologyImport StreetOncologyImport StreetOncologyImport StreetOphthalmologyImport StreetAnti-infectivesImport StreetCNS	SponsorInterestPreclinicalOncologyOncologyOncologyOncologyImage: Specific ConcologyOncologyOncologyOncologyOncologyOncologyOncologyOncologyOncologyOncologyOncologyOncologyImage: Specific ConcologyOncologyImage: Specific ConcologyOncologyImage: Specific ConcologyOncologyImage: Specific ConcologyOncologyImage: Specific ConcologyOncologyImage: Specific ConcologyImage: Specific Concology<	SponsorInterestPreclinicalenablingOncologyOncologyInterestInterestOncologyOncologyInterestInterestOncologyOncologyInterestInterestOncologyOncologyInterestInterestOncologyInterestInterestInterestOncologyInterestInterestInterestOncologyInterestInterestInterestOncologyInterestInterestInterestOncologyInterestInterestInterestInnovate UKAnti-infectivesInterestInterestInnovate UKInterestInterestInterestInnovate UKInterestInterestInterestInnovate UKInterestInterestInterestInnovate UKInterestInterestInterestInnovate UKInterestInterestInterestInnovate UKInterestInterestInnovate UKInterestInterestInterest<	SponsorInterestPreclinicalenablingPhase IOncologyOncologyImage: SponsorImage: SponsorImage: SponsorOncologyOncologyImage: SponsorImage: SponsorImage: SponsorOncologyOncologyImage: SponsorImage: SponsorImage: SponsorOncologyImage: SponsorImage: SponsorImage: SponsorImage: SponsorInnovate UKAnti-infectivesImage: SponsorImage: Sponsor

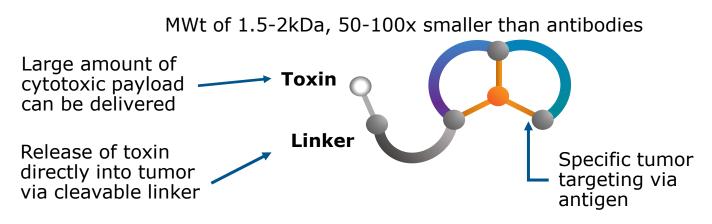
therapeutics

## **Bicycle Toxin Conjugates** (BTCs)



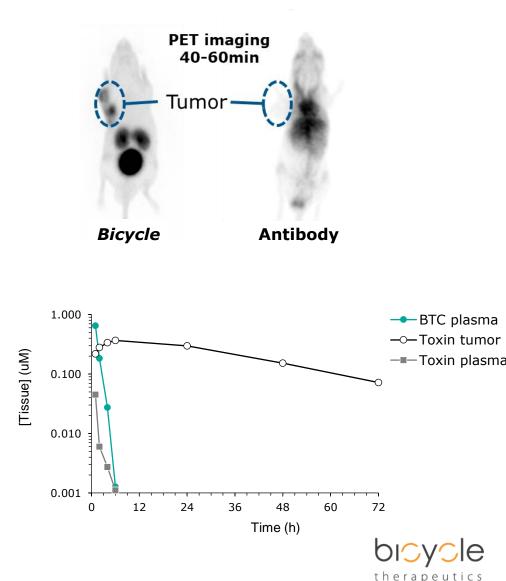
#### BTC IO

# **Bicycle** Toxin Conjugates<sup>®</sup>: Designed to be precision targeting therapeutics

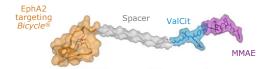


## BTCs offer advantages over antibody drug conjugate (ADC) and small molecule approaches

Property	втс	ADC	Importance
Tumor penetration	$\checkmark$	?	Access to site of action
Tumor retention	~	?	Maintenance at site of action, lower total body burden
Short systemic exposure	~	×	Minimizes toxicity, enhances combinability
Reduced liver metabolism	~	×	Improved safety profile
Renal elimination	$\checkmark$	×	Improved safety profile
Flexible dosing	~	×	Tailored dosing regimen minimizing toxicity



## **BT5528: Exemplifies potential of BTCs to address failed ADC targets**



#### Background

BTC

- BT5528 is highly selective for EphA2, which:
  - Regulates cell migration, adhesion, proliferation and differentiation
  - Is overexpressed in many difficult to treat tumors
  - Has been intractable to ADC approaches

#### Status

- Phase I/II trial ongoing: open-label trial in EphA2(+) solid tumors
- Monotherapy and combination with nivolumab arms continue to enroll
- Patients are selected using proprietary IHC assay
- Topline data expected in 2021

#### Progress

- Clinically derisked coagulopathy and acute liver toxicity associated with EphA2-targeted ADCs
- Dose escalation ongoing; currently administered doses in the predicted therapeutic range
- Preliminary findings consistent with anti-tumor activity have been observed

#### **Patient Population**

 EphA2 is expressed in 52% of pancreatic cases; significant expression (>30%) in NSCLC, gastric, head & neck, and bladder cancers



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## **BT5528 clinical experience**\*

### Experience prior to introduction of selection assay

- $\circ$  19 pts have been dosed between 2.2 and 8.5 mg/m<sup>2</sup>, either in combination with nivolumab (N=7) or monotherapy (N=12)
  - Duration of treatment: 3-34 weeks. Tumor types: pancreatic, ovarian, urothelial, NSCLC, TNBC, upper GI, Ewing's sarcoma
- Dosed up to 8.5 mg/m<sup>2</sup> weekly reversible neutropenia seen (as predicted from preclinical studies)
- One patient from this group continues on study; retrospective analysis shows moderate EphA2 expression

### **Patient selection assay**

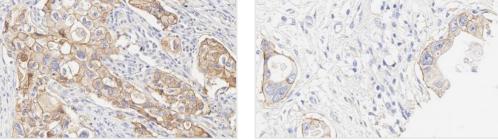
- Proprietary Bicycle IHC assay developed to CAP/CLIA standards
- Measures expression of EphA2 extracellular domain (i.e., Bicycle<sup>®</sup> binding site)
- Multi-indication tumor microarray survey provides guide to frequency of EphA2 patient
- Expression generally increases with stage
- Two patients have been selected by IHC assay
  - $\circ$  Pancreatic (6.5 mg/m<sup>2</sup>Q1W), urothelial (8.5 mg/m<sup>2</sup>Q2W)

### **Next steps**

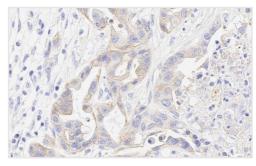
 Focus initially on monotherapy; optimize dose and frequency

#### NSCLC

### Pancreatic



Ovarian







### BT5528-100: Subject 1 summary Monotherapy (assigned 8.5 mg/m<sup>2</sup> Q2W); urothelial cancer

- PR seen after 2 cycles; patient failed prior lines of therapies, including pembrolizumab and enfortumab vedotin
- Substantial reductions in non-target lesions were also observed
- Neutropenia resolved within 7 days; patient remains on study, receiving 6.5 mg/m<sup>2</sup> Q2W

Cycle 1			Cycle 2		Cycle 4		
Day 0	Day 8	Day 15	Day 22	Day 1	Month 2	Day 1	Month 4
8.5 mg/m <sup>2</sup> Q2W	-	Gr3 Neutropenia	SRC review	6.5 mg/m <sup>2</sup> Q2W	43% shrinkage PR	6.5 mg/m <sup>2</sup> Q2W	61% shrinkage PR

#### 76 yo / F

#### Diagnosis = Urothelial cancer EphA2 H-Score: *TM*=*70*, *TC*=*80*

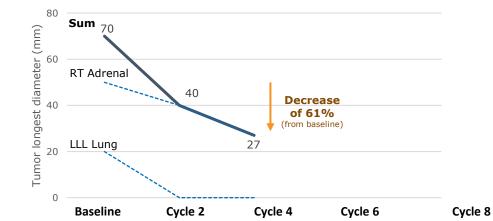
Diagnosed March 2017

<u>Prior Treatment – Non-metastatic</u> 1<sup>st</sup>-Line: MIBC/TURBT (2 months) 2<sup>nd</sup>-Line: Neoadjuvant cisplatin/gemcitabine (3 months) followed by radical cystectomy ("recurrence free" for 1 year) <u>Prior Treatment - Metastatic</u> 1st-Line metastatic: pembrolizumab (7 months) 2<sup>nd</sup>-Line metastatic: enfortumab vedotin x2 cycles complicated with pancreatitis (7 months) 3<sup>rd</sup>-Line metastatic: Carboplatin/gemcitabine (5 months) 4<sup>th</sup>-Line metastatic: CNS RXT (2 months)

#### **Course on Study**

C1D1: 8.5mg/m<sup>2</sup> Q2W (ie, every two weeks) C1D15: Dose hold due to Gr3 neutropenia (resolved within 7 days) C2D1: Lowered to 6.5 mg/m<sup>2</sup> Q2W **RECISTv1.1 best response = Partial Response** 

#### Size of target lesions:



#### Status of non-target lesions:

Small mediastinal LNs	Present	Decreased	
Small liver mets	Present	Absent	
Retroperitoneal LNs	Present	Decreased	

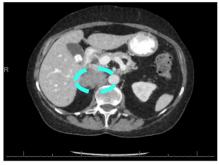




### Target lesion – right adrenal nodule

Pre-treatment

BTC



Post-Cycle 2 on BT5528



50 mm per RECIST

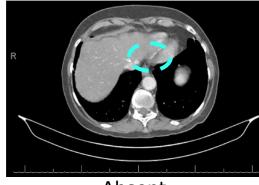
40 mm per RECIST

#### Non-target lesion – liver lesion

Pre-treatment



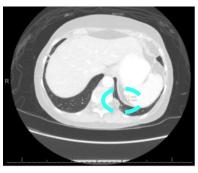
Post-Cycle 2 on BT5528



Absent

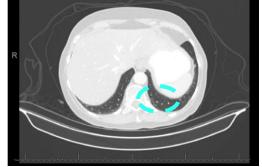
### Target lesion – lower left lung nodule

Pre-treatment



20 mm per RECIST

### Post-Cycle 2 on BT5528



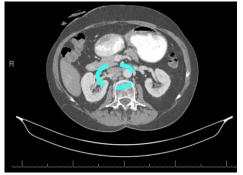
Complete resolution

### Non-target lesion – retroperitoneal lymphadenopathy

#### Pre-treatment



#### Post-Cycle 2 on BT5528



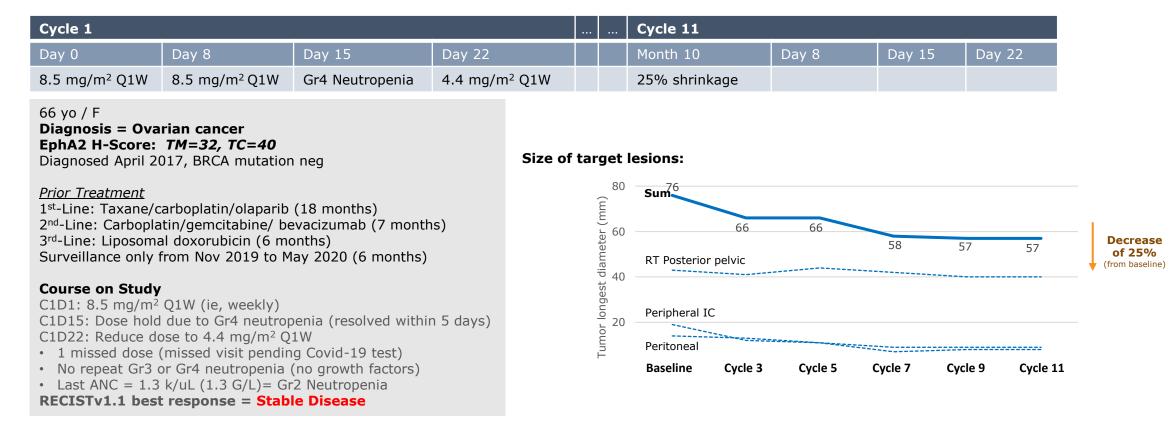


July-21



### **BT5528-100: Subject 2 summary** Monotherapy (assigned 8.5 mg/m2 Q1W); ovarian cancer

- Tumor shrinkage of 25% in ovarian cancer patient; failed prior lines of therapies, including olaparib and bevacizumab
- Patient started study prior to introduction of selection assay
- Patient in Cycle 11 (first dose May 2020) and remains on study; receiving 4.4 mg/m2 Q1W







#### Achieving efficacious MMAE intra-tumor concentrations

- Tumor concentrations of MMAE sustained after dosing
- MMAE tumor concentrations above those required for preclinical efficacy
- ca. 50 nM at 24h post single dose of 1.5 mg/m<sup>2</sup> BT5528 mouse xenograft study (MED)
- Significantly greater than in vitro cytotoxicity IC<sub>50</sub>'s (0.2 to 1.3 nM depending on cell line)

Patient ID	Tumor	Dose	Time	ММАЕ	Concentratio	<b>on</b> (nM)
	type	(mg/m <sup>2</sup> )	post-dose	Tumor	Plasma	Ratio
3000-007	Ewing's sarcoma	4.4	~24h after dose 3	87.5	8.7	10.1
3000-009	Ovarian	4.4	~24h after dose 3	197	21.2	9.3

## Emerging, qualitative metabolic ID data supports the hypothesis that BTCs undergo reduced hepatic metabolism (cf. ADCs) and are renally eliminated

- No circulating metabolites of MMAE have been observed in plasma
  - $^{\circ}~$  No evidence of CYP-mediated hepatic metabolism of MMAE
- Significant amounts of MMAE and peptidyl metabolites observed in urine after 24h
  - $^{\circ}$  Contrast with ADCs where ca. 5% of the dose is excreted as MMAE in the urine and 17% in the feces over 7 days

MED = minimally effective dose

## **BT8009: Nectin-4 BTC fast follower with differentiated profile to approved ADC**



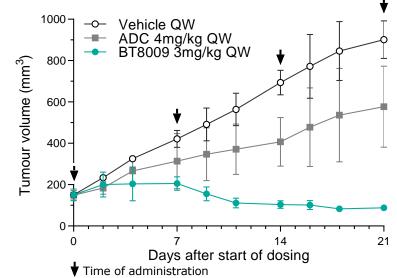
#### Background

BTC

- BT8009 is highly selective for Nectin-4, which:
  - Is believed to play a role in tumor cell growth and proliferation
  - Is overexpressed in common types of cancer
  - Has been validated in the clinic by enfortumab vedotin

#### **Progress**

 Preclinical evidence demonstrates BT8009 has best -in-class potential



### Status

- Phase I trial ongoing: open label, multi-center across US & EU, enrolling patients with Nectin-4(+) tumor types (e.g., urothelial)
- Evaluating BT8009 as a monotherapy and in combination with nivolumab
- Topline data expected in 2021

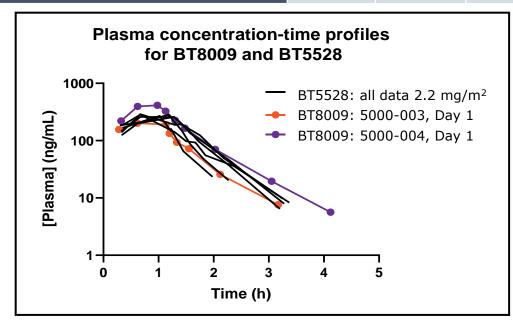
#### **Patient Population**

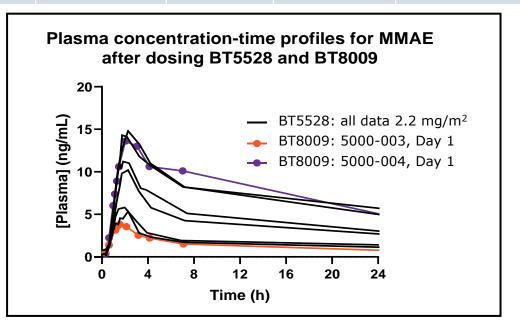
 Nectin-4 is expressed in 98% of bladder, 87% of esophageal and 85% of NSCLC cases



## **BT8009** clinical experience\*

Compound/Cohort	t½	Cmax	AUC∞	CLp	Vss	MMAE Cmax	MMAE AUC24
	(h)	(ng/mL)	(ng.h/mL)	(mL/min/kg)	(L/kg)	(ng/mL)	(ng.h/mL)
BT5528 Cohort 1 (2.2 mg/m <sup>2</sup> )	0.39	274	344	2.85	0.09	10.3	114
	± 0.08	± 13	± 42	± 0.32	± 0.01	± 4.1	± 103
BT8009 5000-003 Day 1 (2.5 mg/m²)	0.500	201	273	3.85	0.12	3.83	34.6
BT8009 5000-004 Day 1 (2.5 mg/m <sup>2</sup> )	0.572	414	530	2.38	0.09	13.6	193





- BT5528 and BT8009 have similar clinical PK profiles
- MMAE has a similar PK profile following administration of either BT5528 or BT8009



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#### BTC IO

# BT1718: Possible first-in-class BTC targeting key tumor antigen

#### Background

- BT1718 is highly selective for MT1-MMP (MMP-14), which:
  - Has established role in cell invasion and metastasis
  - Is highly expressed in tumors of squamous cell origin

#### **Status**

- Phase IIa trial initiated: open label, sponsored by CRUK\*; patients selected based on MT1-MMP expression using proprietary IHC assay
  - Initial cohorts include squamous non-small cell lung cancer (NSCLC) and basket; further cohorts may be added
- Topline data expected in 2021

#### Progress

- Achieved primary objectives of Phase I trial in patients with advanced solid tumors
  - PK in line with preclinical predictions
  - Delivering >4x toxin delivered by ADCs
  - Early signs of activity in difficult to treat patient population



Baseline

68% reduction in a target lesion (SCLC)

### **Patient Population**

 MT1-MMP is expressed in 58% of NSCLC, 76% of esophageal cases; very highly expressed in bladder and ovarian cancers<sup>§</sup>



<sup>\*</sup> Sponsored by Cancer Research UK Centre for Drug Development

## Emerging clinical data support BTCs as a next-generation tumor-targeted delivery platform

Property	BTC	ADC	Importance	
Tumor penetration	$\checkmark$	?	Access to site of action	]
Tumor retention	$\checkmark$	?	Maintenance at site of action, lower total body burden	Precision – Targeting & Efficacy
Short systemic exposure	$\checkmark$	×	Minimizes toxicity, enhances combinability	
Reduced liver metabolism	$\checkmark$	×	Improved safety profile	Maximal - Therapeutic Window
Renal elimination	$\checkmark$	×	Improved safety profile	
Flexible dosing	$\checkmark$	×	Tailored dosing regimen minimizing toxicity	<i>Optimal Patient Experience</i>

We believe that the unique properties of BTCs, which are now being demonstrated clinically, will lead to superior clinical outcomes for patients

BTC

therapeutics

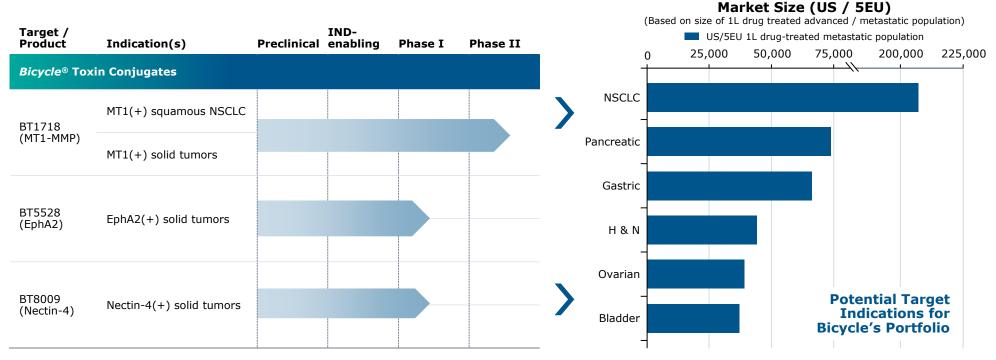
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BTC

### **Bicycle** Toxin Conjugates<sup>®</sup> represent potentially differentiated next-generation cancer therapeutics

First-in-class or best-in-class opportunities

Based on novel technology, designed to overcome ADC failure and other limitations Potential for internal/ external combinations Represent future of tumor-targeted cytotoxic payload delivery



## Immuno-oncology



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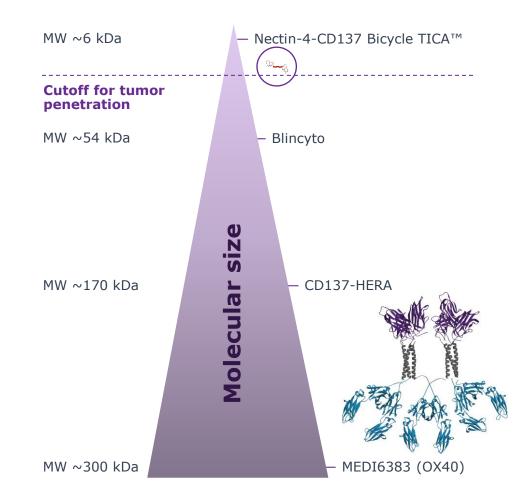
# **Bicycles** are a new class of IO therapies that could overcome limitations of existing approaches

#### **Disadvantages of biologics in IO**

- Very large and complex molecules, poor tumor penetration
- High chance for immunogenicity
- Approach often not generalizable
- Little opportunity to "tune" properties and mitigate toxicities
- Complex, expensive and risky manufacturing

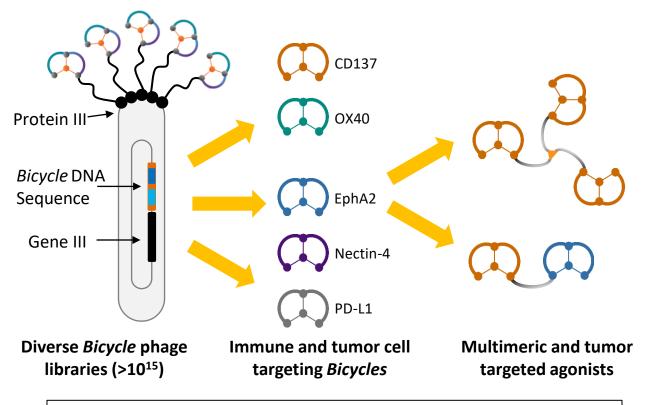
#### Advantages of *Bicycles*

- Smaller than the smallest monovalent antibody, primed for rapid tumor penetration
- Generalizable approach to multiple immune cell receptors
- Chemically synthetic, so easy to "tune" properties
- Simple peptide manufacturing





# **Bicycles** platform is delivering a tool kit of building blocks to create novel IO agonists



### Why CD137?

- Validated target, limited by toxicity
- Unlike CD3, expressed on multiple immune cell types
- Urelumab (BMS), efficacious, but trials halted due to doselimiting liver toxicity, utomilumab (Pfizer), safe, but inactive

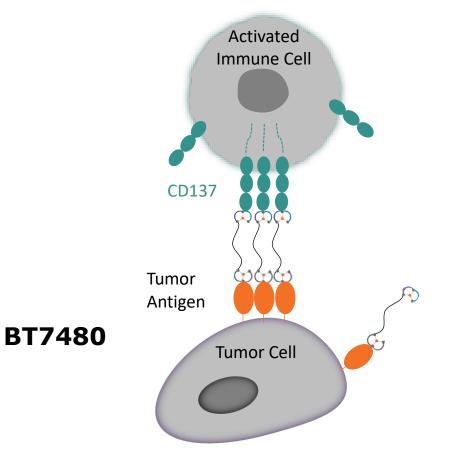
Journal for ImmunoTherapy of Cancer	Anticancer immunit	y induced by a	a
	synthetic tumor-targ	eted CD137 ag	gonist
	Punit Upadhyaya, <sup>1</sup> Johanna Lahdenran Rachel Dods, <sup>3</sup> Eric Haines, <sup>1</sup> Mariana I Jessica Kublin, <sup>5</sup> Rachid Lani, <sup>6</sup> Jun Ma, Katerine Van Rietschoten, <sup>3</sup> Tom Stephe Liuhong Chen, <sup>3</sup> Kevin McDonnell, <sup>1</sup> Phili	Kleyman, <sup>4</sup> Julia Kristensson, <sup>5</sup> Gemma Mudd, <sup>3</sup> Elizabeth I n, <sup>7</sup> Fanglei You, <sup>1</sup> Helen Harr	Repash, <sup>1</sup> ison, <sup>3</sup>
To cite: Upathysys P. Lahdemania, J. Hurov K, et al. Anticanor Immuniky induced UD137 aposisti. Journal for UD137 aposisti. Journal for Immuni07hengy of Cancer 2020;0:e001762, doi:10.1136/ jite-2020-001762 - Additional material is published colline cetly: To view, Additional mat	ABSTRACT Background In contrast to immune checkpoint inhibitors, the use of antibodies as agonists of immune continulatory receptors as cancer therapeutics has largely laide. We sought to address this problem using a new class of modular synthetic drugs, termed tumor-targeted immune cell agonist (TCAs), hased on constrained bicyclic peptides ( <i>Bicycles</i> ). <b>Methods</b> Phage Ibraries displaying <i>Bicycles</i> were panned for binders against tumor nerosis factor (TMP) receptors 20137 and OXA, and tumor antipones EphA2, Nectin-4 and programmed death ligand 1. The CD137 and OX40	cancer immunotherapies with clinical outcomes despite a nistic rationale for utility and p of concept. <sup>24</sup> Translation of preclinical mouse models to h in general, notoriously poor. <sup>5</sup> factors related to the modality duration and location of acti- that have been tested in this to us that a more fit-forpurp logical approach may yield m	strong mecha- reclinical proof f efficacy from uman cancer is, However, other y, including the on of the drugs class, suggested bose pharmaco-
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CRD1 CRD2 CRD4 CRD4			

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therapeutics

## Tumor-targeted immune cell agonists (TICA<sup>™</sup>): Next-generation IO modulators for oncology

- Simple bivalent (or multivalent) molecules using tumor antigens as a scaffold to assemble CD137 signaling complexes *in-trans*
- C Tumor antigen binder arm = Nectin-4 binder
  - $^{\circ}$  Expression in range of solid tumors including bladder, lung and breast
- Immune activator effector arm = CD137 binder
  - $^{\circ}$  Signal 2 costimulatory receptor drives T-cell function and survival, also expressed on NK cells and myeloid cells



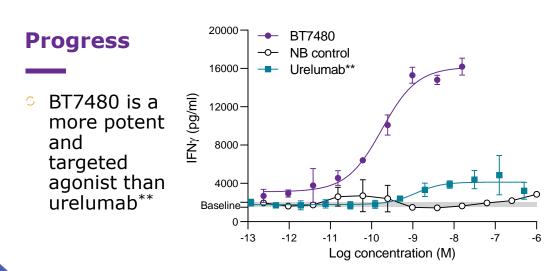


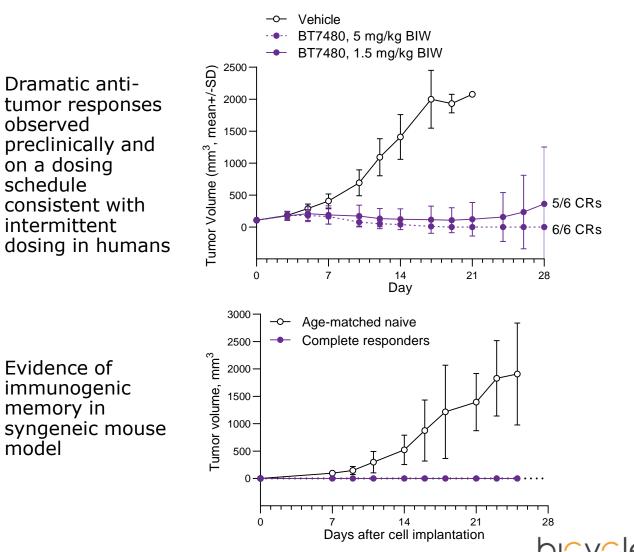
#### BTC IO

## BT7480: Potential first-in-class, highly potent Nectin-4-targeted CD137 agonist

#### **Background & Status**

- More potent than urelumab in Nectin-4 expressing tumors
- Fully synthetic, 30x smaller than antibodies
- Short half life, compatible with intermittent dosing
- Ideal combination partner
- IND-enabling studies ongoing
- Phase I initiation expected in 2H 2021

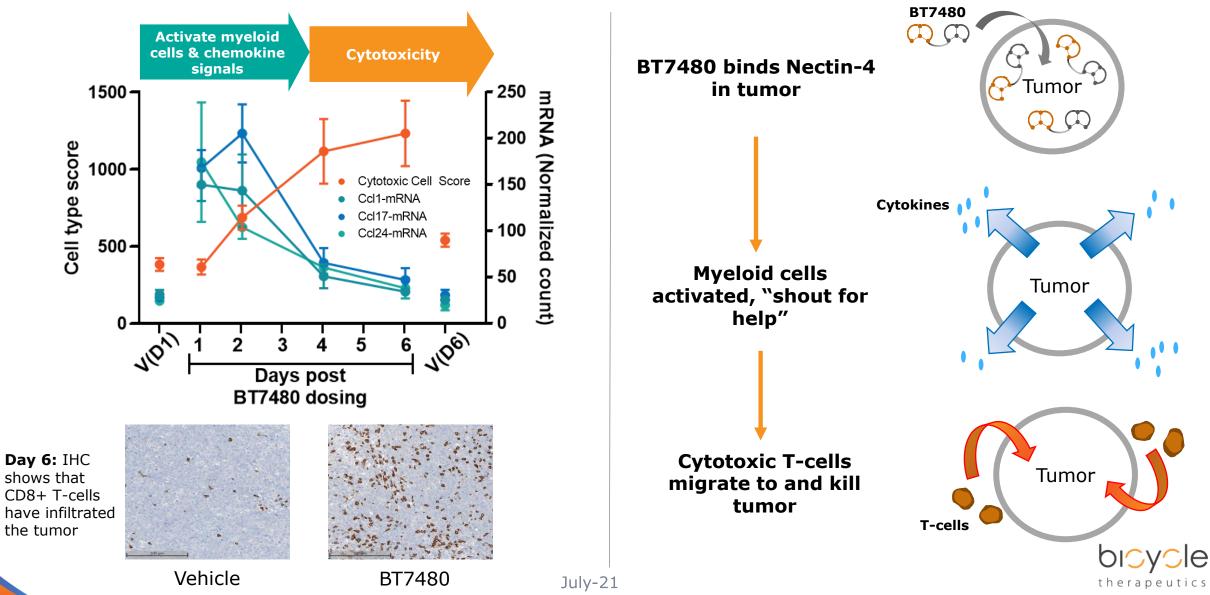




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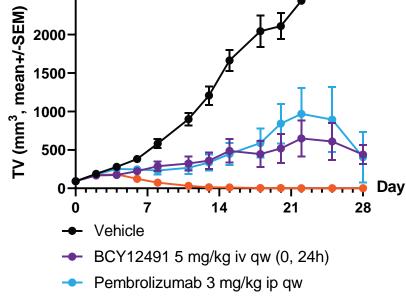
# **BT7480** has a unique and differentiated mechanism of action



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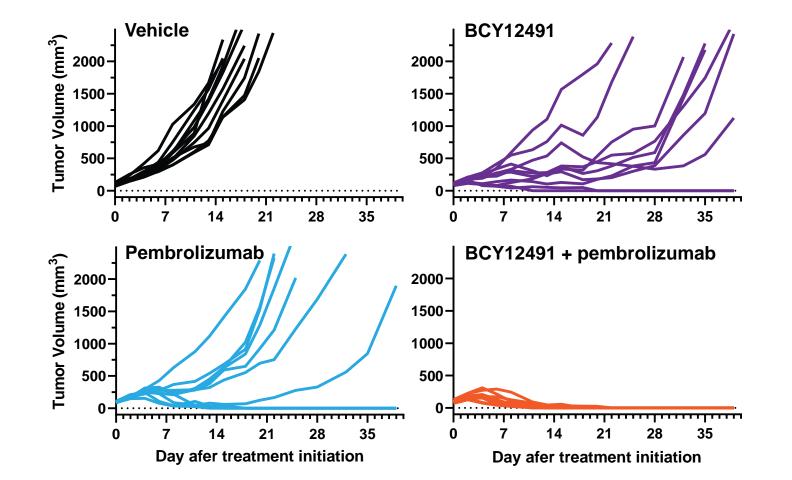
### **100% complete response rate with model CD137 TICA™+ pembrolizumab combination**





- BCY12491 + pembrolizumab

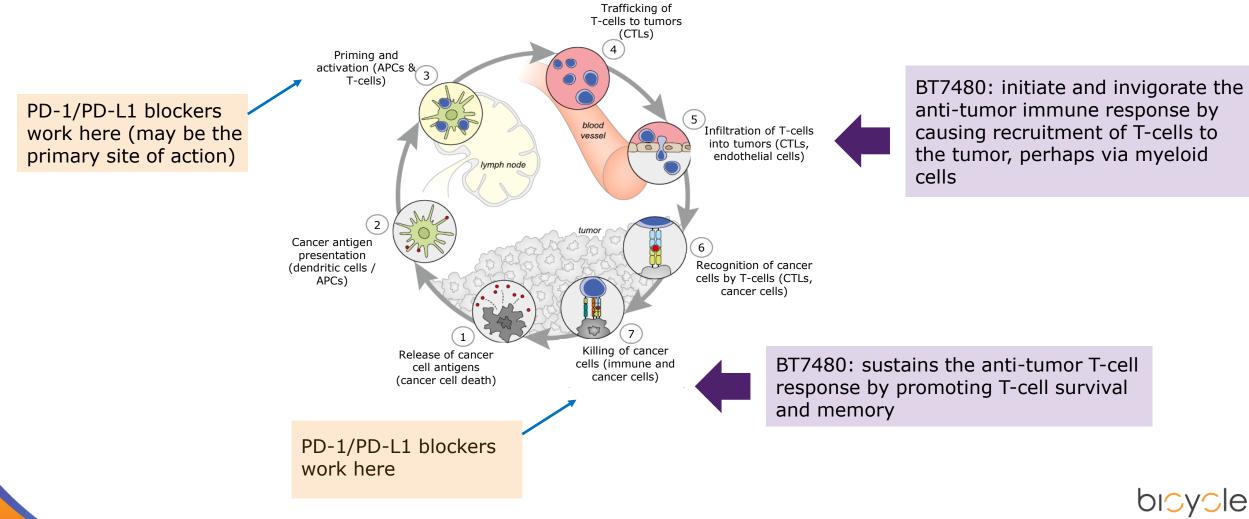
Test Agent	CRs on D39
Vehicle	0/10
BCY12491	2/10
Pembrolizumab	3/10
BCY + pembrolizumab	10/10



BTC

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# BT7480 has the potential to both drive <u>and</u> sustain tumor immunity via targeted agonism of CD137

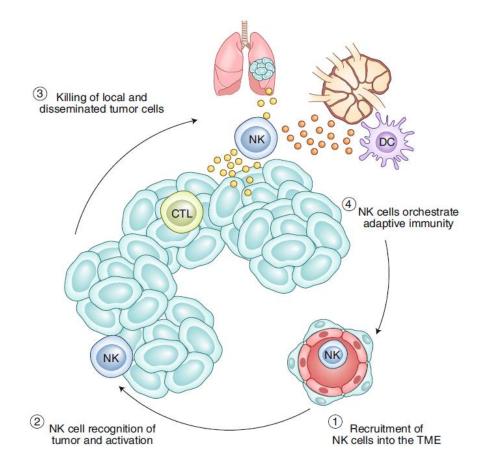


therapeutics



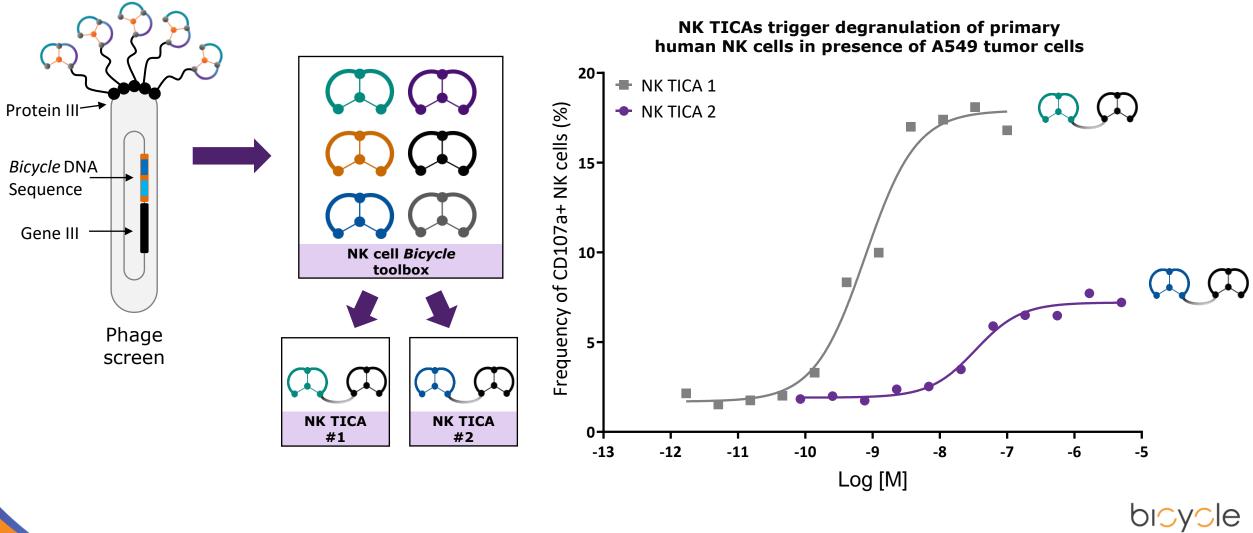
# Natural killer (NK) cells are emerging key players in anti-tumor immunity

- NK cells kill tumor cells through direct cytotoxic mechanisms
- Solution Service New published science has revealed a role for NK cells in orchestrating adaptive tumor immunity
- NK cells are activated through surface receptors excellent opportunity for tumor-targeted *Bicycles*





# Key NK cell receptors are amenable to *Bicycle®* technology and can rapidly be assembled into NK-TICAs

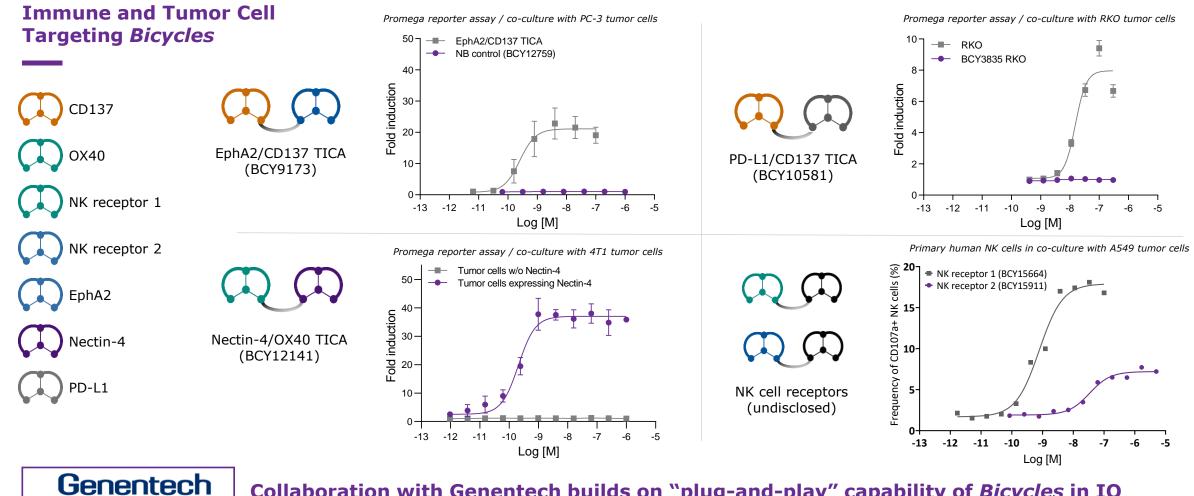


therapeutics



## **Bicycle<sup>®</sup>** TICA<sup>™</sup>: a modular & generalizable platform

Immune cell and tumor targeting *Bicycles* can be rapidly combined and chemically optimized Extending beyond T-cell into multiple immune cell receptor classes



Collaboration with Genentech builds on "plug-and-play" capability of *Bicycles* in IO

therapeutics

A Member of the Roche Group

## Partnerships



## Potential of Bicycle® technology is unconstrained

## **Bicycles** are ideally suited for a broad range of therapeutic interventions and are:

### **Oncology**

- Ideally suited for solid tumor delivery
- Preclinical & clinical evidence of precision targeting

#### Dermatology

- Capable of skin penetration
- Able to potently modulate key inflammatory pathways

#### Respiratory

- Rapid lung penetration and retention
- Potent modulation of key inflammatory pathways

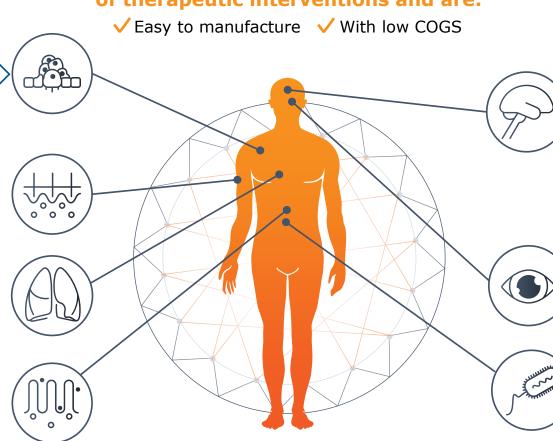
AstraZeneca 😕

Genentech

A Member of the Roche Group

#### Gastrointestinal

- Gut stable, potent immunomodulation
- Intraluminal modulation of GI disease



#### **CNS and Neuromuscular**

- CNS delivery
- Potential next-generation medicines for CNS diseases
   IONIS
- Tissue-targeted delivery of oligonucleotide therapeutics using *Bicycles* with high affinity to TfR1

### **IONIS**

#### Ophthalmology

- Potential for long term modulation
- Proof of concept achieved with clinical evidence of durable activity

 $O \times U R I O N^{\circ}$ 

#### Infectious disease

Modulation key prokaryotic pathways

### Innovate UK



## **Upcoming Milestones**



# Multiple milestones expected across pipeline of wholly-owned clinical & near-clinical assets

Target / Product	Indication(s)	Preclinical	IND- enabling	Phase I	Phase II	Key 2021 Events
<b>Bicycle®</b> Toxin Conjug	ates					
	MT1(+) squamous NSCLC					<ul> <li>Mechanistic data</li> </ul>
BT1718 (MT1-MMP)	MT1(+) solid tumors					<ul> <li>Phase IIa interim update</li> </ul>
BT5528 (EphA2)	EphA2(+) solid tumors					<ul> <li>Site expansion</li> <li>Mechanistic data</li> <li>Phase I interim update</li> </ul>
BT8009 (Nectin-4)	Nectin-4(+) solid tumors					<ul> <li>Site expansion</li> <li>Mechanistic data</li> <li>Phase I interim update</li> </ul>
Immuno-oncology						
BT7480 (Nectin-4/CD13	7 TICA™)					Phase I/II trial initiation
BT7455 (EphA2/CD137	TICA™)					<ul> <li>IND-enabling studies</li> </ul>
						bicycle

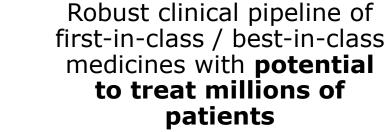
therapeutics

We aim to redefine what's possible for people with cancer and other serious diseases by pioneering a new and differentiated class of innovative treatments



AMGEN

EMD



Cash balance of \$195.6M\* provides runway to support multiple clinical milestones



MERCK Takeda