

Synaffix's Journey to the Top Leads to the Swiss Alps

Creating value for patients through cutting-edge ADC technology platform and matching out-licensing business model

Business Use Only



Dutch Life Sciences
c o n f e r e n c e

Leiden Bio Science Park
December 7, 2023

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Antibody Drug Conjugates: Recognition of Their Potential, Finally... ...Yet Technology Shortcomings Constrain Growth

An increasingly commercially validated therapeutic class...



Non-Proprietary Brand Name	Approval Year	Sponsor	2020 Sales (\$M)	Peak Sales (\$M)
Gemtuzumab ozogamicin	2000, 2017	Pfizer, Wyeth	185	190 (2022F)
Brentuximab vedotin	2011	Seagen, Takeda	1,219	2,285 (2027F)
Trastuzuman emtansine	2013	Genentech, Roche	1,859	2,260 (2023F)
Inotuzumab ozogamicin	2017	Pfizer, Wyeth	N/A	483 (2027F)
Polatuzumab vedotin	2019	Genentech, Roche	180	1,574 (2027F)
Enfortumab vedotin	2019	Astellas, Seagen	343	5,436 (2027F)
Trastuzumab deruxtecan	2019	AstraZeneca, Daichi-Sankyo	284	5,617 (2027F)
Sacituzumab govitecan	2020	Immunomedics	49	3,242 (2027F)
Belantamab mafodotin	2020	GSK	42	866 (2027F)
Loncastuximab teserine	2021	ADC Therapeutics	N/A	270 (2027F)
Tisotumab vedotin	2021	Seagen	N/A	806 (2027F)
	2022	Immunogen		



~96 ADCs in Clinical Pipeline⁽¹⁾



\$23.9 Bn by 2028 with 23.7% CAGR⁽²⁾⁽³⁾

... constrained by technology shortcomings



1 Heterogeneity:



Mixture of payload under/over-loading, variable position

2 Payload Hydrophobicity:



Enhanced clearance and side effects

3 Instability:



Payload release in circulation, less drug on target

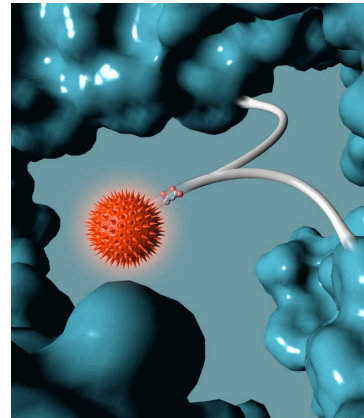
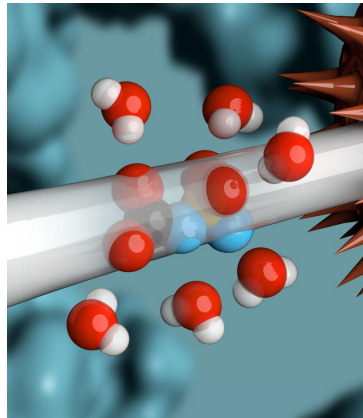
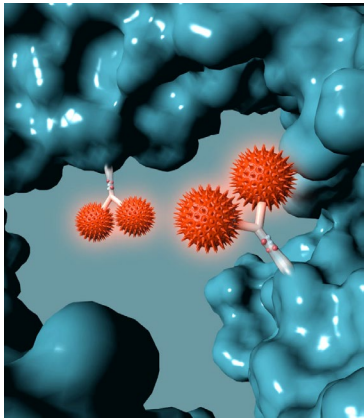
4 Payloads:



Lack of diversity in mode-of-action (MoA)

Synaffix's Consolidated Technology Platform Addresses ADC Shortcomings Providing Best-in-Class Differentiated Therapeutics

A three-prong versatile platform suitable for any antibody and any payload



Glyco Connect®

Site-specific, glycan-based antibody conjugation technology



HydraSpace™

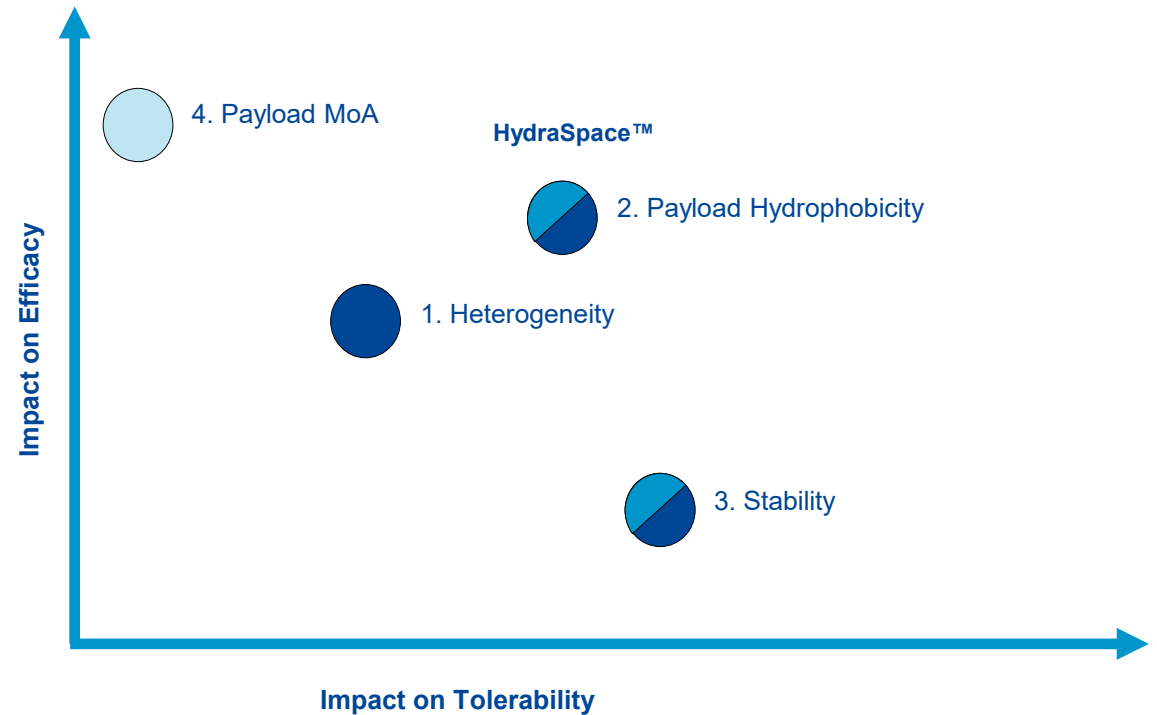
Highly polar spacer technology



toxSYN™
Linker-Payloads

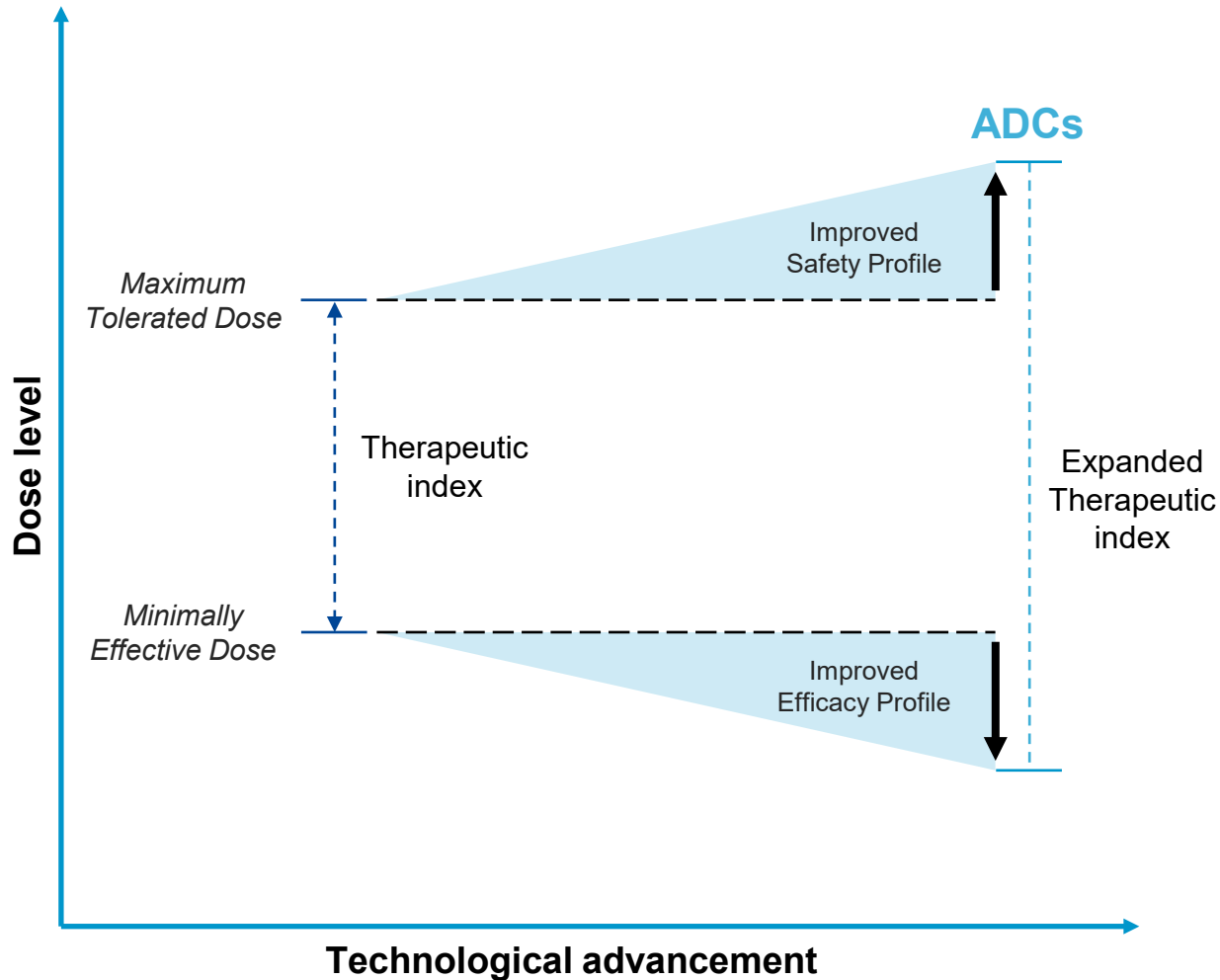
Multiple mechanisms of action (MoAs) to maximize ADC efficacy

Synaffix ADC technologies maximize ADC's therapeutic index Improving both efficacy and tolerability



● Glyco Connect® ● HydraSpace™ ● toxSYN™

Unmet Need Translated Into Vision Statement



1 Be the **preferred** technology provider for the development of ADCs



2 Enable '**Best-in-Class**' targeted therapeutics



3 Become **most prevalent** technology across new clinical-stage ADCs



Platform Technology

For ADCs with Best-in-Class Therapeutic Index

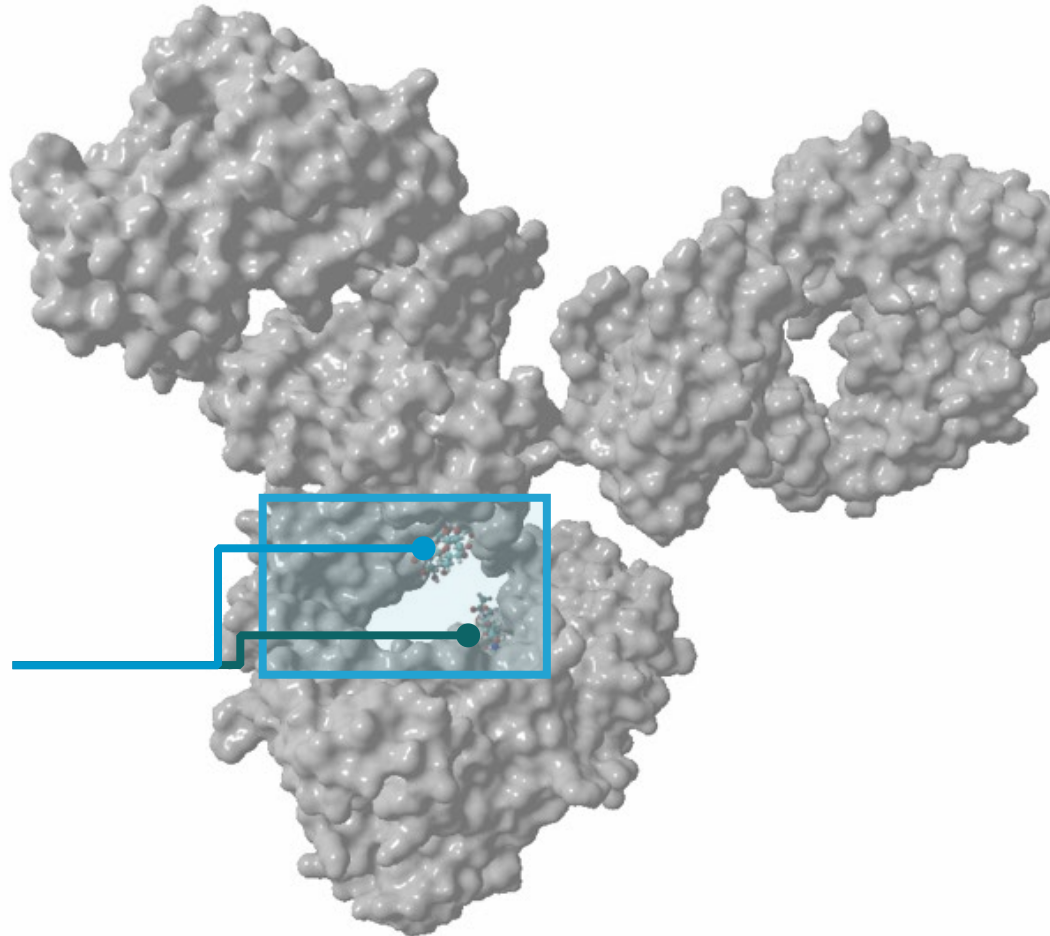


Glyco Connect®

The Glycan Pocket is a Special Place to Hide ADC Payloads

ATOM PROPERTIES

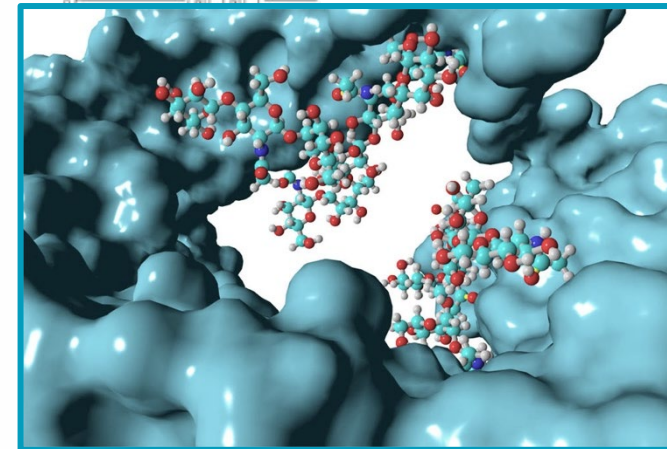
Number:
Name:
Element:
Occupancy: % BFactor:
Residue:
Object:
Position: X = 000000.00000 X
 Y = 000000.00000 X
 Z = 000000.00000 X
Bonds:
1) Type to ()
 Length . . . 30
2) Type to ()
 Length . . . 30
3) Type to ()
 Length . . . 30
4) Type to ()
 Length . . . 30
Marked Distance: Å
Marked Angle: °
Marked Dihedral: °



Glycan Locations

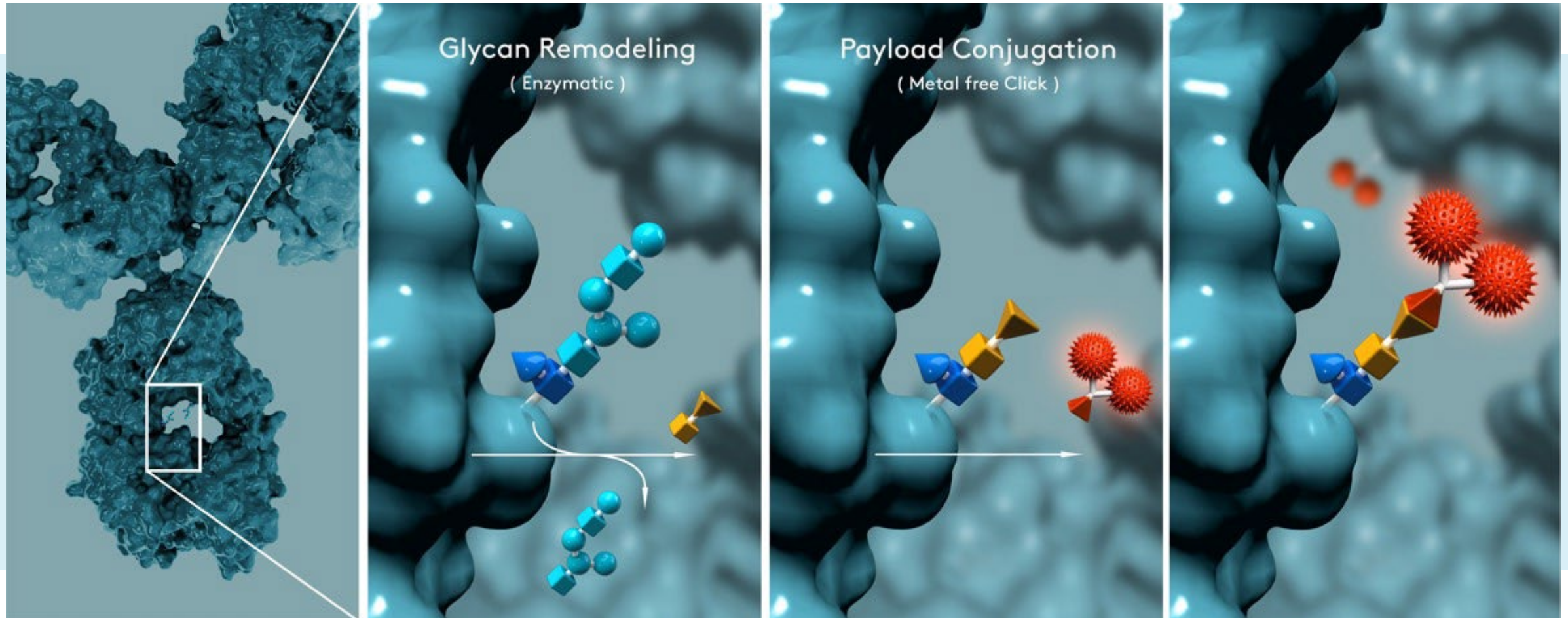
SCENE CONTENT

Obj	Name	Vis	Act	Atom
1	ligy	Yes	Yes	1
2		No	No	
3		No	No	
4		No	No	
5		No	No	
6		No	No	
7		No	No	
8		No	No	



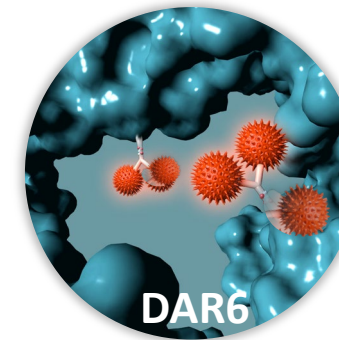
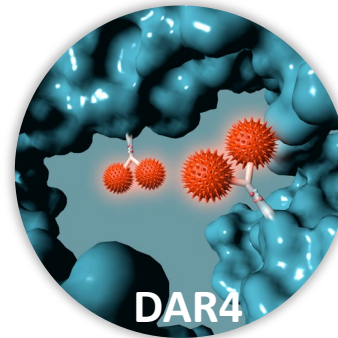
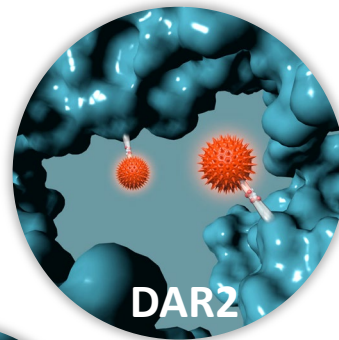
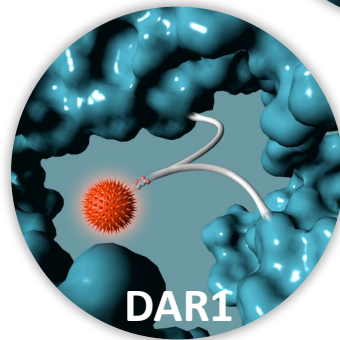
Glyco Connect[®]

Enables Site-Specific ADCs without Antibody Engineering

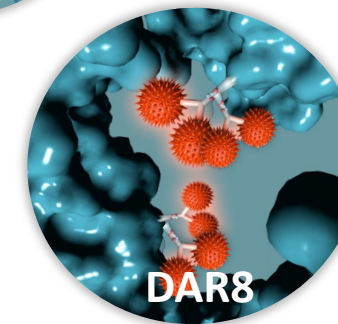


- All clinical-stage and marketed ADCs currently limited to a drug-antibody ratio (DAR) between 2 and 8

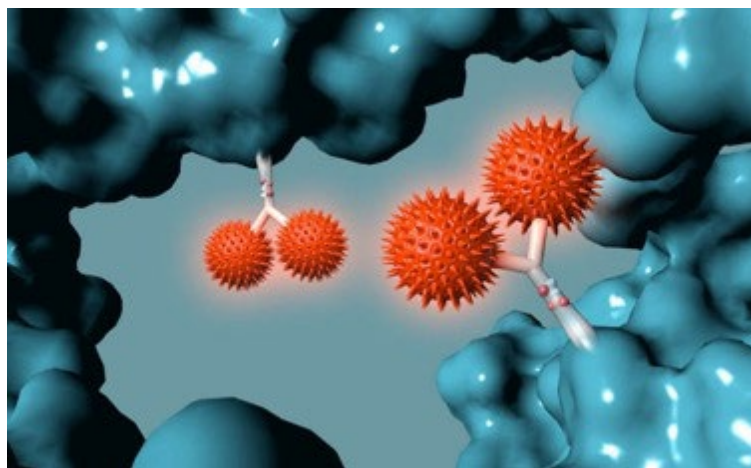
For Higher Potency Payloads,
such as PBD dimers, IGN dimers,
calicheamicin, duocarmycin, PNU159,682,
amanitin and others



For Lower Potency Payloads

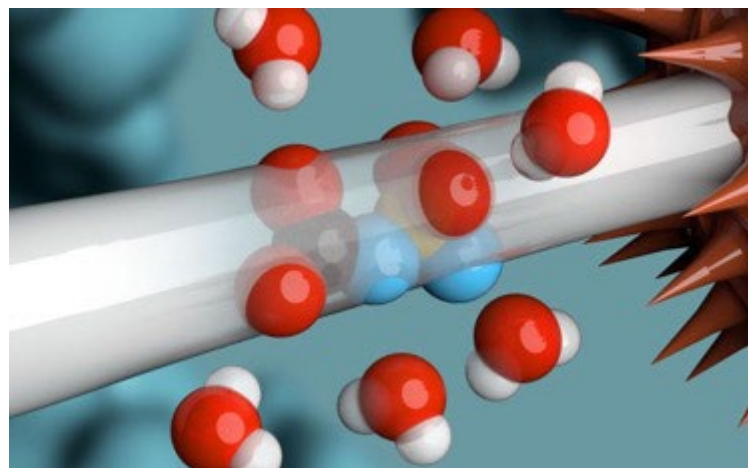


Protected by >30 Patent Families



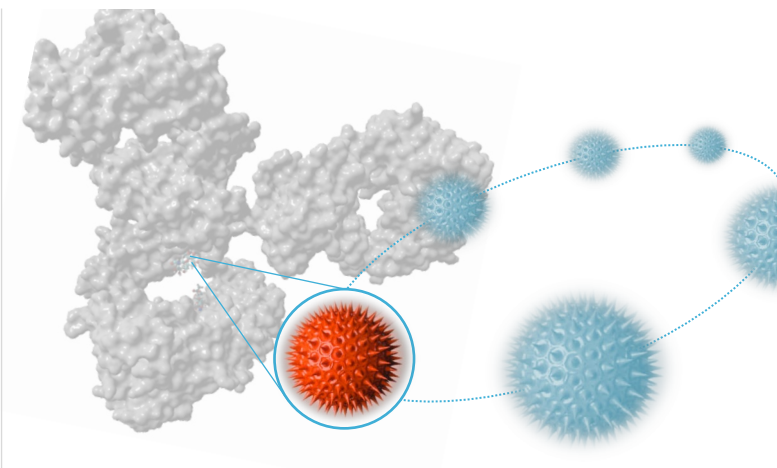
Glyco Connect[®]

Site-specific antibody conjugation technology enabling best-in-class **therapeutic efficacy and tolerability** (DAR1/2/4/6/8)



HydraSpace[®]

Highly polar spacer technology further differentiates the **therapeutic window and stability of Synaffix ADCs**



toxSYN[™]

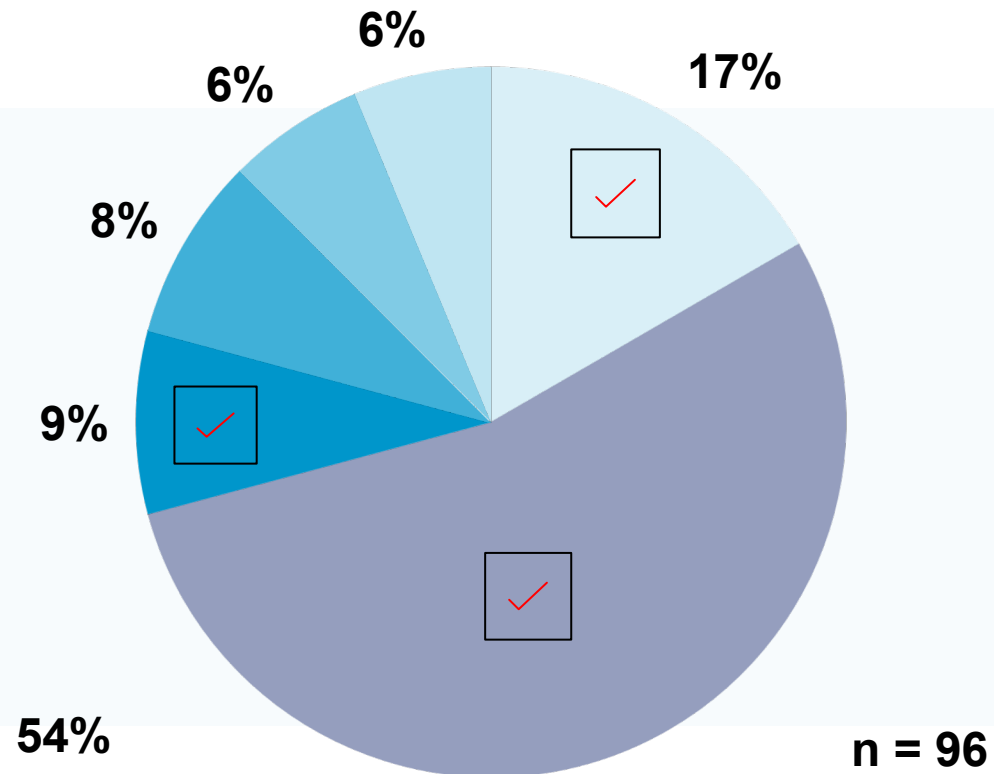
Multiple linker-payloads spanning various mechanisms of action to maximize efficacy **for any ADC target**

Differentiated Impact on Therapeutics Index



Setting the Stage for Benchmarking Experiments

Three Technologies Have Delivered the Vast Majority of Clinical Stage ADCs

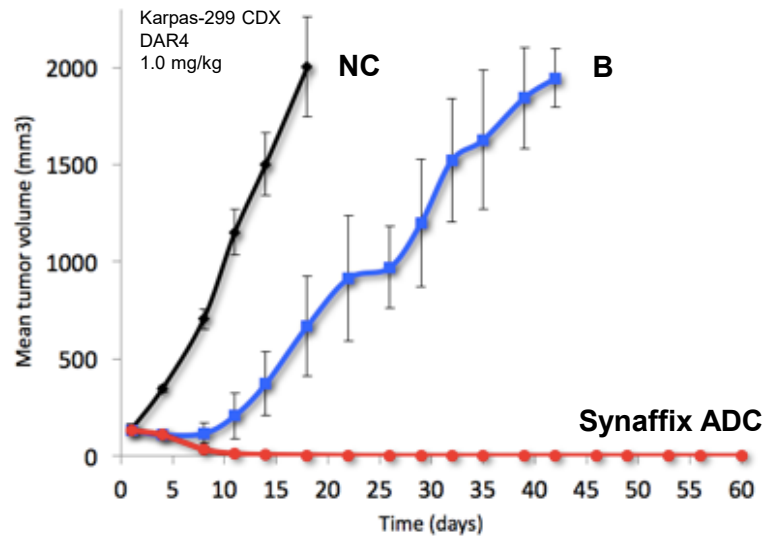


Consistently superior TI versus:

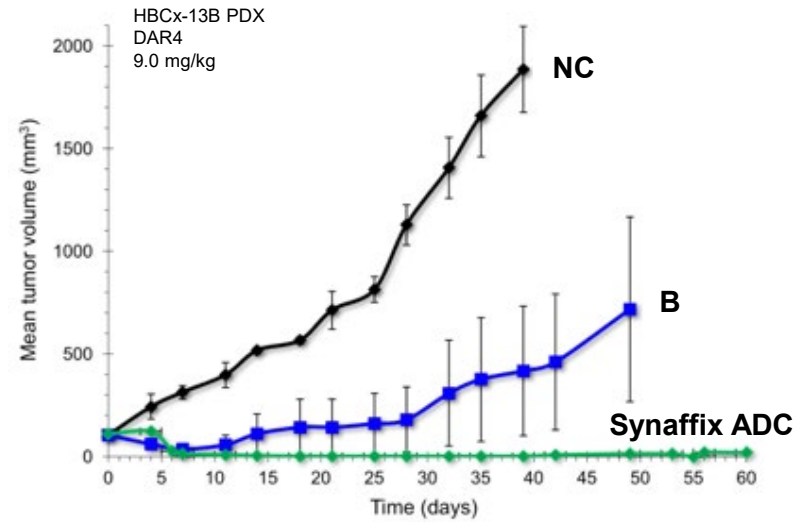
- Random cysteine conjugation
- Random lysine conjugation
- Engineered cysteine conjugation

Synaffix Technology Demonstrates Consistently Superior Therapeutic Index vs. Three Major Clinical-Stage ADC Technologies

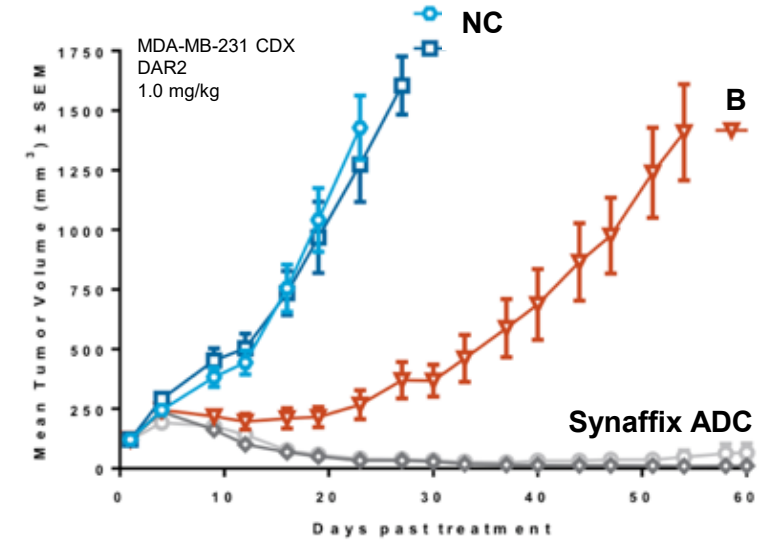
Random conjugation to cysteine (MMAE)



Random conjugation to lysine (maytansinoid)



Site-specific conjugation to engineered cysteine (PBD)



vs. Brentuximab vedotin from pharmacy

vs. Trastuzumab emtansine from pharmacy

vs. ADC Therapeutics' previous lead development candidate for ADCT-601

B = Benchmark ADC NC = Negative Control ADC

Synaffix ADC = same mAb, same payload (Brentuximab vedotin, ADCT-601) or payload class (Trastuzumab emtansine), same DAR as Benchmark ADC

Synaffix Technology Demonstrates Consistently Superior Tolerability in Rats

vs. All Three Major Clinical-Stage ADC Technologies



Random conjugation to cysteine (MMAE)		
Dose (mg/kg)	Brentuximab vedotin (DAR4.0)	Synaffix ADC (DAR3.8)
70	Not Tested	X
60		MTD
40		No DLTs
20		X
15		MTD
4x better tolerability		

vs. Brentuximab vedotin from pharmacy

Random conjugation to lysine (maytansinoid)		
Dose (mg/kg)	Trastuzumab emtansine (DAR3.6)	Synaffix ADC (DAR3.8)
60	Not Tested	MTD
50		X
35		MTD
20		No DLTs
20		No DLTs
1.7x better tolerability		

vs. Trastuzumab emtansine from pharmacy

Site-specific conjugation to engineered cysteine (PBD)		
Dose (mg/kg)	Cysteine-engineered ADC (DAR1.8)	Synaffix ADC (DAR1.8)
6.0	Not Tested	MTD
3.0	X	No DLTs
2.0	MTD	No DLTs
3x better tolerability		

vs. ADC Therapeutics' previous lead development candidate for ADCT-601

Synaffix ADC = same mAb, same payload/payload class and same DAR as comparator ADC MTD = Maximum Tolerated Dose DLTs = Dose-Limiting Toxicities X = severe toxicities observed

Brentuximab vedotin is a US registered trademark of Seagen Inc. Trastuzumab emtansine is a US registered trademark of Genentech USA, Inc.

1 Conjugation Site: ↑ Exposure

2 Lack of Glycan: ↓ On-Target Toxicity

Exemplified on
subsequent slides

3 Homogeneity & Stability: ↓ Off-Target Toxicity, ↑ Efficacy

4 Highly Polar Linker: ↓ Off-Target Toxicity, ↑ Efficacy

Lack of Glycan is Anticipated to Reduce On-Target Toxicities

Abrogation of Binding to Fc- γ and Mannose Receptors May Significantly Reduce Risk for Interstitial Lung Disease

- Lung toxicity is most important adverse events associated with Daiichi-Sankyo tech (Trastuzumab deruxtecan)
- Up to 16% of patient may suffer from interstitial lung disease (ILD) and/or pneumonitis

WARNING: INTERSTITIAL LUNG DISEASE and EMBRYO-FETAL TOXICITY

See full prescribing information for complete boxed warning.

- **Interstitial lung disease (ILD) and pneumonitis, including fatal cases, have been reported with ^{Trastuzumab}deruxtecan. Monitor for and promptly investigate signs and symptoms including cough, dyspnea, fever, and other new or worsening respiratory symptoms. Permanently discontinue ^{Trastuzumab}deruxtecan in all patients with Grade 2 or higher ILD/pneumonitis. Advise patients of the risk and to immediately report symptoms. (2.3, 5.1)**

- Lung toxicity is strongly associated with non-targeted uptake in alveolar macrophages (by Fc- γ receptors, mannose receptor, macropinocytosis) (Cancer Science, Kumagai *et al.*, **2020**)
- Glyco Connect[®] abrogates binding to Fc- γ /mannose receptors, negative charge of HydraSpace[™] may reduces macropinocytosis (t.b.c.) → potential reduced risk/clinical benefit for patients

Early Clinical Read-out is Supporting Translation of Synaffix Technology Benefits in Patients

IBI343: Potential Best-in-Class CLDN18.2 ADC

Preliminary efficacy and favorable safety signals observed with dose escalated to 10mg/kg

Observed better-than-peer safety at high dose level

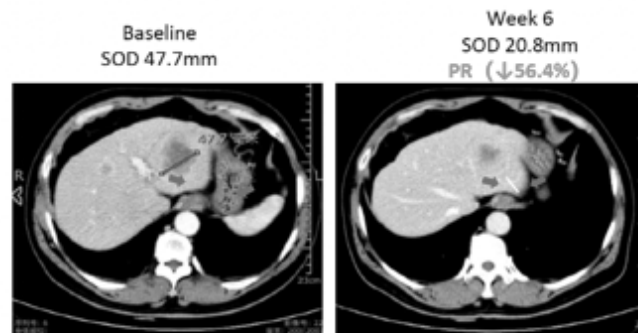
- Dose escalation reached **10mg/kg**.
- Tolerable safety in multiple dose groups.
- Specifically, observed **safer-than-peers** with lower rate of GI AEs and hypoalbuminemia, and lower rate of discontinued treatment due to AEs.

Thoughtful design attributes to the wide therapeutic window:

- The site-specific glycan conjugation technology
- The homogenous DAR4
- The silenced Fc to reduce non-specific uptake

Encouraging ORR and high DCR observed

- Dosed over 60 GC/PDAC patients with CLDN18.2 expression.
- Encouraging ORR observed within short period of follow-up.
- High DCR observed for heavily treated patients.



Note: all numbers above are percentage change of sum of tumor diameters

IBI343 enabled by:

- Glyco Connect[®]
- HydraSpace[™]
- SYNtecan E[™] (Topo 1 inhibitor)

	Trastuzumab deruxtecan	IBI343
Indication	GC / mBC	GC + PDAC
Clinical dose (mg/kg)	6.4 / 5.4	up to 10.0

Superior overall risk/benefit profile than peers

Better opportunities in combination therapy given favorable tolerability

GC
mBC
PDAC

gastric cancer
metastatic breast cancer
pancreatic ductal adenocarcinoma

Value Proposition and Business Model



Over \$9 Billion in Out-Licensing Deals to Date

Driven by Consolidated Offering, Highly Competitive TI and Engineering-free Approach



Consolidated Technology Offering



Consolidated licensing-based solution includes conjugation, spacer and proprietary linker-payload technologies so that any company with an antibody can rapidly develop a proprietary ADC

Highly-Competitive Therapeutic Index (TI)



Synaffix technology consistently delivers ADCs with best-in-class therapeutic index versus the 3 major clinical-stage ADC technologies

Engineering-Free Approach



ADCs rapidly generated and scaled for proof-of-concept and clinical development without any antibody sequence or cell line engineering

DAR Versatility



Precisely tunable drug-antibody ratio (DAR) loading of 1, 2, 4, 6 and 8

Business Model



Target-specific out-licensing of proprietary platform technology

Manufacturing Support



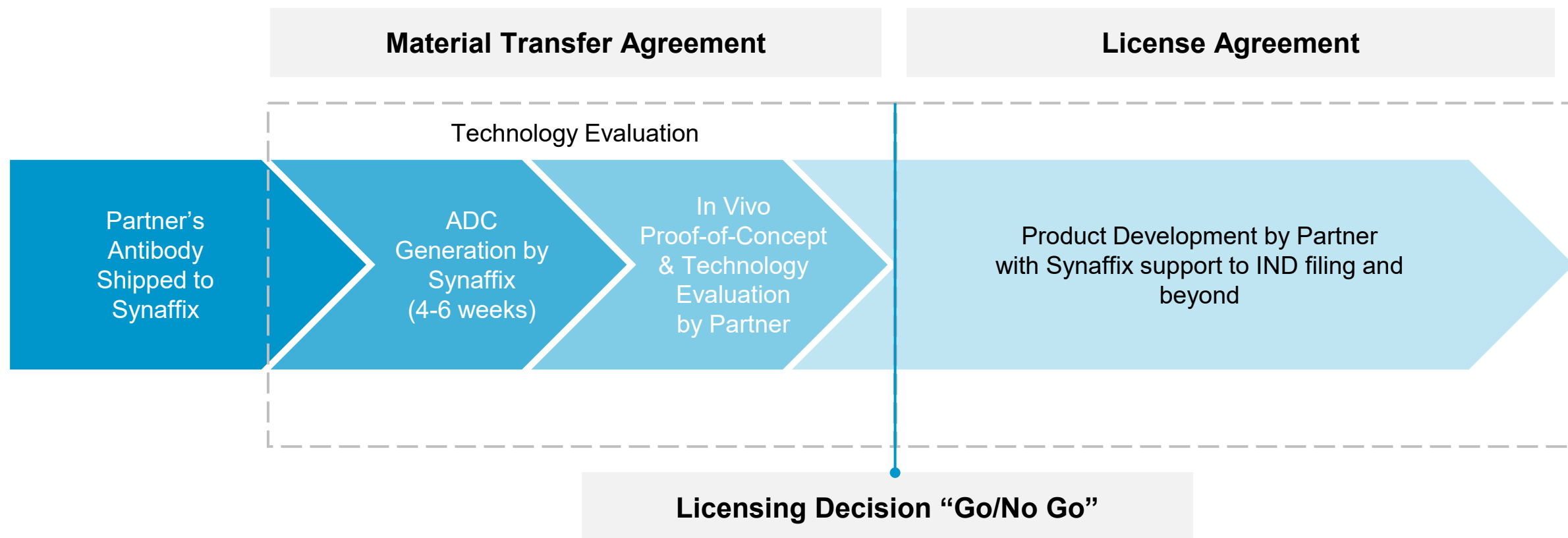
Synaffix acquisition enables end-to-end ADC offering with Lonza

Synaffix Partnering Model:

Evaluation of Development Candidate(s) Prior to Technology Licensing



We embrace research collaborations with companies who look towards external innovation to build their pipelines



Licensing Partners are Rapidly Advancing >20 Programs

Synaffix Deals Represent Over \$9 Billion in Total Potential Deal Value



	Program	Preclinical	Phase 1
ADC Therapeutics	ADCT-601 (Axl)	<div style="width: 70%;"></div>	<div style="width: 30%;"></div>
	Undisclosed	<div style="width: 40%;"></div>	<div style="width: 60%;"></div>
Mersana Therapeutics	XMT-1660 (B7-H4)	<div style="width: 70%;"></div>	<div style="width: 30%;"></div>
	Mersana Therapeutics, Inc. in collaboration with: Janssen Multiple Undisclosed	<div style="width: 20%;"></div>	<div style="width: 80%;"></div>
Miracogen	MRG004A (TF)	<div style="width: 70%;"></div>	<div style="width: 30%;"></div>
	Undisclosed	<div style="width: 25%;"></div>	<div style="width: 75%;"></div>
Innovent	IBI-343 (Claudin 18.2)	<div style="width: 70%;"></div>	<div style="width: 30%;"></div>
	Undisclosed additional target	<div style="width: 25%;"></div>	<div style="width: 75%;"></div>
ProfoundBio	Undisclosed	<div style="width: 20%;"></div>	<div style="width: 80%;"></div>

	Program	Preclinical	Phase 1
Genmab	Undisclosed	<div style="width: 15%;"></div>	<div style="width: 85%;"></div>
MacroGenics	2X Undisclosed	<div style="width: 15%;"></div>	<div style="width: 85%;"></div>
Kyowa Kirin	2X Undisclosed	<div style="width: 15%;"></div>	<div style="width: 85%;"></div>
Emergence* Therapeutics	Undisclosed	<div style="width: 15%;"></div>	<div style="width: 85%;"></div>
Hummingbird Bioscience	Undisclosed	<div style="width: 15%;"></div>	<div style="width: 85%;"></div>
Amgen	Undisclosed additional target	<div style="width: 15%;"></div>	<div style="width: 85%;"></div>
Ching Kun Dang Pharma	Undisclosed	<div style="width: 15%;"></div>	<div style="width: 85%;"></div>
ABL Bio	Undisclosed	<div style="width: 15%;"></div>	<div style="width: 85%;"></div>
Sotio	Undisclosed	<div style="width: 15%;"></div>	<div style="width: 85%;"></div>

* As of 24th August 2023, is a wholly owned subsidiary of Eli Lilly & Co.

Award-Winning ADC Platform Technology



As awarded by ADC industry
experts at World ADC Awards
2022



As awarded by biotech industry
peers at LSX European Lifestars
Awards 2022



As awarded by the expert judging
panel at Scrip Awards 2022


From Start-Up to Global Leading CDMO

Advancing Partnered Pipeline Requires
Evolving Value Proposition and Offers Novel
Growth Opportunities



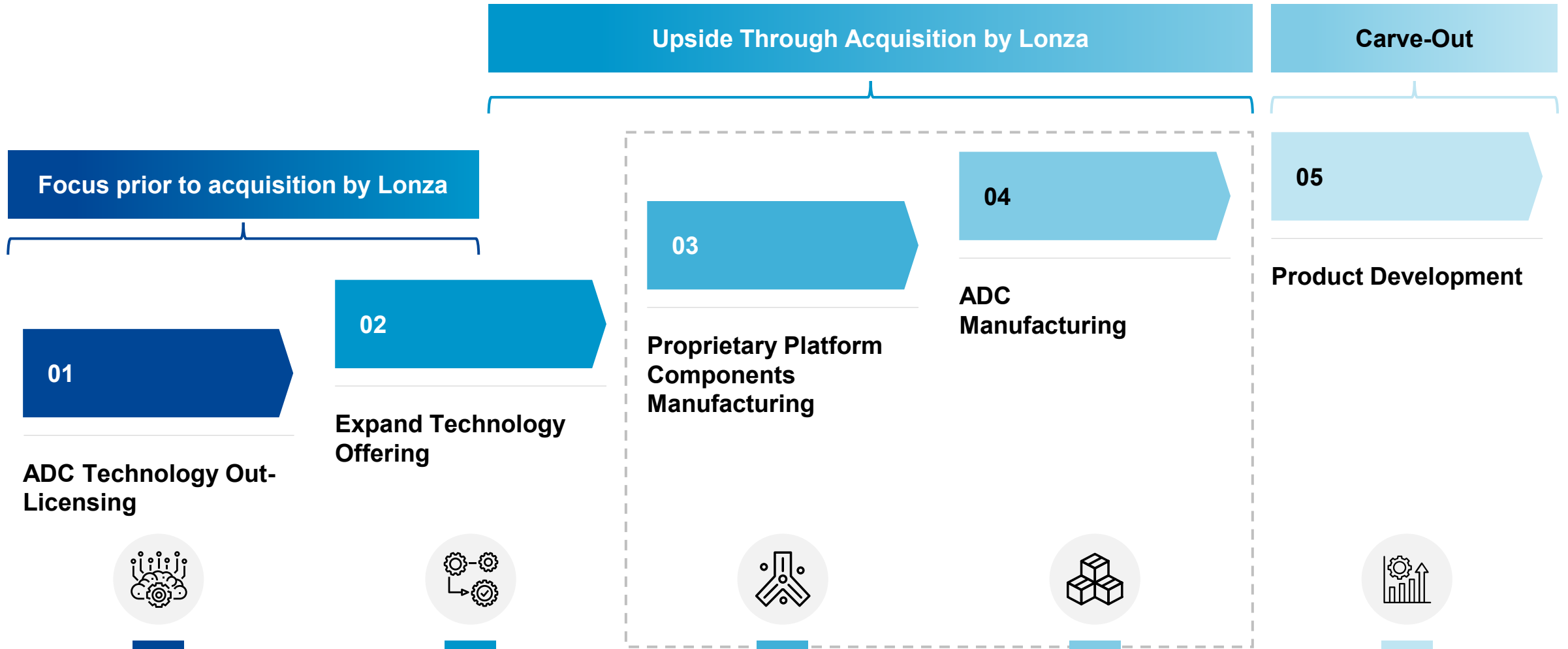
Synaffix Continues to Experience Strong Technology Out-Licensing Business Growth



Founding & Early Fundraising		ADC Technology Development				Commercial Traction					
2010	2012	2014	2016	2016	2017	2019	2020	2021	2021	2022	2023
Synaffix Founded	Glyco Connect® Launched	Series A Financing	SAB Established	Hydra Space™ Launched	toxSYN™ Linker-Payloads Launched	1st Glyco Connect® ADC Enters Clinic (ADCT-601)	2nd Glyco Connect® ADC Enters Clinic (XMT-1592)	>\$2 Billion in Out-Licensing Deals Secured	3rd Glyco Connect® ADC Enters Clinic (MRG004a)	>\$3 Billion in (Out-Licensing) Deals Secured	>\$9 Billion in Out-Licensing Deals Secured
		Brabantse Ontwikkelings Maatschappij	High Potency Lab Opened								Lonza Acquisition by Lonza
Technology Out-Licensing Deals											
		BOM		ADC Therapeutics		Miracogen		ProfoundBio		Janssen	Amgen
		Aravis								Mersana Therapeutics, Inc. collaboration with	CKD
		M. Ventures					Innovent		MacroGenics	Emergence Therapeutics*	Hummingbird Bioscience
		BGV				Mersana Therapeutics		Kyowa Kirin	Genmab	ABL bio	Sotio

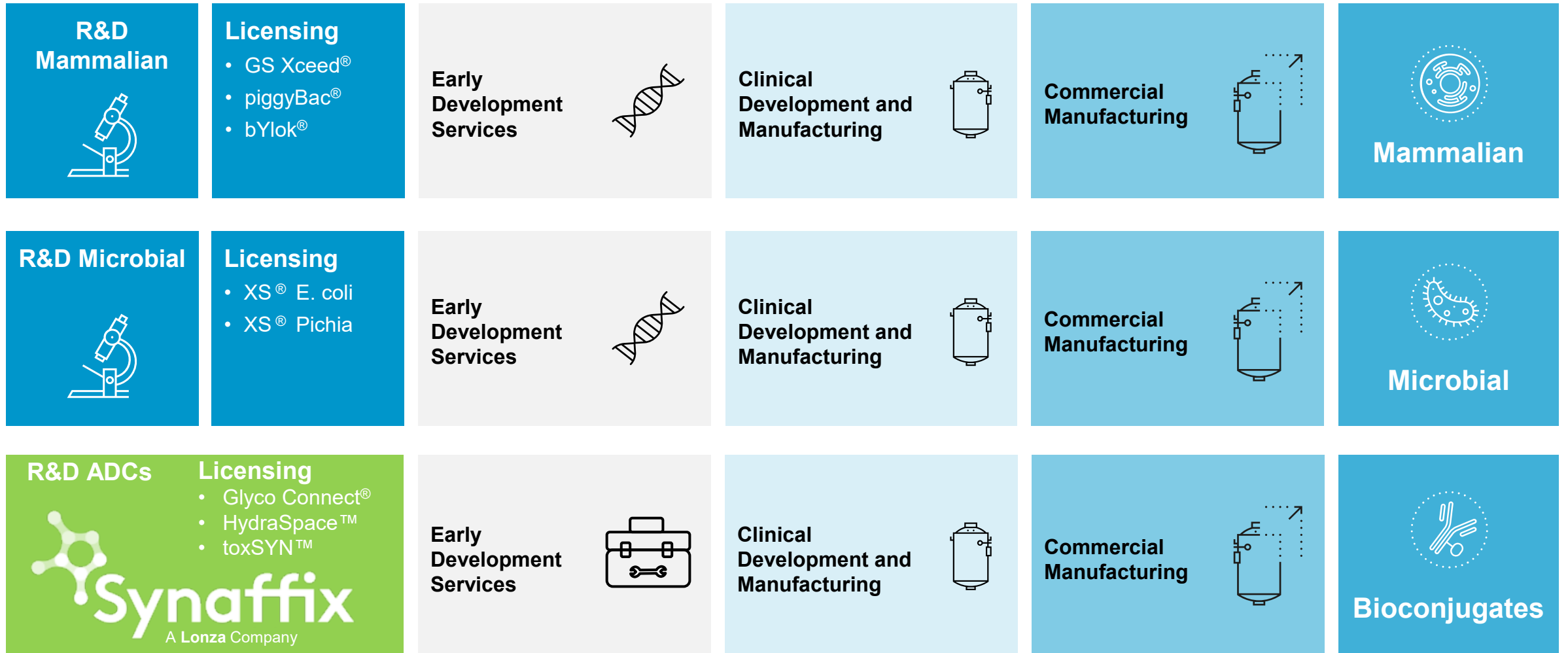
Numerous Growth Strategies to Accelerate Commercial Success

Acquisition by Lonza in Combination with Carve-Out of Pre-Clinical Pipeline of Proprietary ADCs Unlocks most Value for Both Patients and Shareholders



Synaffix Acquisition Enables End-to-End ADC Offering for Lonza

Essential ADC Technology and Services for Early Discovery, Clinical Development and Manufacturing





 Synaffix
A Lonza Company

 **Synaffix**
A **Lonza** Company