Antigenix THERAPEUTICS

Precision Antibody-Based Therapeutics

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My education journey

Bachelor's degree - Biology

Master's degree - Molecular Biology

Thesis: Evaluate transposable elements in purple sea urchins (*Strongylocentrotus purpuratus*)

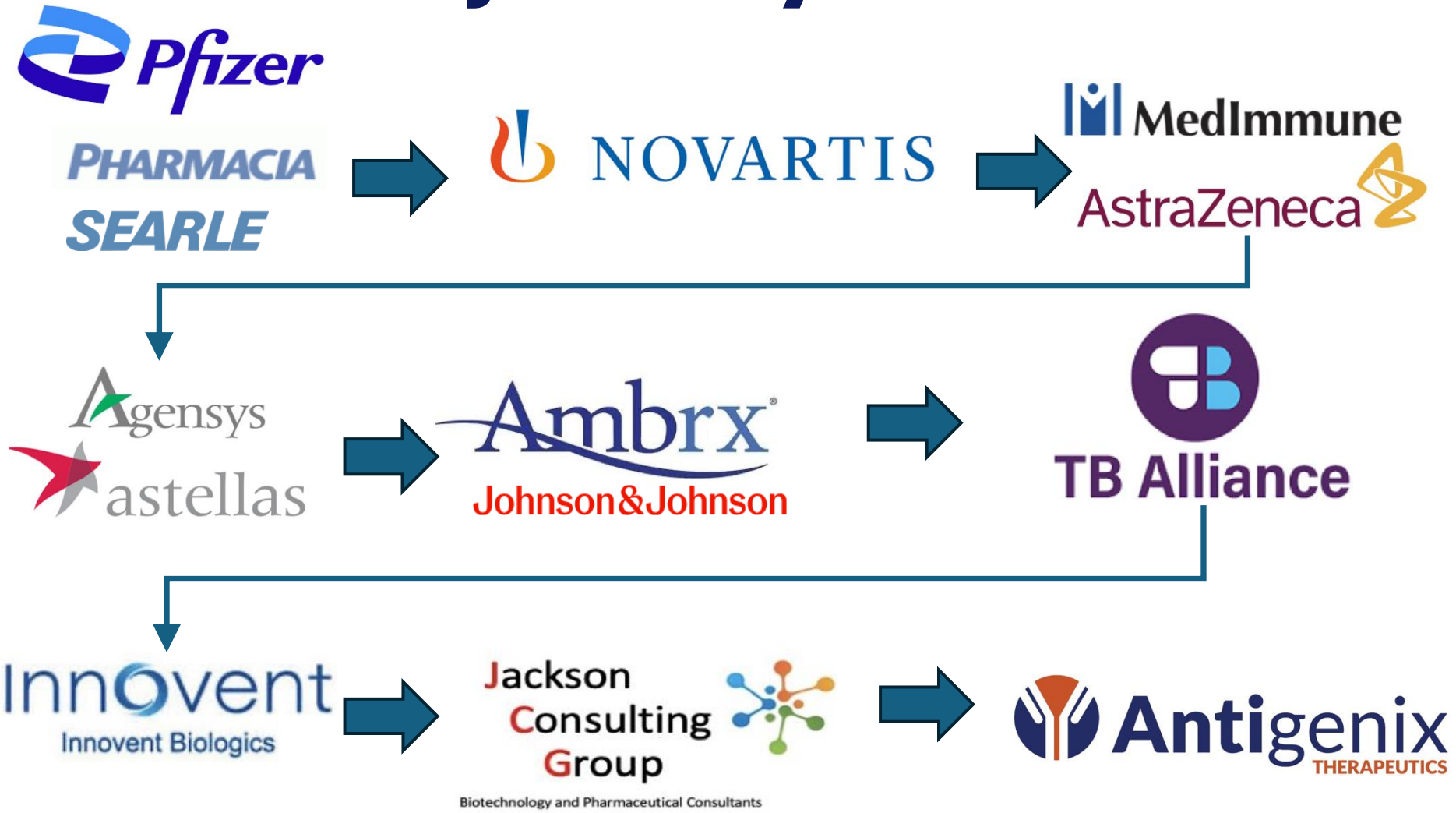
Doctorate degree – Molecular Biology/Biophysics

Thesis: Identified the angiogenic and anti-angiogenic properties of proliferin and proliferin related protein.
Science, 2 Dec 1994, Vol 266, Issue 5190, pp. 1581-1584

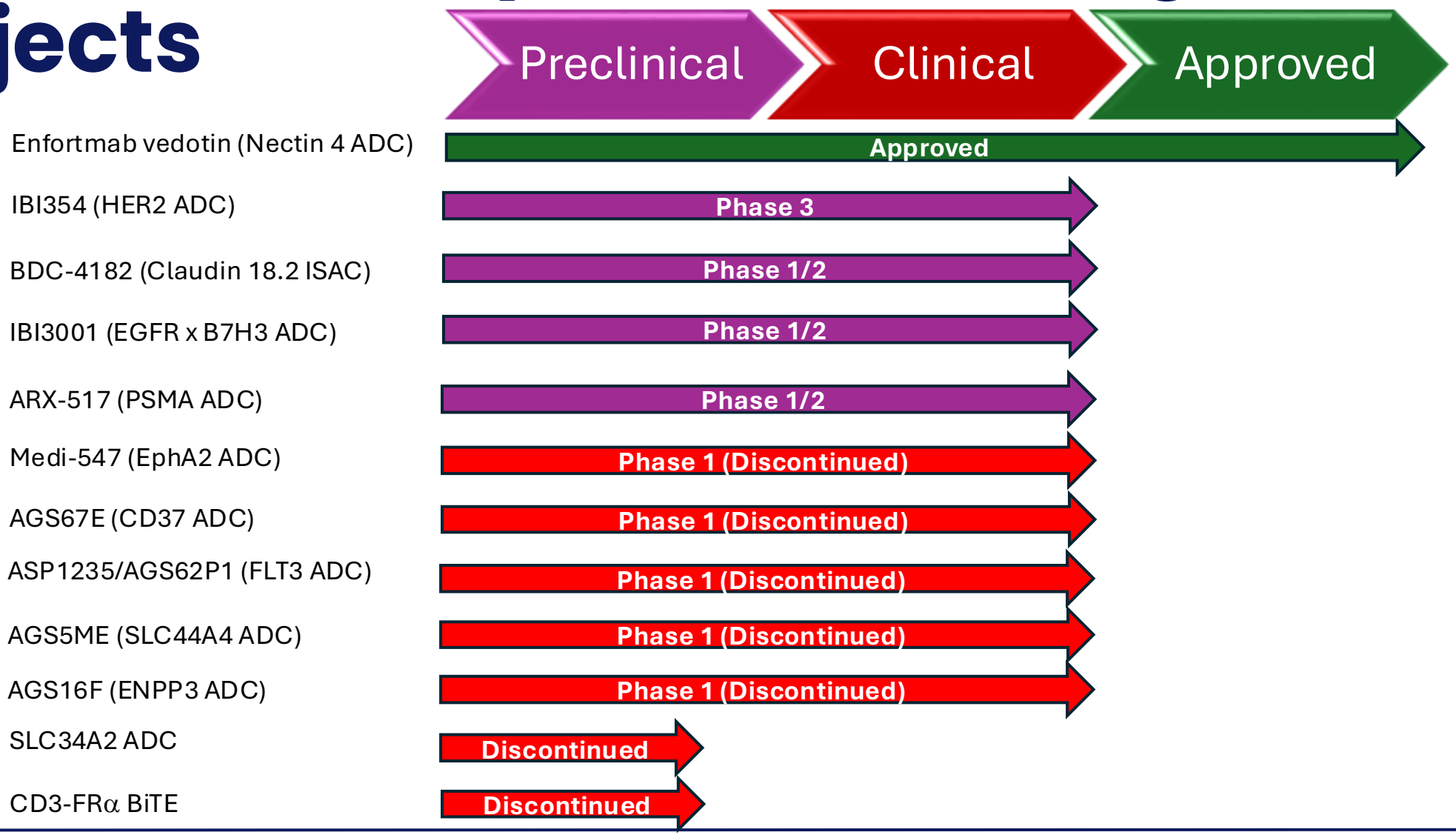
Postdoctoral fellow

Project: Evaluate the angiogenic properties of Ephrins and Eph receptors on tumor angiogenesis.

My career journey



Clinical development of biologics projects



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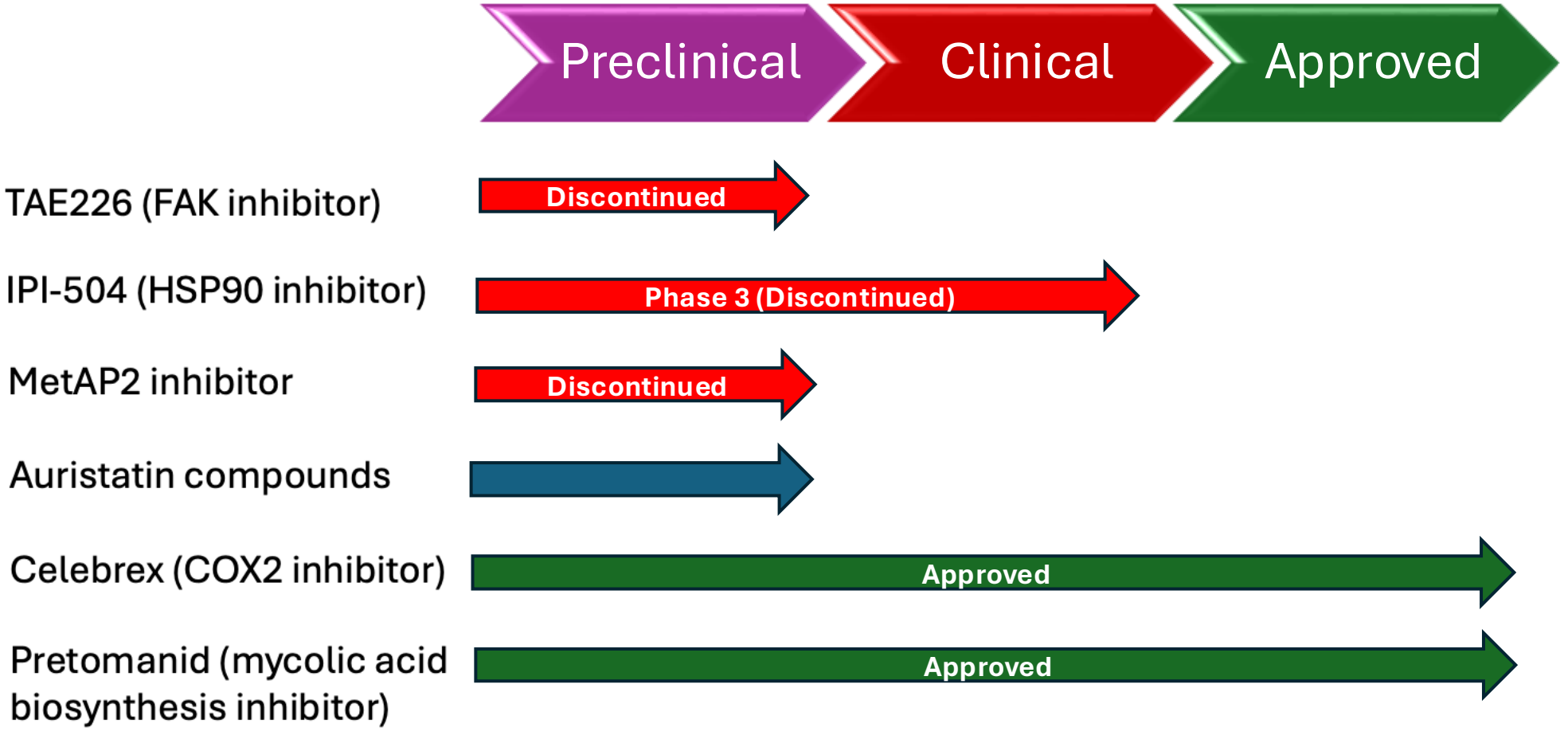
Clinical development of small molecule projects



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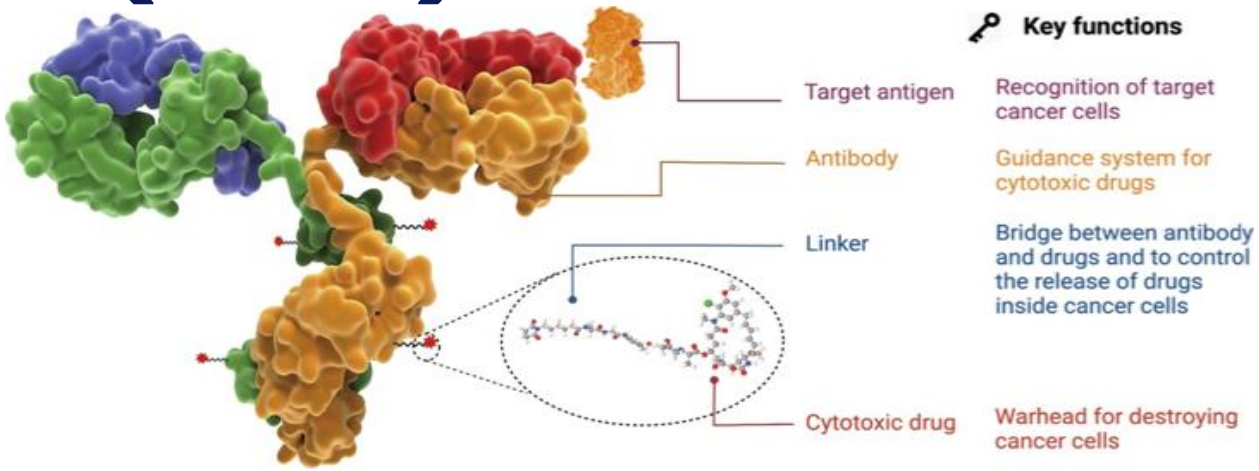
Antigenix Therapeutics

- Antigenix is focused on developing the next generation of antibody drug conjugates (ADCs) that have improved anti-tumor efficacy while reducing the side effects patients experience from various the previous generation of ADCs and chemotherapy.
- We are located in the Princeton Innovation Center BioLabs.
- We currently have five members on our team.

❖ We are actively searching for a post-doc to support our research efforts.

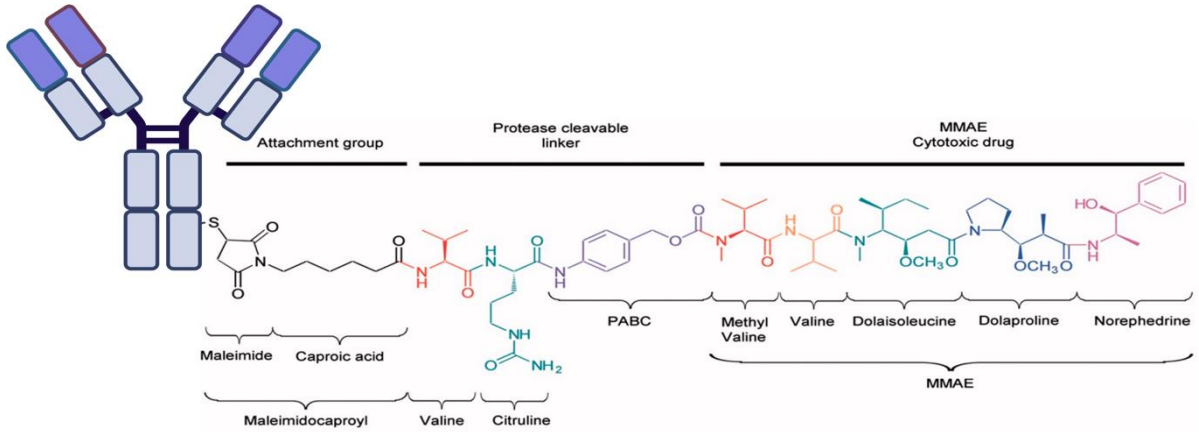
What is an antibody drug conjugate (ADC)?



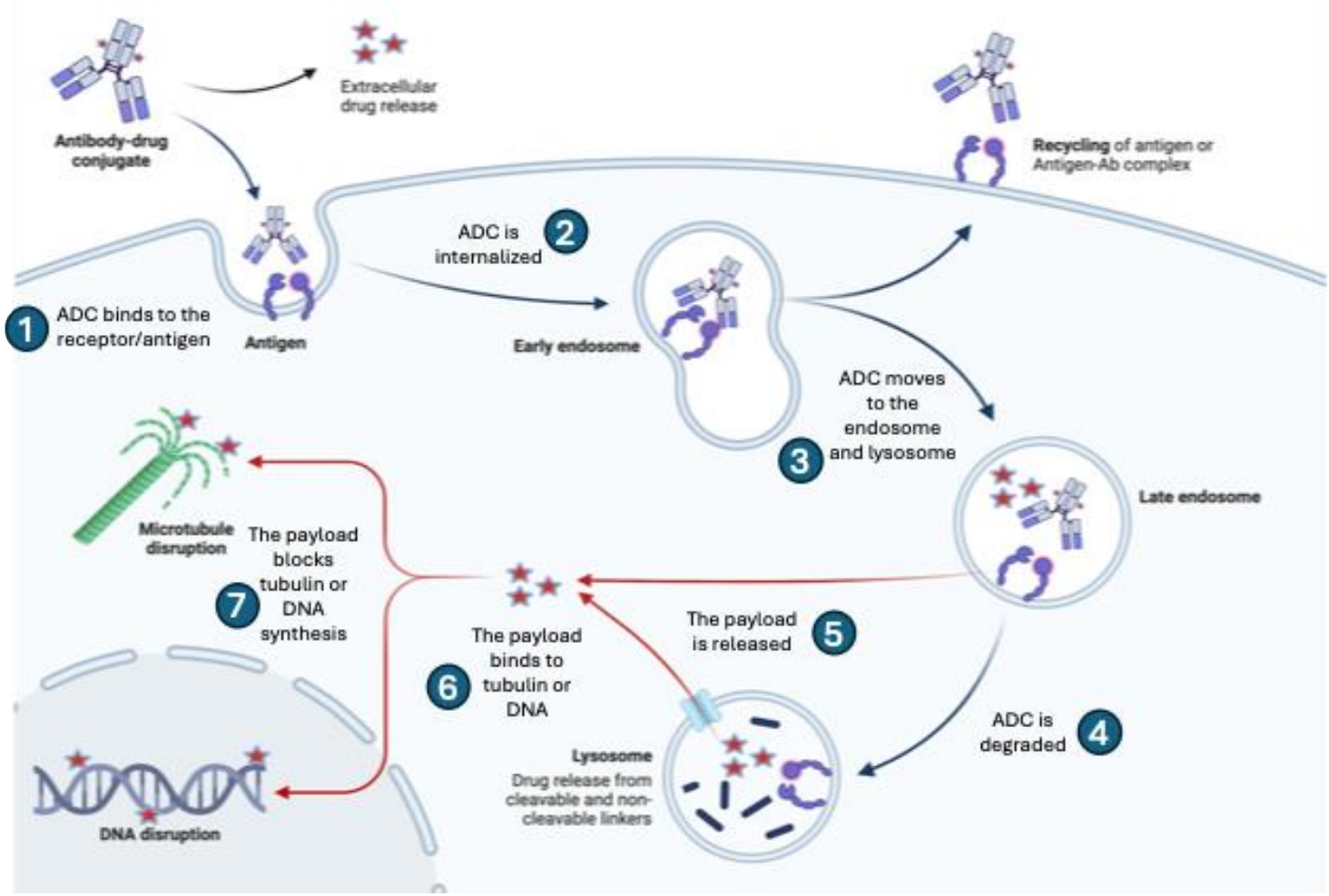
Type of linkers

- Protease cleavable
- Non-protease cleavable
- pH/acid cleavable
- Glutathione cleavable
- Sulfatase cleavable
- Linear
- Branched

Signal Transduction and Targeted Therapy (*Sig Transduct Target Ther*) ISSN 2059-3635 (online)



How do antibody drug conjugates work?



- ADCs bind to the cell surface receptors on cancer cells.
- The ADCs is internalized where it moved to the lysosomes.
- Once at the lysosomes, the antibody is degraded and the low pH aids in the release of the payload.
- The payload binds to either tubulin or DNA and inhibits the tubulin function or DNA synthesis.
- This results in apoptotic cell death

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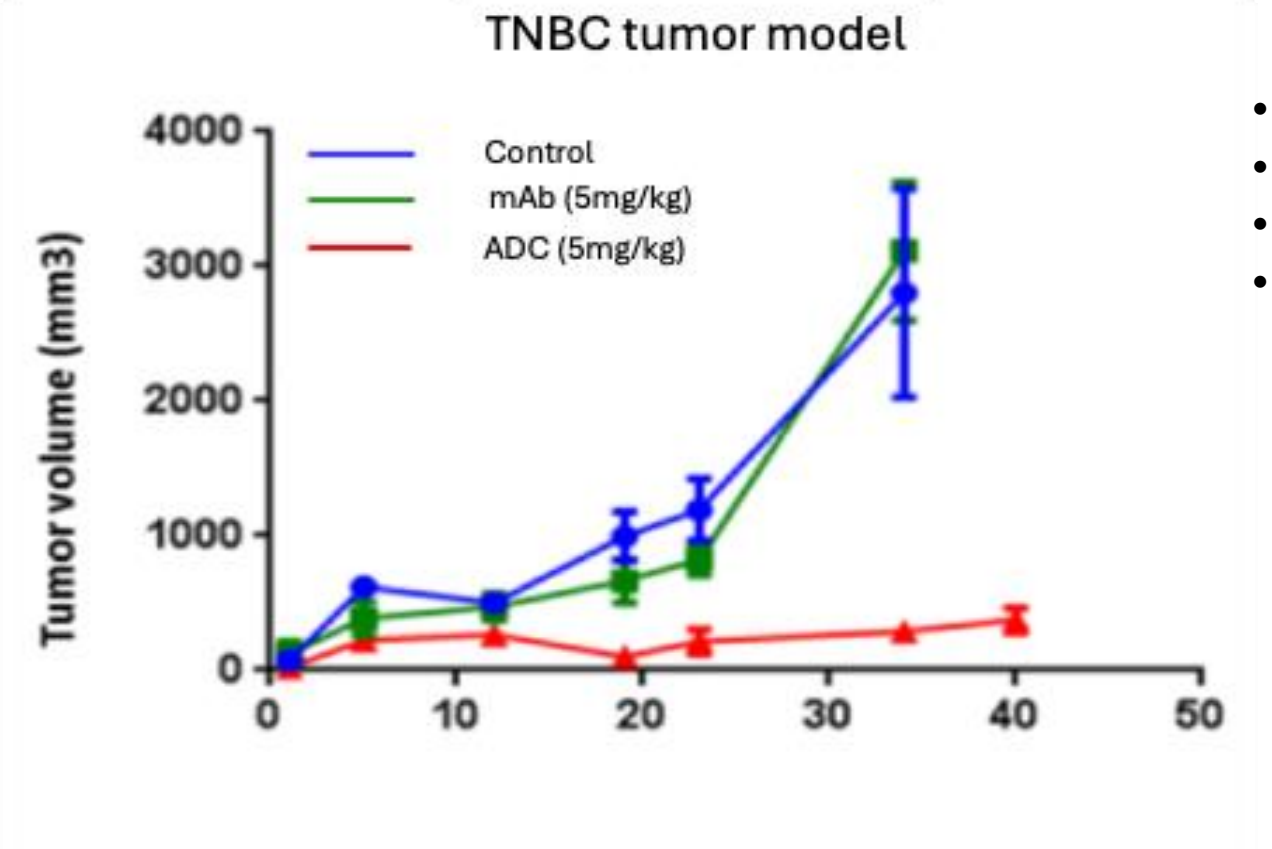
Our ADC Inhibits Tumor Growth in a Triple Negative Breast Cancer (TNBC) Tumor Model



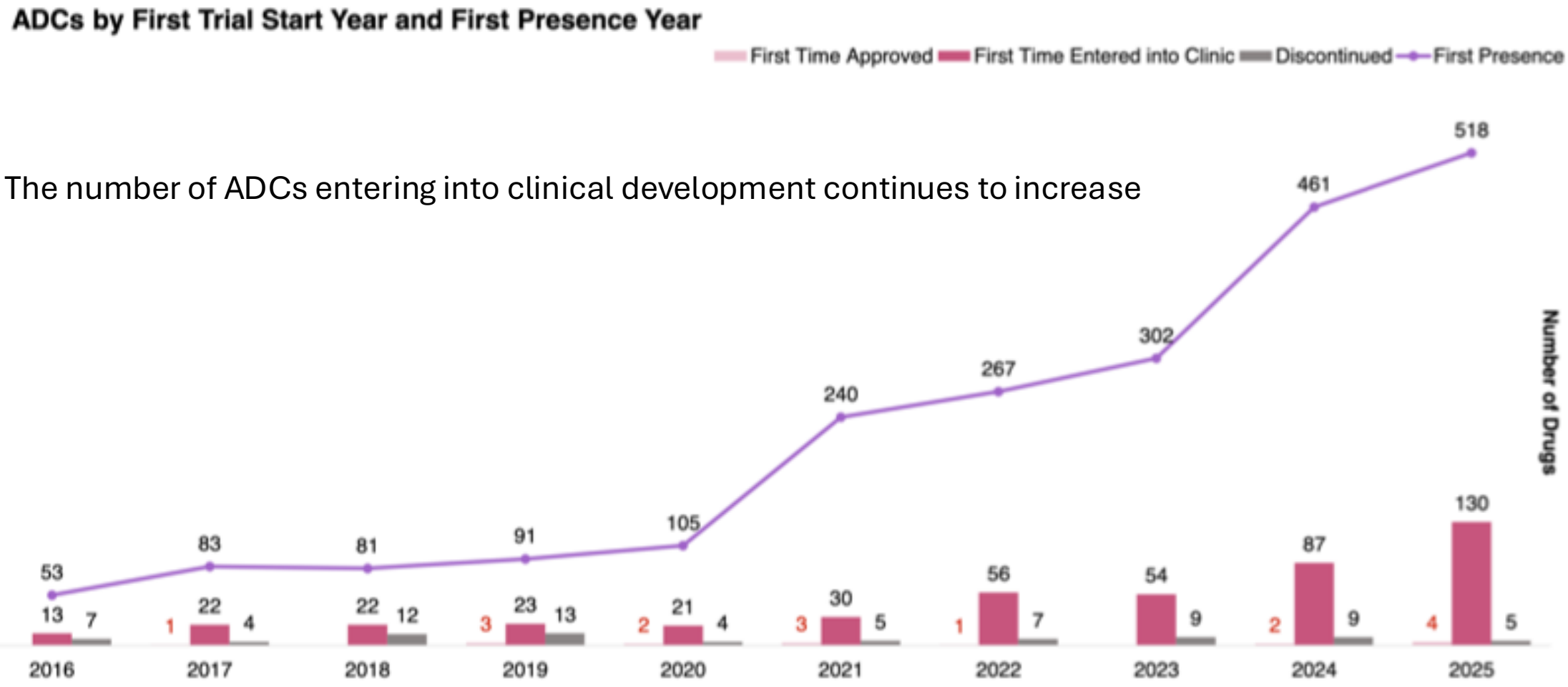
- Mice were implanted with TNBC tumor cells.
- Mice were treated with two doses of our ADC
- Our ADC inhibits tumor growth *in vivo*
- No weight loss was noted

20 ADCs have been approved

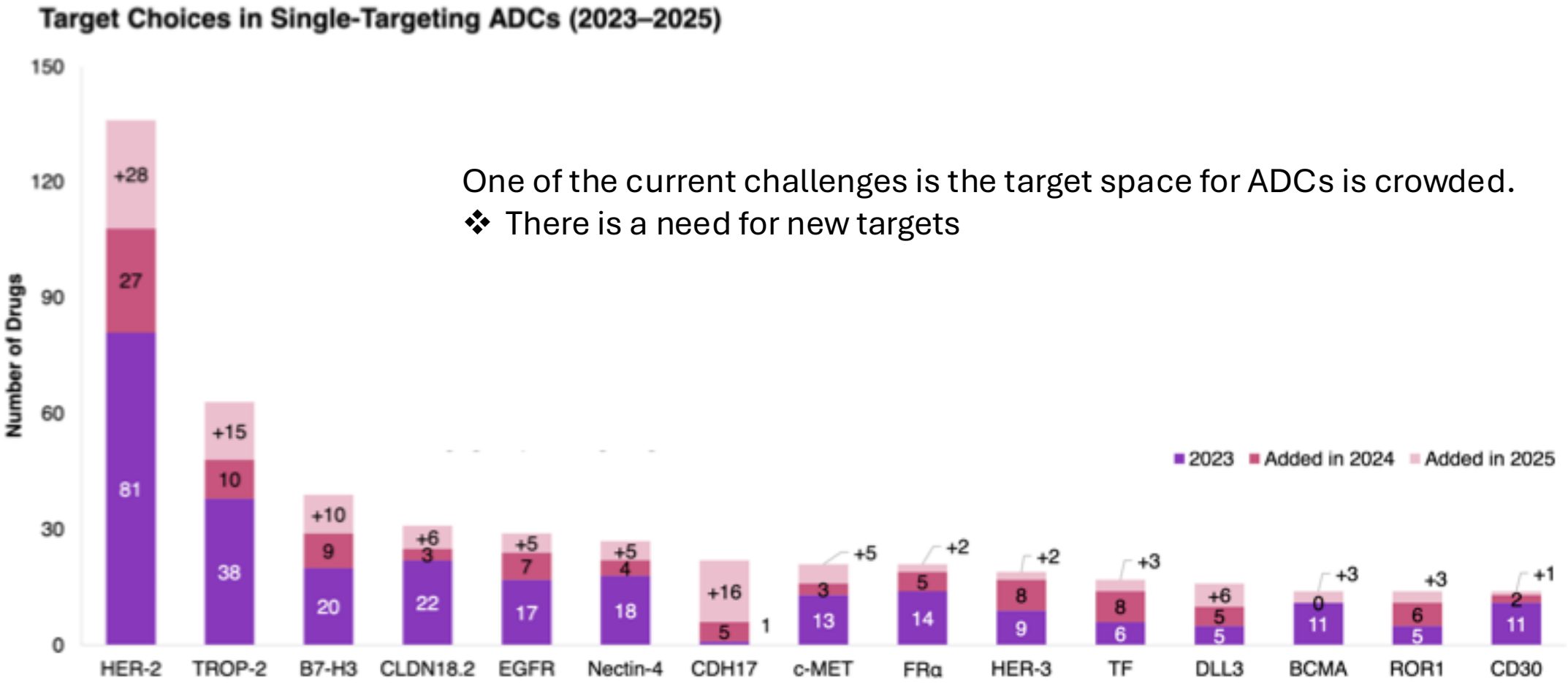
ADC	Target	Linker	Payload	Region(s) of approval	Year approved	Indications of approval
Brentuximab vedotin	CD30	Protease-cleavable dipeptide (Val-Cit)	MMAE	US, EU, Japan, Canada, others	2011	Hodgkin lymphoma; systemic ALCL; other CD30-positive lymphomas
Trastuzumab emtansine	HER2	SMCC	DM1	US, EU, Japan, Canada, China, others	2013	HER2-positive metastatic breast cancer; HER2-positive early breast cancer with residual disease after neoadjuvant therapy
Inotuzumab ozogamicin	CD22	Acid-labile hydrazone	Calicheamicin	US, EU, Japan, others	2017	Relapsed/refractory B-cell precursor ALL
Polatuzumab vedotin	CD79b	Val-Cit-based protease-cleavable linker	MMAE	US, EU, Japan, Canada, others	2019	Relapsed/refractory DLBCL; frontline DLBCL in some settings
Enfortumab vedotin	Nectin-4	Val-Cit-based protease-cleavable linker	MMAE	US, EU, Japan, others	2019	Locally advanced/metastatic urothelial carcinoma; combination use with pembrolizumab in some regions
Trastuzumab deruxtecan	HER2	Tetrapeptide-based cleavable linker	DXd (deruxtecan)	US, EU, Japan, China, UK, others	2019	HER2-positive breast cancer; HER2-low metastatic breast cancer; HER2-positive gastric/GEJ cancer; HER2-mutant NSCLC; HER2-positive colorectal cancer
Sacituzumab govitecan	TROP-2	CL2A	SN-38	US, EU, UK, others	2020	Metastatic TNBC; HR-positive/HER2-negative metastatic breast cancer; urothelial cancer
Gemtuzumab ozogamicin	CD33	Acid-labile hydrazone	Calicheamicin	US, EU, Japan, others	2000	CD33-positive AML
Tisotumab vedotin	Tissue factor	Val-Cit	MMAE	US, EU	2021	Recurrent/metastatic cervical cancer
Mirvetuximab soravtansine	FRα	Sulfo-SPDB	DM4	US, EU	2022	FRα-positive platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer
Trastuzumab botidotin	HER2	Val-Cit	Duostatin5 (MMAF)	China	2024	HER2-positive cancer
Trastuzumab rezetecan	HER2	GGFG	HS-9265 (Rezetecan)	China	2024	HER2-positive cancer
Sacituzumab tirumotecan	TROP-2	CL2A	KL610023 (Belotecan and analogues)	China	2024	TROP-2–positive cancer
Becotatug vedotin	EGFR	Val-Cit	MMAE	China	2024	EGFR-positive cancer
Telisotuzumab vedotin	c-MET	Val-Cit	MMAE	US	2024	c-MET–positive NSCLC
Datopotamab deruxtecan	TROP-2	GGFG	DXd	US, EU, Japan	2024	TROP-2–expressing NSCLC / breast cancer indications depending on region
Disitamab vedotin	HER2	Val-Cit	MMAE	China	2020	HER2-positive gastric/GEJ and urothelial carcinoma
Belantamab mafodotin	BCMA	MC	MMAF	US	2020/2025	Relapsed/refractory multiple myeloma
Ujvira	HER2	SMCC	DM1	India	2019	HER2-positive breast cancer
Loncastuximab tesirine	CD19	Val-Ala	Tesirine (SG3249 / SG3199)	US, EU, UK	2021	Relapsed/refractory DLBCL

Clinical Trends for ADCs

The number of ADCs entering into clinical development continues to increase



The ADC Target Space is Crowded



One of the current challenges is the target space for ADCs is crowded.

- There is a need for new targets

What's Unique About Antigenix's Approach To Targeted Therapies

- We have a novel cell surface target that is selectively and highly expressed in multiple tumor types and is not expressed or has very low expression in normal tissues.
- We are evaluating ADC technologies that improves payload release in the tumor and reduces normal tissue toxicities.
- Preclinical data shows our ADC has activity in tumors where the competitor ADCs had no activity.

Antigenix is Developing Multiple Targeted Antibody Formats

Antibody Drug Conjugate (ADC)

Immediate focus

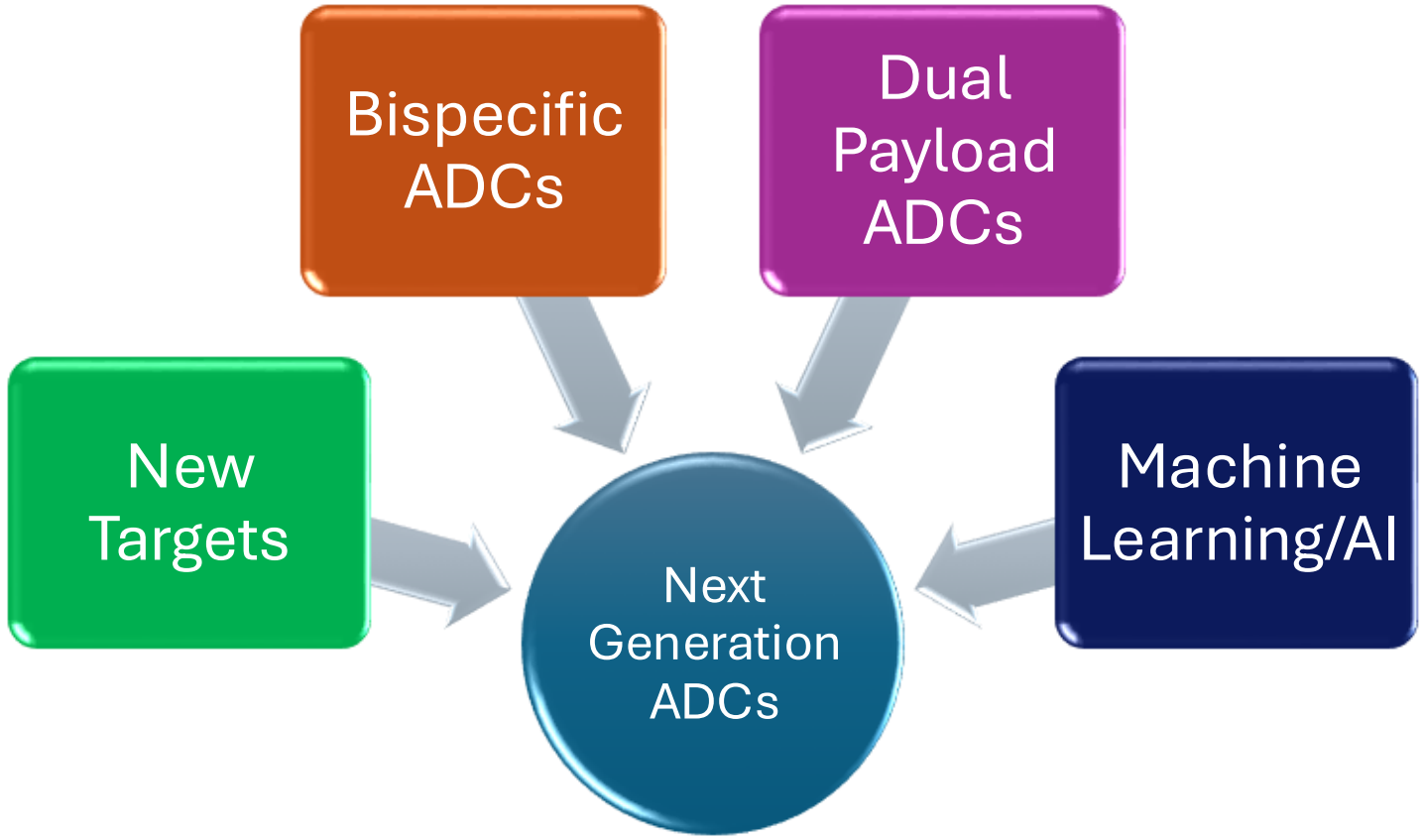
Bispecific ADC

We have identified potential targets for the bispecific ADC

Radioimmuno Conjugate

Future focus

Trends for developing the next generation ADCs



Antigenix Therapeutics – Overview

- Completed our pre-seed and seed round of funding.
- Currently humanizing antibodies against our novel target.
- Evaluating different linker-payload technologies to support our preclinical studies and IND enabling studies.

Summary

- Antigenix Therapeutics is an exciting new biotech startup that is developing next generation ADCs against an interesting new target.
- I have been in the biotech/pharmaceutical industry for 28 years and have been developing ADCs for 15 years.
- I have been fortunate to have worked in teams where we have had successes and failures.
  - Learn from the failures and apply those learnings to the next projects
- Enjoy the journey!

What have I learned along the way?

Big pharma/Biotech vs. small startups

Big Pharma/Biotech

Pros:

1. Well financed and resourced projects
2. Able to learn drug development from experts
3. Possible to work on and lead international project teams
4. Able to attend meetings and present
5. Good pay and benefits

Cons:

1. Lack of innovation
2. Slow to make decisions due to layers of bureaucracy
3. Lots of unnecessary meetings
4. Internal politics
5. High risk of layoffs
6. Easy to be siloed and work on a very defined assay/study
7. Dealing with lawyers and IP concerns

Small biotech startup

Pros:

1. Able to work on multiple projects
2. Very dynamic and fast paced data driven decisions
3. Able to have an immediate impact on projects
4. More opportunities to publish and present at meetings
5. Wear many hats/multi-tasking
6. Potential for a large payout if company is sold from stock options

Cons:

1. Limited funding
2. Longer work hours
3. Pay and benefits may not be comparable to big pharma
4. Can have less structure and too many changes too quickly

Learning from successes and failures

- Having a great team and great leadership is important to the success or failure of a project.
  - Being able to have open and reasonable exchange of ideas in critical.
  - Decisions are transparent and based on the totality of the information.
- Don’t be afraid to terminate a project.
- Find a good mentor.
- Seek constructive feedback.
  - Listen to the feedback and make the changes necessary to improve.

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Thank You