ASX Release

12 October 2023

AROVELLA LICENSES NOVEL SOLID TUMOUR TARGETING TECHNOLOGY

- Arovella has entered into a global, exclusive license with Sparx Group to develop a world-first iNKT cell therapy targeting a validated target, Claudin 18.2 (CLDN18.2), which is expressed in gastric cancers (GC), gastroesophageal junction cancers (GEJC) and pancreatic Cancer (PC).
- Equity-based upfront licencing fee and future stage-gated fees with industry-standard milestone payments in cash and equity.
- Licensed technology is based on Sparx's Phase 1 ready CLDN18.2 antibody, SPX-101, which has shown to outperform zolbetuximab in internal preclinical studies, and has an open IND with the FDA.
- Zolbetuximab (Astellas Pharma Inc.) is expected to be the first CLDN18.2-targeting therapy available for GC/GEJC, with FDA approval expected in January 2024
- The intellectual property has long-life, is granted in the US and has been filed in other major territories worldwide (inc. Europe, Japan, China and South Korea).
- Arovella's CLDN18.2-iNKT cells will be the only off-the-shelf CAR-iNKT cell therapy being developed for this target and will significantly increase the value of Arovella's pipeline
- CLDN18.2-iNKT cells with direct cancer-killing ability are expected to provide superior cancer killing properties relative to an antibody alone.
- Arovella's potential market for an FDA approved CLDN18.2-targeting product is supported by Astellas' forecast peak annual sales for zolbetuximab which are US$0.6-1.3 billion.
- Arovella's CEO and MD Dr Michael Baker will host an investor webinar discussing this announcement at 11am AEDT on Thursday 12 October. Please register here.

Accompanying Video Presentation: https://bit.ly/Arovella-CLDN-licence

MELBOURNE, AUSTRALIA 12 October 2023: Arovella Therapeutics Ltd (ASX: ALA) has signed a global, exclusive License Agreement with Sparx Group (Sparx) for the use of a novel monoclonal antibody (mAb) sequence targeting Claudin 18.2 (CLDN18.2) in cell therapies. The mAb, known as SPX-101, has completed all preclinical proof-of-concept, safety and specificity studies and toxicology studies required to commence a Phase 1 trial to treat gastric cancers.

Arovella will use the SPX-101 sequence to generate a chimeric antigen receptor (CAR) that will be incorporated into Arovella's iNKT cell platform to target gastric cancer (GC), gastroesophageal junction cancer (GEJC), pancreatic cancer (PC), and other solid tumours. CLDN18.2-iNKT cells with direct cancer-killing ability are expected to provide superior cancer killing properties relative to an antibody alone.

CLDN18.2 is a validated target, demonstrated by the fact that there are several products currently in clinical development. The most advanced of these is zolbetuximab, which was acquired by Astellas Pharma after compelling phase 2 data, during its takeover of Ganymed Pharmaceuticals in 2016 for €422 million up-front and the potential for €860 million in milestones. Zolbetuximab has also been awarded Priority Review for treating GC and GEJC by the FDA, highlighting the high unmet need for patients with these diseases. The FDA's decision to approve zolbetuximab is expected in January 2024. Astellas has forecast peak annual sales of US$0.6-1.3 billion for zolbetuximab. Although Arovella's CLDN18.2-iNKT program is preclinical and yet to

demonstrate efficacy, these forecasts support the potential market for an FDA approved therapeutic targeting CLDN18.2.

Arovella's CEO and MD, Dr Michael Baker, commented: "We are very excited to have licensed the CLDN18.2 mAb sequence for use in cell therapy. Sparx has completed excellent work demonstrating the superior activity of its CLDN18.2 mAb, and also its robust safety and specificity. CLDN18.2 is an exciting target, generating a lot of interest globally. Arovella will be the only company in the world developing a CAR-iNKT cell therapy targeting CLDN18.2. The natural benefits that iNKT cells may bring to solid tumours, combined with the CLDN18.2 CAR, is a compelling concept for cancer patients."

Sparx Therapeutics CEO and MD, Gui-Dong Zhu, commented: "Our partnership with Arovella represents a transformative phase in advancing mAb-based therapies. Arovella's cutting-edge CAR-iNKT platform, encapsulating advanced techniques for in vitro expansion and post-infusion persistence of iNKT cells, underscores their leadership in this domain. We profoundly acknowledge CLDN 18.2-iNKT cell therapy as a groundbreaking paradigm in oncological therapeutics."

SPX-101 has superior target affinity, specificity and anti-tumour activity in mouse models, compared to a version of zolbetuximab manufactured internally by Sparx. Arovella will use the SPX-101 sequence to generate CLDN18.2-targeting CAR-iNKT cells that it will develop to treat GC, GEJC and pancreatic cancers. Using the antibody to create CAR-iNKT cells with direct cancer-killing ability is expected to provide superior cancer killing properties relative to the antibody alone.

Cancer targets and unmet need

CLDN18.2 is expressed in a high proportion of gastric cancers (GC), gastroesophageal junction cancers (GEJC) pancreatic cancers (PC), and other solid tumours. GC and GEJC continue to present as high unmet medical needs with over one million new cases diagnosed per annum globally and 789,000 deaths, making it the fourth most fatal cancer globally.[1] Over 496,000 individuals were diagnosed with PC worldwide in 2020 with an estimated 466,000 deaths the same year.[2] Stage 4 pancreatic cancer has a five-year survival rate of 1% with the average patient living for approximately 1 year after their diagnosis.[3] The global gastric cancer market size was valued at $2.1 billion in 2021, and is projected to reach $10.7 billion by 2031, growing at a CAGR of 17.9% from 2022 to 2031.[4]

CLDN18.2 is expressed in very few healthy tissues, lowering the risk of off-target effects for a product targeting this antigen. Furthermore, when CLDN18.2 is expressed in healthy tissue, the protein is sequestered in tight junctions, hidden between the cells and not accessible to bind to the CAR-iNKT cells. During tumour development, the normal tissue structure of the cells is disrupted, exposing the CLDN18.2, making it accessible to treatments such as CAR-iNKT cells. In addition, unlike many targets that can be downregulated, CLDN18.2

[1] https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(22)00134-1/fulltext
[2] https://acsjournals.onlinelibrary.wiley.com/doi/10.3322/caac.21660
[3] https://www.hopkinsmedicine.org/health/conditions-and-diseases/pancreatic-cancer/pancreatic-cancer-prognosis
[4] https://www.alliedmarketresearch.com/gastric-cancer-market-A74458#:~:text=The%20global%20gastric%20cancer%20market,cells%20lining%20of%20the%20stomach

is retained upon malignant transformation and is expressed in a large proportion of primary gastric cancers and metastases.[5]

Differentiation of Arovella's CLDN18.2-targeting technology

Arovella's CLDN18.2-iNKT cells will be the only CAR-iNKT product in development. iNKT cells are an off-the-shelf solution that have inherent properties that may make them amenable to targeting solid tumours, such as (i) the ability to infiltrate tissues and tumours[6,7], (ii) the ability to block or kill cells that promote tumour survival such as myeloid-derived suppressor cells (MDSCs) and tumour-associated macrophages (TAMs),[8] and (iii) the ability to release cytokines to stimulate an immune response and recruit other immune cells to target the tumour cells.[9,10]

Key Terms of The Licence Agreement

The terms of the licensing agreement provide no immediate material financial impact on the Company as a result of signing the agreement, which has no conditions precedent and is effective immediately. Capital requirements to demonstrate the potential of the technology through proof-of-concept studies, complete the first milestone and confirm the viability of the program, are anticipated to be <A$500k over the next 12 months and will be funded out of Arovella's existing cash reserves. Once this data is generated, the Company will be able to determine the costs associated with further development and if it makes commercial sense to proceed.

The licensing payments include an upfront fee of A$300k payable in equity subject to 12-months escrow, and stage-gated, industry-standard milestone payments in cash and equity for achieving milestones such as confirming the use of the mAb sequence in CAR format, IND acceptance, initiating Phase 2 and Phase 3 clinical trials, receipt of FDA approval of the product and approval in other major territories (inc. Europe and Australia). The upfront fee represents 4,347,826 shares at the relevant 5 day VWAP of $0.069 ea., which will be issued under existing LR 7.1 capacity. The remaining contingent milestone equity payments total A$0.9 million which, if all were to be achieved, represent 13,043,478 shares at the current VWAP, which can be issued under existing LR 7.1 capacity. The number of Shares that shall be issued to Sparx for each milestone equity payment shall be calculated based on the five (5) day volume weighted average price (VWAP) of the Shares as quoted by the ASX, immediately before (and not including the day of) the ASX announcement of the relevant milestone.

The potential contingent cash milestone payments total US$14 million, US$12.5 million of which is payable on US FDA marketing approval. The contingent milestone payment for FDA regulatory approval may require additional funding at that time. The timing of the cash milestones is contingent on pre-clinical development success and, thereafter, clinical trial success. The majority of the contingent cash milestone payments are due upon market approvals. Accordingly, and based on other therapeutic drug development programs, this would typically be longer than 7 years.

[5] https://pubmed.ncbi.nlm.nih.gov/19047087/
[6] https://pubmed.ncbi.nlm.nih.gov/29967365/
[7] https://pubmed.ncbi.nlm.nih.gov/33046868/
[8] https://pubmed.ncbi.nlm.nih.gov/19411762/
[9] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4517377/
[10] https://doi.org/10.4049/jimmunol.163.9.4647

The Licence Agreement contains standard termination provisions, and there are no associated termination fees. The Agreement shall expire, on a country-by-country and Licensed Product-by-Licensed Product basis on the fifth (5th) year after the last to expire patents or 5 years after expiring of any exclusivity, or price, reimbursement protection. ALA has confirmed Sparx's ownership of the licensed technology and the validity of the licence agreement. Sparx has completed its obligations as required for ALA to commence development and commercialise the technology.

Investor webinar

Dr Michael Baker will hold an investor webinar for shareholders and interested parties to discuss this announcement and development for Arovella.

Time: 11am AEDT

Date: Thursday 12 October 2023

Registration: https://us02web.zoom.us/webinar/register/WN_XO31IvmYTaqEJvTjXeV8EA

Further details on how to attend will be provided by email following registration.

A recording of the session will be made available via the Company's website and social media channels following the event.

Questions can be submitted on the day or sent in advance to investor@arovella.com.

Release authorised by the Board of Directors of Arovella Therapeutics Limited.

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NOTES TO EDITORS:

About Arovella Therapeutics Ltd

Arovella Therapeutics Ltd (ASX: ALA) is a biotechnology company focused on developing its invariant natural killer T (iNKT) cell therapy platform from Imperial College London to treat blood cancers and solid tumours. Arovella is also expanding its DKK1-peptide targeting technology licenced from MD Anderson and used in conjunction with its iNKT cell therapy platform. Arovella's lead product is ALA-101. ALA-101 consists of CAR19-iNKT cells that have been modified to produce a Chimeric Antigen Receptor (CAR) that targets CD19. CD19 is an antigen found on the surface of numerous cancer types. iNKT cells also contain an invariant T cell receptor (iTCR) that targets α-GalCer bound CD1d, another antigen found on the surface of several cancer types. ALA-101 is being developed as an allogeneic cell therapy, which means it can be given from a healthy donor to a patient.

Glossary: iNKT cell – invariant Natural Killer T cells; **CAR** – Chimeric Antigen Receptor that can be introduced into immune cells to target cancer cells; **TCR** – T cell receptors are a group of proteins found on immune cells that recognise fragments of antigens as peptides bound to MHC complexes; **B-cell lymphoma** – A type of

cancer that forms in B cells (a type of immune system cell); **CD1d** – Cluster of differentiation 1, which is expressed on some immune cells and cancer cells; **aGalCer** – alpha-galactosylceramide is a specific ligand for human and mouse natural killer T cells. It is a synthetic glycolipid.

For more information, visit www.arovella.com

About SparX Group

A research-driven, development-stage biopharmaceutical trailblazer, SparX has a mission of "amplifying human immunity with groundbreaking antibody therapies." Through the utilization of big data analytics, including machine learning, SparX decrypts potential interactions within the vast complexity of biological information. With meticulous pharmacological analyses, backed by in vitro and in vivo evaluations using advanced mouse models, SparX is on a relentless quest to develop unparalleled or superior therapeutics. SparX's robust target discovery platform, combined with the multifaceted SAILING™ antibody optimization system and groundbreaking bi-ADC technology, is poised to redefine the success metrics of empowered antibody drug development. Equipped with in-house cGMP facilities, SparX is on track to become a self-sustaining, fully integrated biopharmaceutical entity.

For more information, visit https://sparxbio.com

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ASX:**ALA**

arovella THERAPEUTICS

Sparx

CLDN18.2 License

Novel monoclonal antibody sequence targeting Claudin 18.2 for use in cell therapy

October 2023

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Arovella licences novel tumour-targeting technology

Off-the-shelf iNKT cell platform

Developing off-the-shelf iNKT cell therapies to target blood cancers and solid tumour cancers

Novel technology targeting Claudin 18.2

Arovella to combine a novel monoclonal antibody (mAb) sequence targeting Claudin 18.2 (CLDN18.2) with its iNKT cell platform

Claudin 18.2 is a validated target

CLDN18.2 is a well documented target for immunotherapy that is overexpressed in multiple cancer types

Excellent safety profile

The mAb has been subjected to rigorous analysis confirming safety and specificity, including in non-human primate models

Commercially attractive deal

Stage-gated approach with upfront licence fee funded through Arovella's equity with industry standard milestone payments

Robust intellectual property

Clear patent protection with composition of matter claims, long patent life, granted in the US and filed in major territories

iNKT cells to target solid tumours

Arovella is implementing its strategy to target and kill solid tumours – 90% of newly diagnosed cancer cases[1]

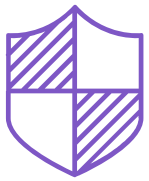
1. *https://www.cancer.gov/types/common-cancers*

Arovella's strategies to combat solid tumours

Arovella is using three approaches to expand the iNKT cell platform into solid tumours

License novel cancer targets

Identify and license new targets that are expressed in multiple cancers to incorporate into Arovella's iNKT celll therapy platform



Armour iNKT cells

Enhance the performance of iNKT cells by equipping iNKT cells with novel armouring technologies

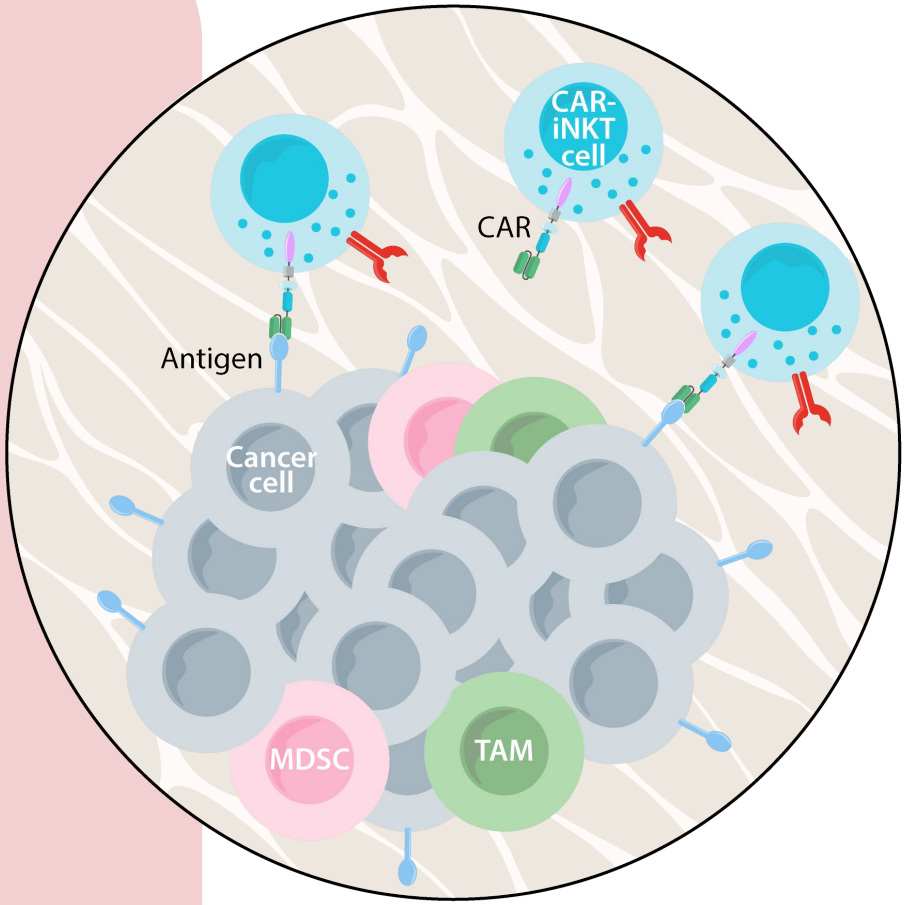
Create unique partnerships

Create partnerships to use novel combination therapies with synergistic effects

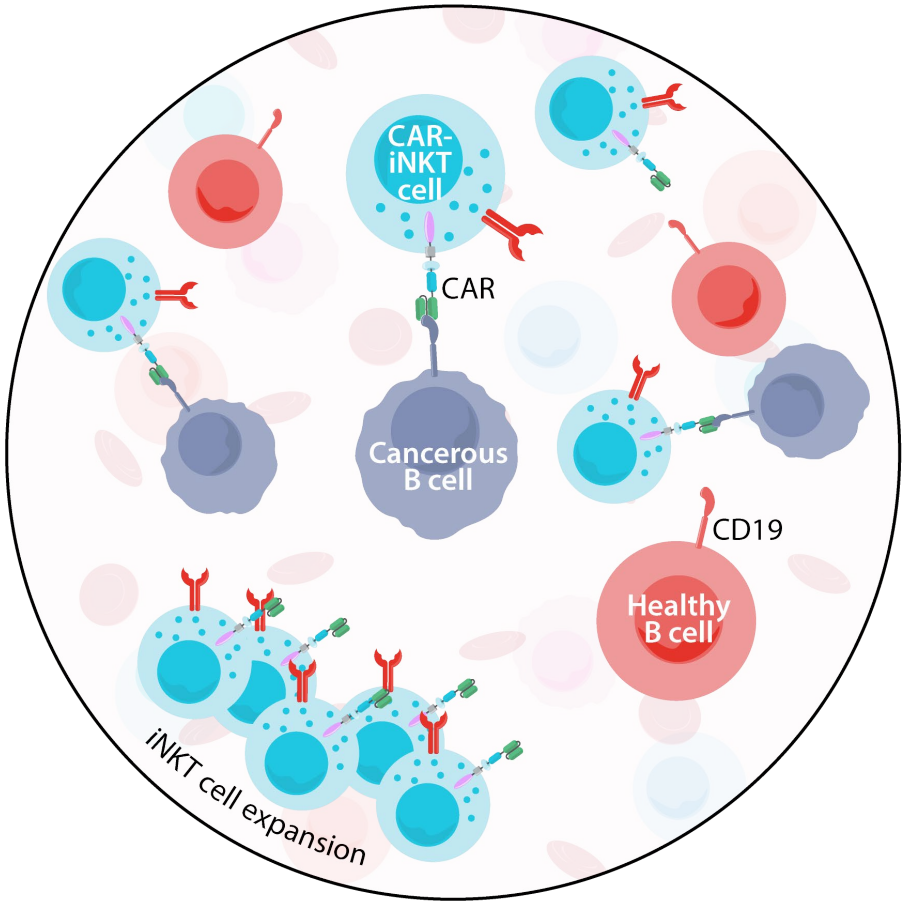
Solid tumours pose challenges to cell therapies

Solid tumours are more
difficult to treat with cell therapies

- Access to tumour
- Antigen specificity and uniformity
- Tumour microenvironment contains pro-tumour cells



Solid tumour

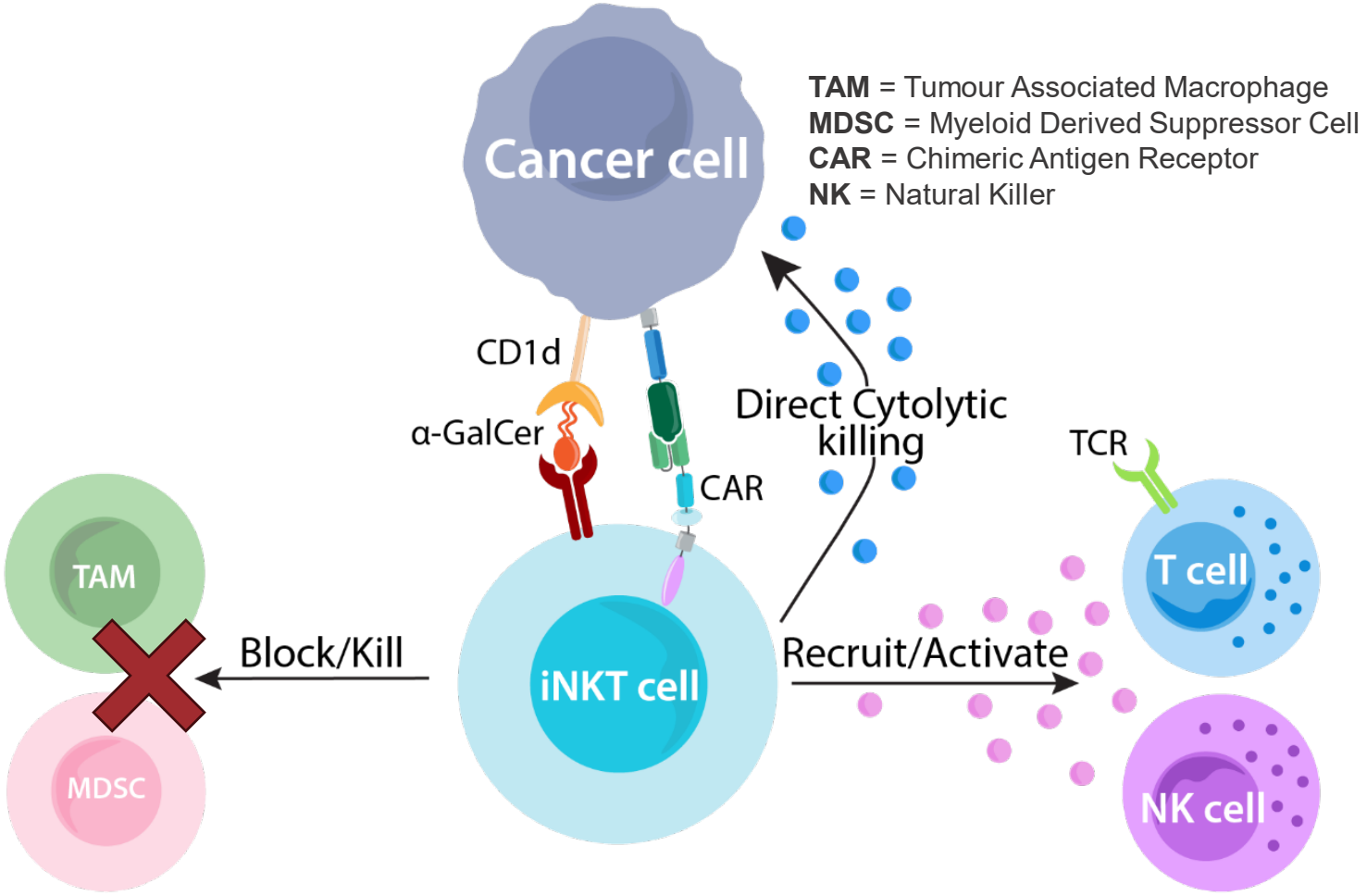


Blood cancer

TAM = Tumour Associated Macrophage; MDSC = Myeloid Derived Suppressor Cell; CAR = Chimeric Antigen Receptor

iNKT cells to combat solid tumours

iNKT cells have several properties to attack solid tumours



Modification of the tumour microenvironment

ESSENTIAL FOR SUCCESS

iNKT cells

- Home to tissues and infiltrate tumours[1,2]
- Block or kill cells that promote tumour growth[3]
- Recruit other immune cells that can also kill tumour cells[4,5]

1. Crosby and Kronenberg 2018 Nat Rev Immuno - 10.1038/s41577-018-0034-2; 2. Heczey et al., 2020 Nature Medicine - 10.1038/s41591-020-1074-2; 3. Song et al., 2009 J Clin invest - 10.1172/JCI37869; 4. Gottschalk et al., 2015 Front Immunol - 10.3389/fimmu.2015.00379; 5. Carnaud et al., 1999 J Immunol - 10.4049/jimmunol.163.9.4647

Add additional CARs for novel targets

STRATEGY 1

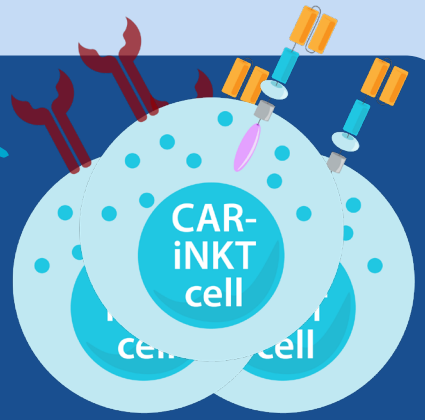
Arovella's manufacturing process can be leveraged for multiple cancer types

MANUFACTURING

CARs targeting novel antigens specific for solid tumours

can be incorporated into iNKT cells

using the same manufacturing process



New lentiviral vector generated for each new CAR

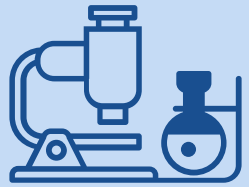
Introducing Claudin 18.2 (CLDN18.2)

A promising solid tumour target

CLDN18.2 overexpression has been

identified in several types of cancers

- gastric cancer **(GC)**
- gastroesophageal junction cancer **(GEJC)**
- pancreatic cancer **(PC)**
- esophageal cancer **(EC)**
- ovarian adenocarcinoma **(OAC)**
- lung cancers **(LC)**



Validated target

with first monoclonal antibody expected to be **approved in 2024**

Gastric cancer

market alone expected to reach **$10.7 billion** by 2031[1]

1. *https://www.alliedmarketresearch.com/gastric-cancer-market-A74458#:~:text=The%20global%20gastric%20cancer%20market,cells%20lining%20of%20the%20stomach*

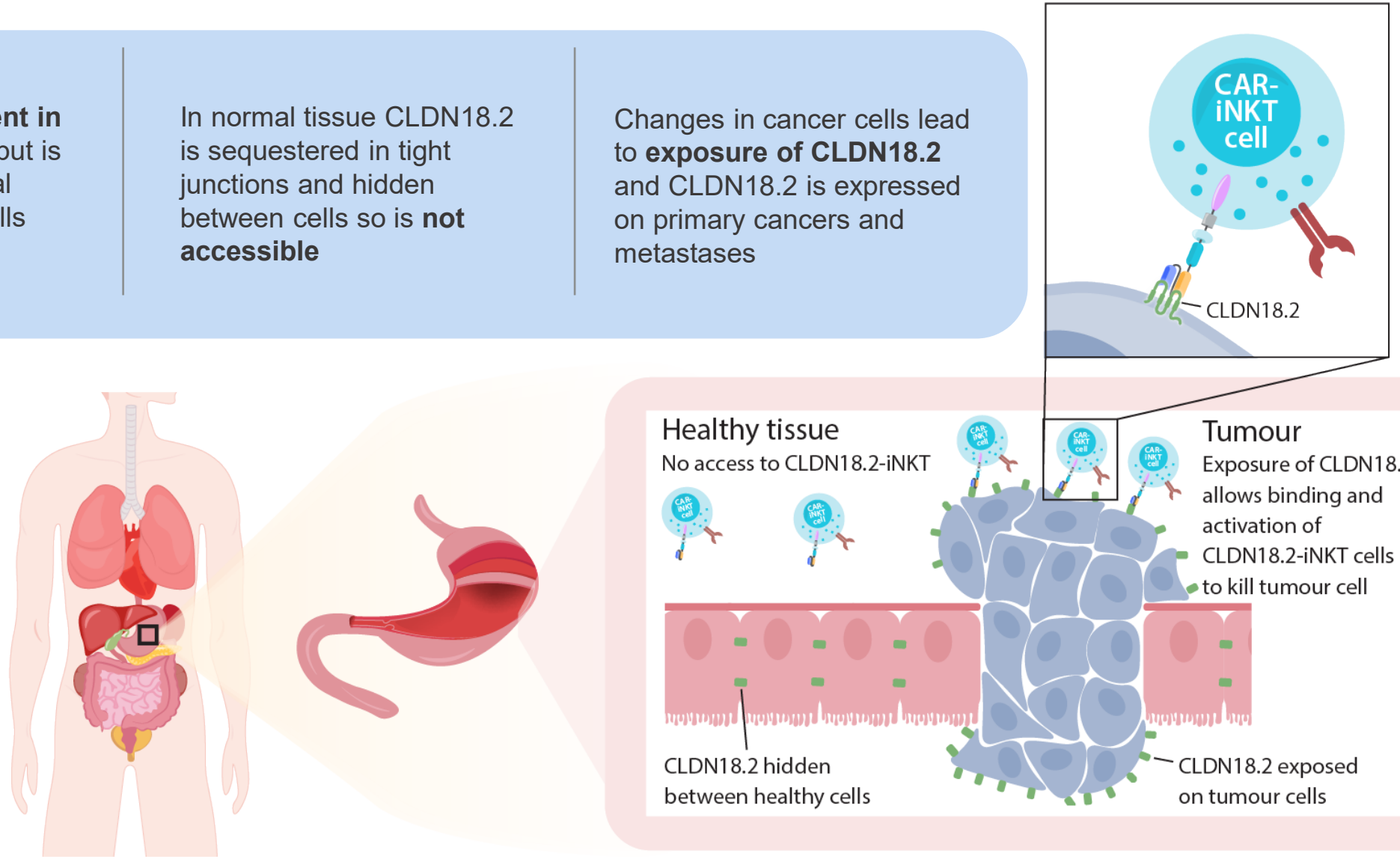
CLDN18.2 is a validated target

CLDN18.2 is hidden in healthy tissues and exposed on tumour cells

CLDN18.2 is **not present in most healthy tissues** but is found in gastric mucosal membrane epithelial cells (lining of GI tract)

In normal tissue CLDN18.2 is sequestered in tight junctions and hidden between cells so is **not accessible**

Changes in cancer cells lead to **exposure of CLDN18.2** and CLDN18.2 is expressed on primary cancers and metastases

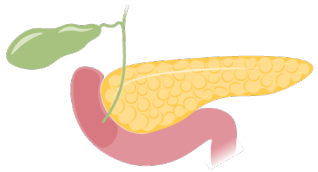


Targeting tumours of high unmet need

CLDN18.2 is found in a high proportion of gastric and pancreatic cancers

Gastric Cancer

>1,000k cases per annum globally[1]	**770k deaths** per annum globally[1]	**~6-33%** Regional and distant 5-year survival[2]	**4th highest** cause of cancer death annually[1]



Pancreatic Cancer

496k cases[3] per annum globally	**466k deaths** per annum globally[3]	**~3-15%** Regional and distant 5-year survival2[4]	**No effective standard of care** For late-stage diagnosis

1. Morgan et al 2022 eClinicalMedicine - 10.1016/j.eclinm.2022.101404; 2. https://www.cancer.org/cancer/types/stomach-cancer/detection-diagnosis-staging/survival-rates.html; 3. Sung et al 2021 - 10.3322/caac.21660; 4. https://www.cancer.org/cancer/types/pancreatic-cancer/detection-diagnosis-staging/survival-rates.html

A Claudin 18.2 mAb is effective in gastric cancer

The mAb, zolbetuximab, is expected to be approved in Q1 2024

Zolbetuximab

completed phase 3

and is expecting **approval in Jan 2024**

FDA granted

Priority Review Biologics License Application (BLA)

Priority Review **only granted for major advances in therapy** or where no adequate therapy exists

FDA

2.4 months increase in overall survival

relative to standard of care in phase 3 study for gastric and gastroesophageal junction cancers*

Astellas acquired zolbetuximab

through the **acquisition of Ganymed in 2016** for an upfront payment of **€422 million** and milestones of **€860 million** and

expects peak sales of US $0.65-$1.3 billion

*Increase in progression free survival from 8.67 months to 10.61 months and overall survival from 15.54 to 18.23 months for zolbetuximab plus chemotherapy vs chemotherapy alone

Arovella to develop CLDN18.2 iNKT cell therapy

Exclusive licence to novel mAb sequence targeting CLDN18.2 for cell therapies

arovella THERAPEUTICS + Sparx

Exclusive global licence with Sparx Therapeutics

to use the patented SPX-101 sequence to develop cell therapies

Upfront payable in equity

modest short-term capital requirements

Industry-standard milestones

payable in cash and equity

SPX-101 technology → **TARGET SOLID TUMOURS** ← **iNKT** cell therapy platform

Arovella will combine the SPX-101 technology with its iNKT cell therapy platform to target solid tumours

Gastric cancer and pancreatic cancer are priority targets

The licence provides an **exciting new program** for Arovella in solid tumours, leveraging its progress on ALA-101

SPX-101 has an **excellent safety and efficacy** profile in pre-clinical studies

First off-the-shelf CAR-iNKT cell product

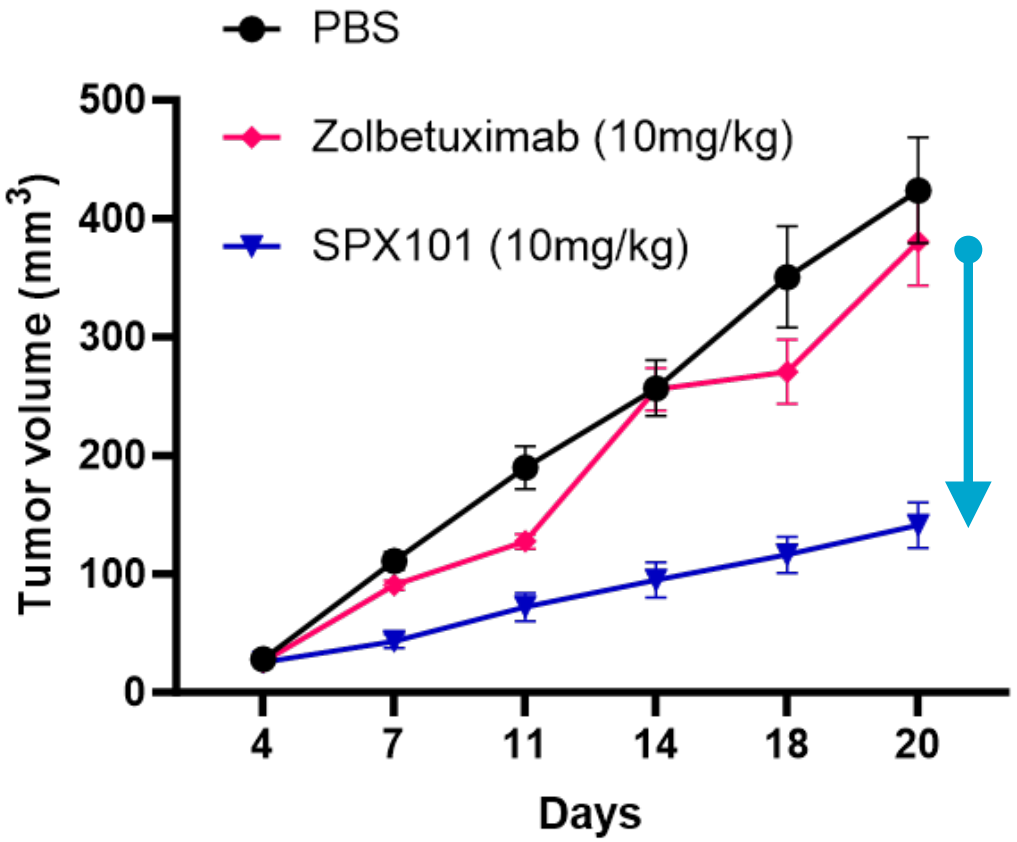
targeting CLDN18.2

SPX-101 has superior properties on a validated target

Excellent safety profile and demonstrated efficacy in animal models

SPX-101 is superior to zolbetuximab[1]

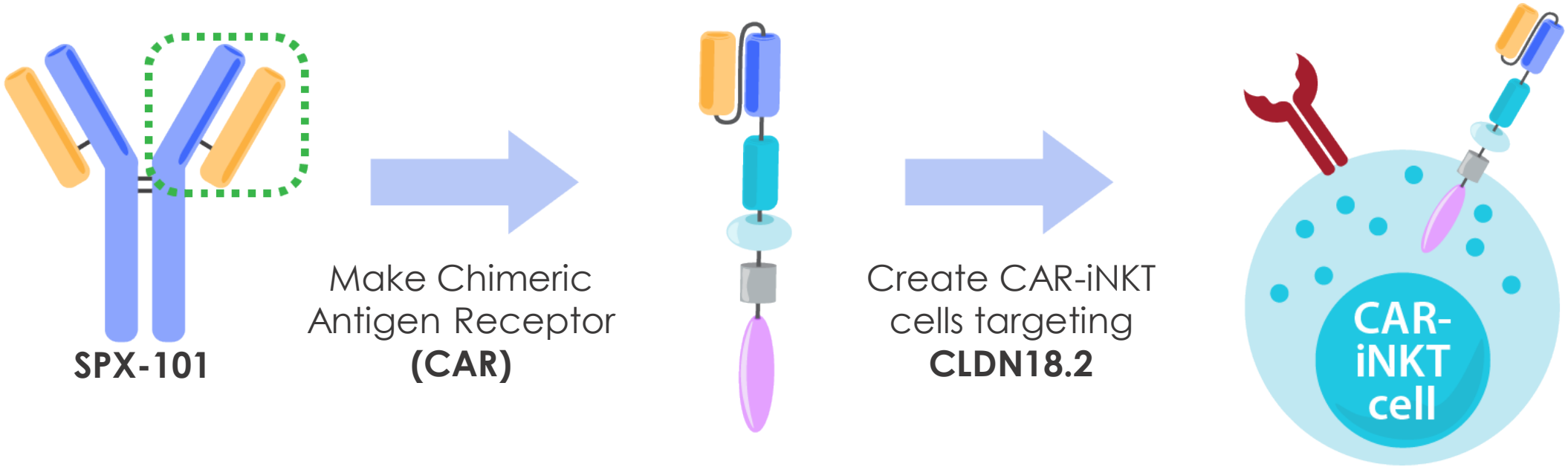
- Sparx has compared SPX-101 to an internally manufactured version of zolbetuximab
- ~30-fold higher affinity for CLDN18.2
- Superior efficacy and survival in MC38 mouse xenograft model (see graph)
- Sparx have an open IND to commence a Phase 1 clinical trial in patients with gastric cancer



1. Zolbetuximab used in these studies was made internally by Sparx using the zolbetuximab sequence

Leverage the mAb to create CLDN18.2-CAR-iNKT cells

Cell therapies generally expected to have better efficacy than mAbs

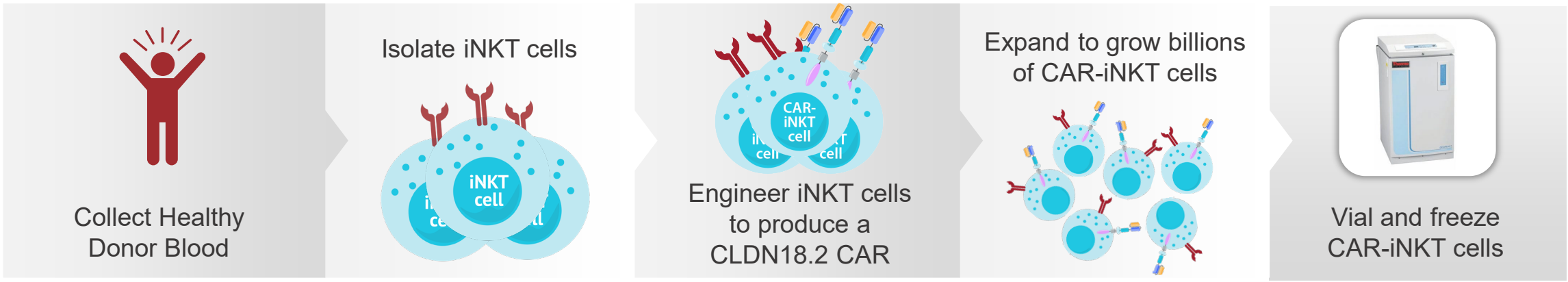


- The CLDN18.2-binding domain of SPX-101 will be used to create a CAR and incorporated into the iNKT cell platform
- This will be the **first off-the-shelf CAR-iNKT cell product targeting CLDN18.2**
  - An autologous CLDN18.2 CAR-T product is in Phase 1 and has demonstrated promising data

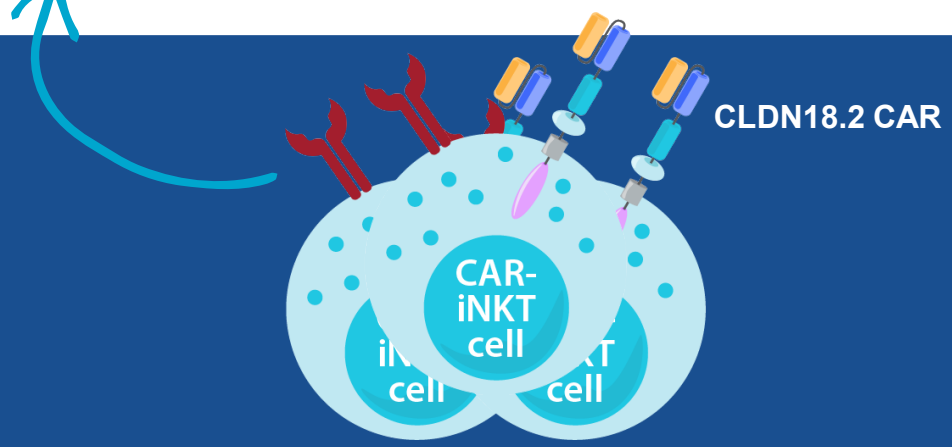
Manufacturing CLDN18.2-iNKT cells

Generation of CLDN18.2-iNKT cells will leverage existing manufacturing process

MANUFACTURING



Arovella will use its **proprietary manufacturing process** to create CLDN18.2-iNKT cells



Robust intellectual property

Patent life until 2038

Composition of matter claims for a unique CLDN18.2 monoclonal antibody sequence

Patent granted in the US

Patent pending in Europe, China, Japan and South Korea

US 20200207857A1

(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2020/0207857 A1**

Zhu et al. (43) **Pub. Date: Jul. 2, 2020**

(54) **BINDING MOLECULES SPECIFIC FOR CLAUDIN 18.2, COMPOSITIONS AND METHODS THEREOF, FOR THE TREATMENT OF CANCER AND OTHER DISEASES**

(71) Applicant: **Sparx Therapeutics Inc.**, Mt. Prospect, IL (US)

(72) Inventors: **Guidong Zhu**, Gurnee, IL (US); **Jingdong Ye**, Vernon Hills, IL (US); **Jingdong Qin**, Woodridge, IL (US); **Jichun Ma**, Germantown, MD (US)

(73) Assignee: **Sparx Therapeutics Inc.**, Mt. Prospect, IL (US)

(21) Appl. No.: **16/727,554**

(22) Filed: **Dec. 26, 2019**

Related U.S. Application Data

(60) Provisional application No. 62/786,012, filed on Dec. 28, 2018.

Publication Classification

(51) **Int. Cl.**

C07K 16/28	(2006.01)
C12N 15/85	(2006.01)

(52) **U.S. Cl.**

CPC ***C07K 16/2827*** (2013.01); ***C12N 15/85*** (2013.01); *C07K 2317/515* (2013.01); *C07K 2317/54* (2013.01); *C07K 2317/51* (2013.01); *C07K 2317/622* (2013.01); *C07K 2317/734* (2013.01); *C07K 2317/732* (2013.01); *C12N 2015/8518* (2013.01); *C07K 2317/55* (2013.01)

(57) **ABSTRACT**

Compositions and methods of making isolated binding molecules (e.g. an antibodies) or antigen-binding fragment thereof useful as therapeutics for treating and/or preventing diseases associated with cells expressing claudin18.2, including tumor-related diseases such as gastric cancer, esophageal cancer, pancreatic cancer, lung cancer, ovarian cancer, colon cancer, hepatic cancer, head-neck cancer, and cancer of the gallbladder are described. Also, described are pharmaceutical formulations comprising the described compositions for the treatment of diseases either as single agent (e.g., naked antibodies) or as adjuvant therapy with other antigen-binding anticancer agents such as immune checkpoint inhibitors (e.g., anti-CTLA-4 and anti-PD-1/PD-L1 monoclonal antibodies), and/or by combination therapies where the anti-claudin18.2 antibodies are administered before, after, or concurrently with chemotherapy.

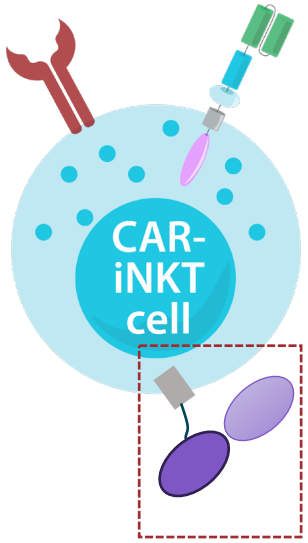
Specification includes a Sequence Listing.

“Armouring” iNKT cells

STRATEGY 2

Cytokine technology enhances activity of iNKT cells in solid tumours

Cytokine Technology



Cytokine Technology

Adding specialised cytokines to iNKT cells can **increase persistence of the cells** *(how long they last in the body)* and increase anti-tumour activity

Exclusive option

with University of North Carolina for cytokine technology developed by Prof. Gianpietro Dotti

Cytokine technology is incorporated into the lentiviral vector and **does not require change to manufacturing process**

iNKT cells + cytokine technology

Expand more and survive for longer

than CAR-iNKT cells lacking the cytokine

10x more circulating CAR-iNKT cells

4 weeks after treatment in a mouse model

Superior anti-tumour activity

compared to CAR-iNKT cells lacking the cytokine

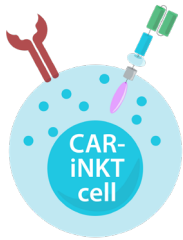
75%+

of mice treated with CAR-iNKT cells containing the cytokine were **alive at 61 days**

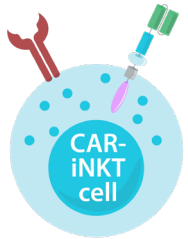
VS

Mice treated with CAR-iNKT cells lacking the cytokine **all died within 49 days**

Arovella's expanding pipeline

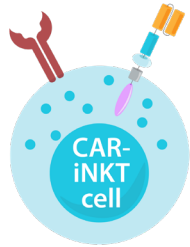


CD19-CAR



CD19-CAR

Oncolytic virus
CF33-CD19



Novel Targets

Introduction of CLDN18.2

ALA-101

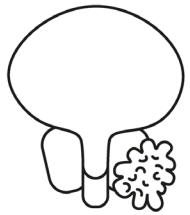
ALA-101 + onCARIytics

CLDN18.2

Cytokine Technology

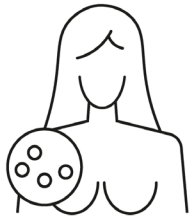
Non-Hodgkin's Lymphoma

Head and Neck Cancer



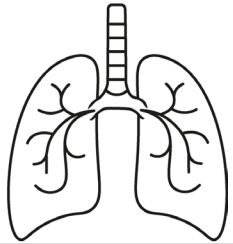
Prostate Cancer

Brain Metastases

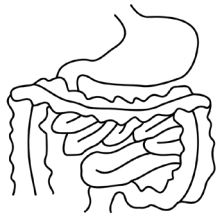


Triple negative breast cancer

Pancreatic Cancer



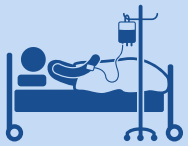
Lung Cancer



Gastric Cancers

Milestones for FY2024

	June 2023	December 2023	June 2024
ALA-101	▪ Complete process optimisation and scale-up in preparation for cGMP manufacture ▪ Complete production of cGMP lentiviral vector ▪ Finalise clinical trial plan for phase I study	▪ Complete cGMP manufacture for phase I clinical trials ▪ Complete preparatory activities for phase I study, including submission of regulatory dossier.	
iNKT Cell Therapy Platform	▪ Confirm the activity of CAR19-iNKT cells when combined with Imugene's onCARlytics to target solid tumours in animal model ▪ Analyse additional CARs to add to the platform ▪ In-licence cytokine technology currently under option (pending due diligence)	▪ **Initiate proof-of-concept testing for CLDN18.2-iNKT cells to expand iNKT platform for treatment of solid tumours**	



Expect to advance ALA-101 to phase I first-in-human clinical trial during 2024

Non-Hodgkin's lymphoma patients, dose escalation, primary end point – DLTs, secondary endpoint – efficacy signals

Continue to enhance the platform and expand the pipeline

Expand the use of the iNKT platform to treat solid tumours

DLTs – Dose Limiting Toxicities
cGMP – Current Good Manufacturing Practice

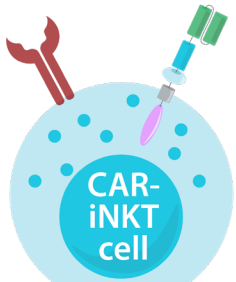
Summary

Novel allogeneic CAR-iNKT cell platform

iNKT cells serve as an excellent platform to develop allogeneic, or “off-the-shelf”, cell therapies to treat cancer

Lead product progressing to clinical trials

ALA-101, a potential treatment for CD19-expressing blood cancers, is being progressed to phase I clinical trials, expected to commence in 2024



Arovella’s CAR-iNKT Cell Platform

CAR-iNKT cells have multiple anticancer properties

CAR-iNKT cells are dual-targeting with enhanced cancer killing ability

iNKT cells have properties that may assist targeting solid tumours

Arovella continues to expand the iNKT cell platform to potentially treat solid tumours

Improved manufacturing logistics

Allogeneic CAR-iNKT cells will significantly improve logistics and increase patient access

Arovella is expanding its pipeline

Arovella has added a novel CLDN18.2 CAR to its platform, to target gastric and pancreatic cancer

ASX:**ALA**

arovella
THERAPEUTICS

Thank You

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Investor Webinar

Dr. Michael Baker
CEO & MANAGING DIRECTOR

DATE: Thur, 12 Oct 2023

TIME: 11:00 AM (AEDT)

https://us02web.zoom.us/webinar/register/WN_XO31IvmYTaqEJvTjXeV8EA