CHIMERIC THERAPEUTICS

Newsletter September 2021

Meet Dr Hua, he leads his own laboratory at the University of Pennsylvania where he and his team focus on discovering and developing new cancer therapies

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Jennifer's update

JENNIFER CHOW
CHIEF EXECUTIVE OFFICER
AND MANAGING DIRECTOR

Hello! I truly hope that this finds you and your loved ones all staying safe and healthy.

These past few months have been an incredibly busy time for our team at Chimeric. We have very exciting news to share with you about the expansion of our pipeline, the ongoing development of our CLTX CAR T and how we have further enhanced our in-house cell therapy expertise.

To the big news first – after months of negotiations, our team was thrilled to announce that we have exclusively licensed a novel CDH17 CAR T cell therapy from world renowned cell therapy centre, the University of Pennsylvania.

Within this newsletter I'm going to share with you the background on the team that invented this novel CDH17 CAR T cell therapy and highlight just a small fraction of the work that they have put into its development over the past decade. I believe you'll be as excited as our team is as you're able to see for yourself what promise this new CAR T cell therapy has for patients!

In their report assessing our new CDH17 CAR T cell therapy we were very pleased that the Edison Group recognised its potential, resulting in a valuation for Chimeric of A$327m or $0.99 per share. There's more information on the Edison Group report on page 7 of this newsletter.

While we have been in negotiations for the CDH17 CAR T cell therapy we have also remained fully committed to advancing the development of our CLTX CAR T cell therapy.

In our last newsletter we were pleased to announce that we had successfully completed the 1st dose cohort in our phase 1 clinical trial with no safety concerns. Now, we are pleased to let you know that the trial has continued to advance with patients in the 2nd dose cohort having already received their therapy. We also recently received our first IND clearance from the US Food and Drug Administration for our CLTX CAR T cell therapy. This is a key milestone for us as it provides the foundation for us to further advance development of our CLTX CAR T. More information on the CLTX CAR T can be found on page 8.

For anyone that has heard me speak, they have probably heard me talk about the expert team we have at Chimeric. I am incredibly proud of the team that we have built and continue to enhance and truly believe that it is this group of cell therapy pioneers and experts that makes Chimeric different from other companies that are developing cell therapies.

Cell therapy development can be challenging as it involves complex technical operations and novel regulatory standards. Teams that are inexperienced in cell therapy development often run into challenges that they were not able to predict or overcome because they have never experienced them before- they are unique challenges associated specifically with cell therapy development.

Having a team at Chimeric that has worked on the development of over 25 cell therapies, including 4 out of 5 of the FDA approved CAR T cell therapies gives us a competitive advantage. Not only are we able to foresee the challenges of development, we are able to leverage our expertise and resources to easily overcome them.

In the past few months, we have added two new cell therapy experts to the Chimeric team to enhance our technical operations. Dr Li Ren has joined our management team as Vice President, Technical Operations and Dr George Matcham has joined our board as a non-executive director.

Both Li and George have extensive technical operations expertise and experience and will be instrumental to our ongoing development and growth. I invite you to get to know them both better on pages 9 and 10 of this newsletter.

Finally, I am pleased to share with you that we continue to be in a healthy position to drive our growth and development having closed our year with ~A$22.5m in the bank and having funded our new asset licensing through existing cash reserves.

As we head into the 2nd half of the year our team will continue to focus on driving the development of both our CLTX CAR T and our CDH17 CAR T, discovering additional novel cell therapies to enhance our pipeline and expanding our team to ensure we are right-sized to drive our development.

I look forward to updating you later this year on our continued progress in pursuit of our mission and hopefully one day soon being able to meet many of you in person.

With warmest regards,

JENNIFER CHOW

Exclusive Licensing – Novel 3rd Generation CDH17 CAR T cell therapy

In late July, we were thrilled to announce that we have acquired the exclusive license to a novel, 3rd generation CDH17 CAR T cell therapy that meets all of our criteria. The CDH17 CAR T brings cutting edge science together with world renowned leaders in cell therapy development and has already demonstrated the promise of curative potential for patients.

Building a pipeline

In our last newsletter we talked about our goal to build a Chimeric pipeline. We highlighted that traditional drug development focuses on delaying disease progression in cancer – not on finding a cure – and that our mission at Chimeric is more ambitious.

We believe that novel cell therapies have the promise to cure cancer because we have seen it first-hand.

Our mission is to bring that promise to life for more patients with cancer by discovering, developing and commercialising cell therapies with the most curative potential.

In pursuit of our mission our team has been meeting with scientists and clinicians from all over the world, seeking to discover assets and technologies that we believe have the best chance of bringing curative potential to cancer patients.

We have been looking for assets that integrate the best science and collaborators that have the agility and experience in cell therapy to partner with us to bring the promise to life for patients.

THE QUICK FACTS

CDH17 CAR T cell therapy

Chimeric exclusively licensed the novel, 3rd generation CDH17 CAR T cell therapy from the University of Pennsylvania in July 2021

Extensive preclinical data for the CDH17 CAR T has demonstrated safety with potent efficacy

A Phase 1 clinical trial is planned to begin in 2022 at the University of Pennsylvania

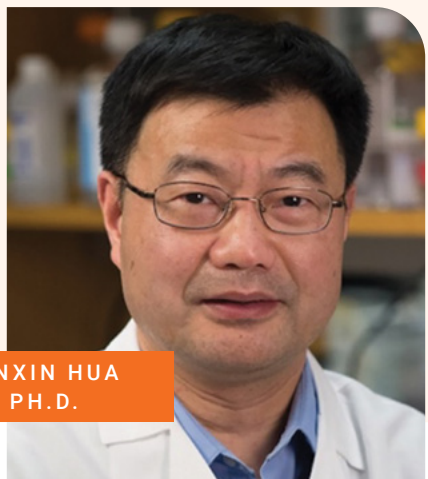
The CDH17 CAR T was acquired with attractive licensing fees funded through existing Chimeric cash reserves

A 3 year scientific research commitment has been entered into with the University of Pennsylvania and Chimeric for further development

Where was the CDH17 CAR T Cell invented?

The CDH17 CAR T cell therapy was invented and developed at the University of Pennsylvania (Penn). Penn is globally recognised as a leader in cellular immunotherapy discovery and development and is widely known for being the home to the 1st FDA approved CAR T cell therapy.

Penn
University of Pennsylvania



DR. XIANXIN HUA
M.D., PH.D.

Who was the CDH17 CAR T cell therapy invented by?

Dr Xianxin Hua is the scientific inventor of the CDH17 CAR T cell therapy. Dr Hua is an incredibly accomplished scientist who is a Professor of Cancer Biology at the University of Pennsylvania's Perelman School of Medicine, an investigator at the Abramson Family Cancer Research Institute and a Harrington Scholar Innovator.

Dr Hua leads his own laboratory at the University of Pennsylvania where he and his team focus on discovering and developing new cancer therapies. Dr Hua is widely published in top tier scientific journals and has won numerous awards and grants recognising his expertise in oncology research and development.

Chimeric is very pleased to have a 3 year scientific research collaboration commitment to further development with Dr Hua and his extended team at The University of Pennsylvania.

Exclusive Licensing – Novel 3rd Generation CDH17 CAR T cell therapy (cont.)

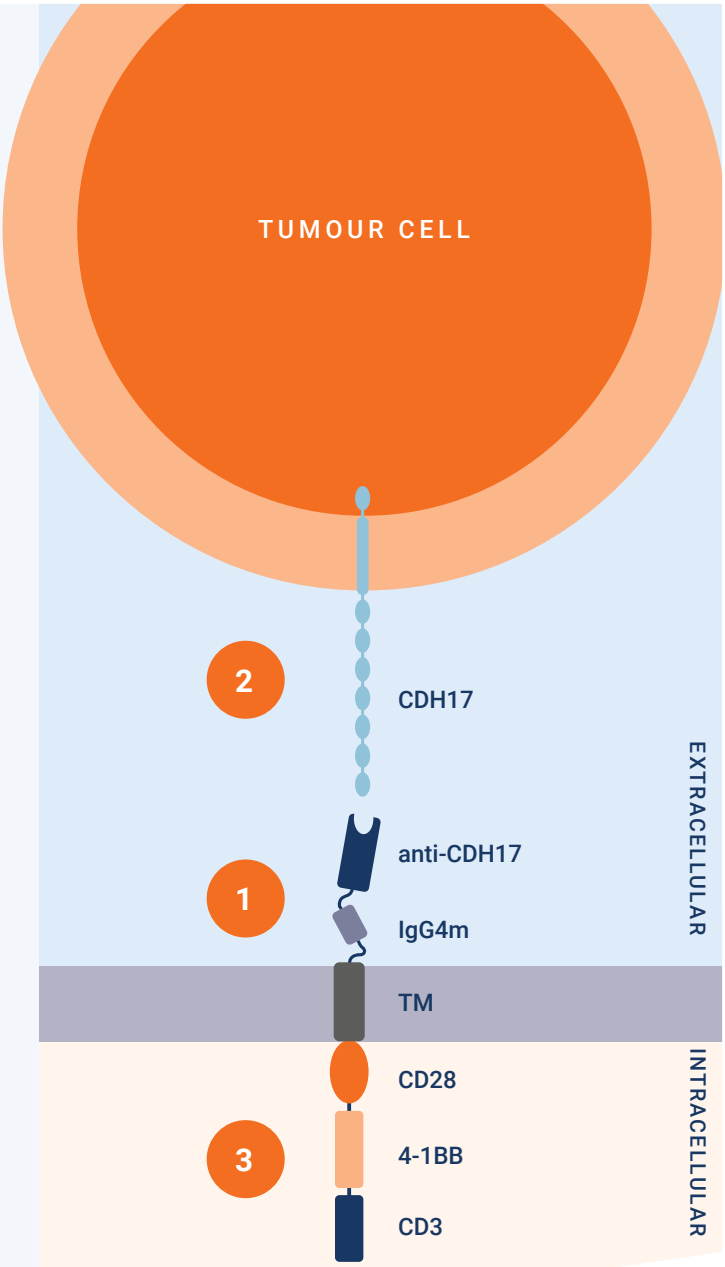
Dr Hua and his team at Penn have spent over 10 years developing and optimising the CDH17 CAR T cell therapy that Chimeric has licensed.

What was the invention process for the CDH17 CAR T cell therapy?

1. **Anti Cancer Antibody (single domain antibody) Development**
   The first step for Dr Hua and his team was to find an antibody that could best recognise and bind to tumour cells. Using a process developed by Dr Hua and patented by the University of Pennsylvania, Dr Hua was able to identify an optimal single domain antibody, that is often referred to as a nanobody, that specifically and preferentially bound to neuroendocrine tumour cells.

2. **CDH17 Identification**
   For the second step, Dr Hua and his team underwent a robust scientific process to identify and validate CDH17 as the antigen target for the optimal antibody they had identified.

3. **3rd Generation CDH17 CAR T Construct Optimisation**
   Finally, the team spent years optimising the CDH17 CAR T construct using the optimal antibody and testing it on CDH17 expressing tumour cells. This optimisation led to the invention of a 3rd generation CDH17 CAR T cell therapy.

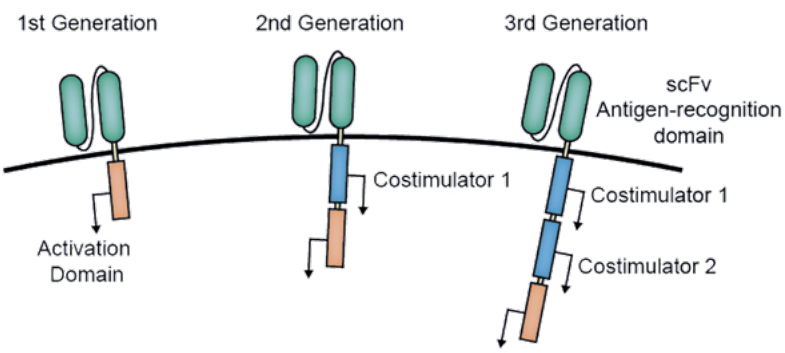


What makes a 3rd generation CAR T?

First Generation CAR T
Only have a CD3ζ activation domain giving them limited signaling capabilities that provide lasting responses.

Second Generation CAR T
Have the CD3ζ activation domain as well as a costimulatory signaling domain (most commonly CD28 or 4-1BB) which improves responses.

Third Generation CAR T
Have the CD3ζ activation domain as well as two costimulatory signaling domains (most commonly CD28 and 4-1BB) which improve T cell activation, enhanced survival and effective expansion of the modified T cells.



Is there any data on the efficacy of the CDH17 CAR T?

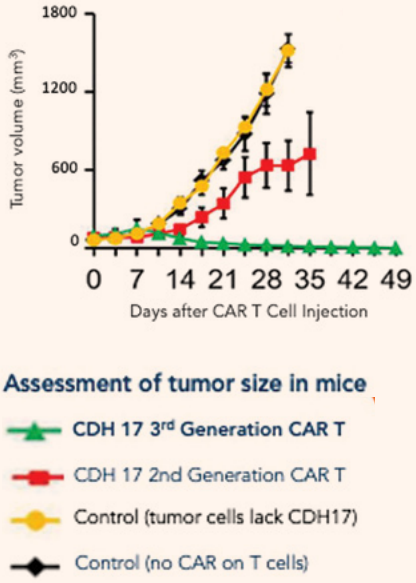
Preclinical studies have shown incredibly promising efficacy. With the 3rd generation CDH17 CAR T **complete tumour elimination with no relapse** was shown in mouse xenograft models.

In this preclinical experiment, the yellow and black lines are controls that show us how fast and how large the tumour continues to grow with no treatment.

The red line shows us one of the earlier versions of the CAR T cell therapy that Dr Hua and his team worked on during their decade of development.

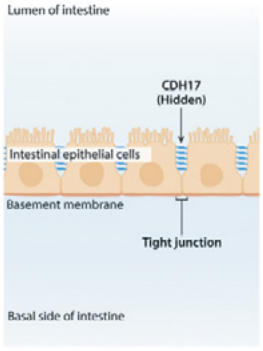
Although the red line shows us that the earlier version had some effect in slowing tumour growth, it was not considered good enough.

The green line is Chimeric's new 3rd generation CDH17 CAR T cell therapy. The green line shows us that our 3rd generation CDH17 CAR T cell therapy completely eliminated all tumour cells quickly and that the tumour cells never came back or relapsed.

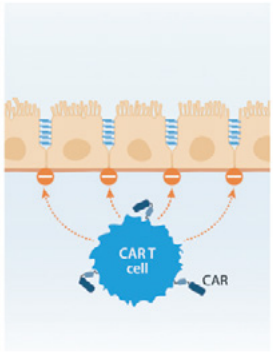


What about the safety of the CDH17 CAR T?

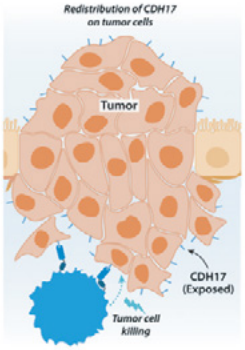
The safety of the 3rd generation CDH17 CAR T cell therapy was also extensively studied during its development. In preclinical experiments, it was shown that although the CDH17 CAR T cell therapy completely eliminated cancer cells that expressed the CDH17 antigen, it did not attack or eliminate normal cells, even when they too expressed the CDH17 antigen.



In normal cells, CDH17 is inaccessible as it is hidden beneath tight junctions that reinforce the barries of normal cells.



CAR T cells are not able to reach the CDH17 on normal cells due to the tight junctions.



In cancer CDH17 upregulation results in exposed of the CDH17 on the cancer cell surface allowing the CAR T to detect and bind to it.

The preclinical studies indicate that our CDH17 CAR T marks the recognition of an entirely new class of solid tumour antigen targets, that are highly susceptible to CAR T attack on tumour cells yet masked from attack by the CAR T in normal tissues

DR XIANXIN HUA, CDH17 CAR T CELL THERAPY SCIENTIFIC INVENTOR

Exclusive Licensing – Novel 3rd Generation CDH17 CAR T cell therapy (cont.)

What tumour types will you be able to treat with the CDH17 CAR T cell therapy?

With the potent preclinical efficacy and safety that was shown, we have made the decision to focus our initial development on 4 different tumour types that express high levels of CDH17; neuroendocrine tumours, colorectal cancer, pancreatic cancer and gastric cancer.

The combined impact of these four tumour types on patients and their families is incredibly significant as they are some of the most common and most deadly cancers today.

NEUROENDOCRINE TUMOURS

6.5x
Increase in incidence

15%
5-year survival for metastatic disease

GASTRIC CANCER

5th
Most common cancer

6%
5-year survival for metastatic disease

COLORECTAL CANCER

3rd
Most common cancer

14%
5-year survival for metastatic disease

PANCREATIC CANCER

8th
Most common cancer

3%
5-year survival for metastatic disease

When will clinical trials start?

A phase 1 clinical trial is planned to begin in 2022 in neuroendocrine tumours, colorectal, gastric, and pancreatic cancer. The trial will be designed to primarily look at the safety and maximum tolerated dose of the CDH17 CAR T cell therapy. The trial will be initiated at the University of Pennsylvania and will then expand to additional clinical sites.

Why was Chimeric chosen to license this therapy?

Chimeric was very proud to be selected as the successful licensee for the CDH17 CAR T as it was a highly competitive process due to the extensive asset optimisation and strong preclinical evidence.

To learn more about the CDH17 CAR T cell therapy and how Chimeric was chosen as the licensee, visit our website:
www.chimerictherapeutics.com

DR HUA INDICATED THAT HE CHOSE CHIMERIC FOR THREE MAIN REASONS:

01 The depth of Chimeric's cell therapy experience and expertise

02 The ease of open and transparent communication between the Chimeric and Penn teams

03 The shared passion of Chimeric to develop the CDH17 CAR T for patients

Feedback from the market on the CDH17 CAR T cell therapy licensing

Chimeric has received incredibly positive feedback on our exclusive licensing of the CDH17 CAR T cell therapy.

In their evaluation, the Edison Group noted that Chimeric had acquired "a promising first in class CAR T asset" giving Chimeric a valuation of A$327m or $0.99 per share.

Within their review, Edison made a point of noting that this valuation does not yet include the potential value of the CDH17 CAR T cell therapy, which they see as potentially transformative for Chimeric.

"Because the CDH17 programme is not yet in the clinic, we are not including it in our valuation yet, per Edison standard methodology. Once included, it may have a meaningful impact upon our valuation due to the size of the markets targeted by the company. To provide some perspective, we attribute a A$305m value to CLTX CAR T, a Phase I programme targeting GBM which has a US incidence of around 12,000 per year. Total incidence for the cancers targeted by the CDH17 programme is estimated to be 248,490 in the US. Hence this may be a truly transformational acquisition by the company."

To read the full Edison report on the CDH17 CAR T cell therapy licensing to Chimeric:

https://www.edisongroup.com/publication/acquiring-a-promising-first-in-class-car-t-asset/29767

CLTX update

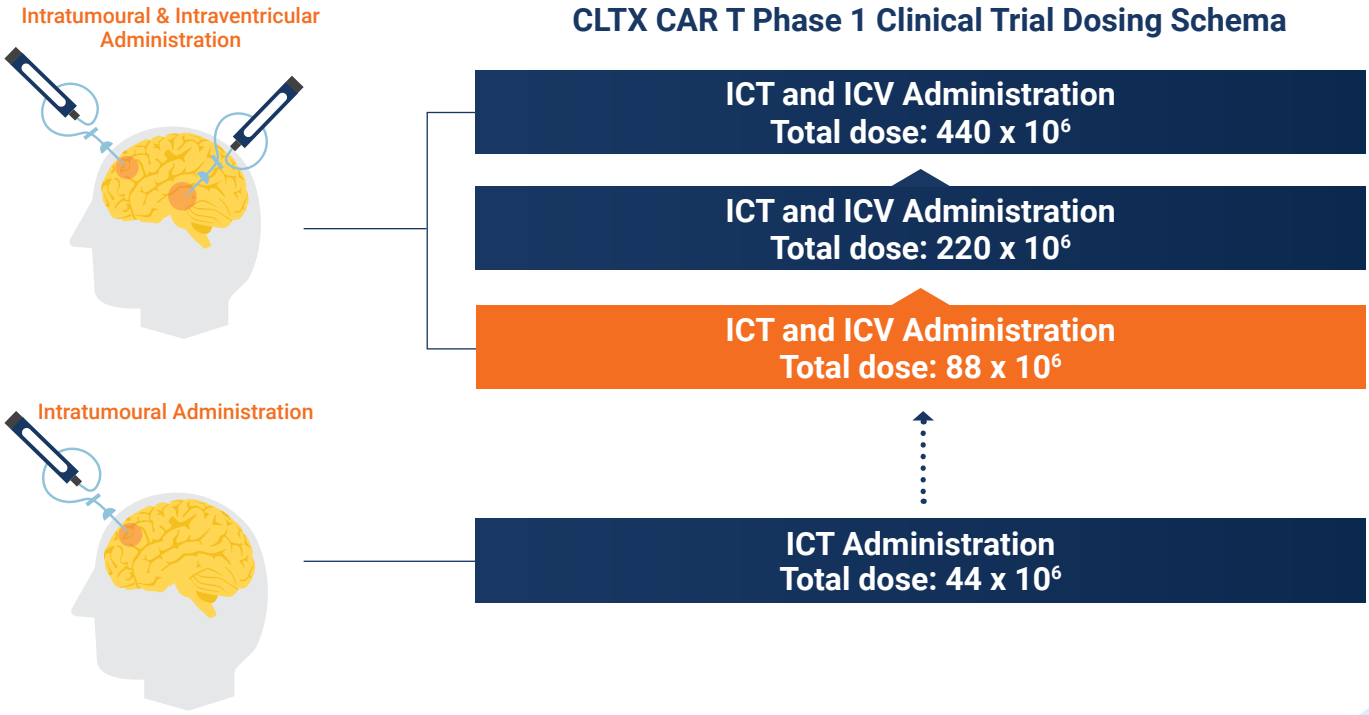
Although we are excited to have acquired the CDH17 CAR T cell therapy we have also remained sharply focused on advancing the development of our CLTX CAR T cell therapy for patients with Glioblastoma.

Our CLTX CAR T cell therapy is a first and best in class CAR T for patients with Glioblastoma that is in a phase 1 clinical trial at the City of Hope cancer centre in California.

In our last newsletter we were very pleased to have announced that we completed dosing patients in the 1st dose cohort without any dose limiting toxicities.

As a result of this early safety in patients we were able to advance the trial to the 2nd dose level and were pleased when the first patient of the second dose cohort was treated in May. Patients at this 2nd dose level receive CLTX CAR T cells through two catheters placed in their brain (intratumoural and intraventricular) for a total dose of 88 X 106 CLTX CAR T cells.

We look forward to providing a clinical update on the patients in this trial late in 2021. In the meantime we continue to develop plans for the phase 2 registration trial as well as for a phase 1 basket trial in solid tumours such as melanoma, prostate cancer and colorectal cancer.



CLTX CAR T IND clearance from the FDA

In August we were thrilled to receive our first IND clearance from the US Food and Drug Administration (FDA) for our CLTX CAR T cell therapy for patients with Glioblastoma.

For Chimeric, this IND clearance marks a significant milestone as it enables us to expand the development program for our CLTX CAR T.

Our first step will be to open additional phase 1 clinical trial sites under the current study protocol.

This will allow us to accelerate the phase 1 clinical trial recruitment which will be particularly important as we head towards the expansion phase of the protocol.

With this foundational IND we will also be able to further advance our plans for a phase 1 basket trial in solid tumours and a phase 2 registration trial in Glioblastoma.

Expanding our Cell Therapy Expertise

One of the things that strongly differentiates us from other companies is our people.

We have an industry leading team of cell therapy pioneers and experts that have deep, global expertise in cell therapy development. Our team has worked on the development of over 25 cell therapies including 4 of the 5 FDA approved CAR T cell therapies.

Development of over **25 therapies**

4/5 of the FDA approved CAR T cell therapies

Abecma

TECARTUS (brexucabtagene autoleucel)

Breyanzi

YESCARTA (axicabtagene ciloleucel)

We recently added a new member to our team, Dr Li Ren, who has joined Chimeric as the Vice President, Technical Operations.

Li brings extensive cell therapy experience, most recently from Bristol-Myers Squibb (BMS) where she oversaw technology transfers from Juno Therapeutics. Prior to joining BMS, Dr. Ren spent nearly 15 years at Celgene and Celgene Cellular Therapies (CCT) leading CMC efforts to advance CAR T, TCR and NK cell therapies to clinic.

We are thrilled to have Li on our team and asked her a few questions to let you get to know her better...

Q: What was the last movie you watched?

A: "Soul". It is a great movie and it reminds me to live in the moment, enjoy the little things, and appreciate what I have.

Q: Where is your favourite vacation spot?

A: Italy. With many beautiful cities, incredible museums, spectacular landscapes, art and fashion, and delicious food, I would say Italy is my favourite vacation destination in Europe.

Q: If you could play an instrument, what would it be?

A: Guitar. I wish I could learn guitar and play my favourite songs.

Q: What is your favourite food?

A: I love delicious food in general, but I would say my favourite food is Chinese food. I grew up in China and Chinese food is still my favourite.

Q: When you were a kid, what did you want to be when you grew up?

A: I always wanted to be a scientist when I was a kid. Science and technology were fascinating to me. Later on, I studied biology, entered the biotech industry, and developed drugs for patients in need. I am very fortunate to be able to do the things that I love.

Q&A

Gaining expert guidance

DR GEORGE MATCHAM
BOARD OF DIRECTORS

Meet Dr George Matcham

Our team at Chimeric is very fortunate to be guided and receive counsel from an experienced board of directors compromised of biotech entrepreneurs and industry veterans. We were thrilled to recently announce that Dr George Matcham, a cell therapy technical operations expert had joined the Chimeric Board of Directors.

Dr Matcham brings to Chimeric a wealth of experience in the biopharma sector, following an instrumental three decades with cell therapy giant Celgene Corporation. At Celgene, Dr Matcham championed the introduction of cellular immunotherapy and led the establishment of cell therapy and biologics technical development. Vital to the growth of cell therapy at Celgene, Dr Matcham held several senior positions, including Chief Operations Officer of Celgene Cellular Therapeutics and Senior Vice President of CAR T CMC Development, where he oversaw clinical supply.

The year ahead

We are immensely excited about what the rest of 2021 will bring, and we look forward to providing you with updates as it continues to unfold.

You can expect to see news as we move our new asset, the CDH17 CAR T cell therapy towards the clinic.

You can also expect to see the first clinical data for our CLTX CAR T towards the end of the year as the phase 1 clinical trial continues to progress.

We will share with you additional information as we develop our plans to explore CLTX CAR T in other solid tumours and also explore potential opportunities for collaborations and complementary technologies with CLTX and our CDH17 CAR T.

Finally, we look forward to introducing you to new innovative technologies that will continue build out our pipeline and the new team members that will bring the right expertise and experience to Chimeric to allow us to bring the promise of cell therapy to patients with cancer.

A final word from our Chairman and Founder

It has been an exciting ride since our listing in January – thank you for your interest and support during that time.

Our goal is to build a pre-eminent cell therapy and CAR T company, and I believe we are well on our way to achieving that vision.

We already have two exciting assets, one now in the clinic, and the second to enter clinical trials in 2022 – there are no companies in Australia in the cell therapy field with this depth of pipeline.

In the biotech game, the next most important asset after the core technology, is the management team, and in this regard Chimeric is ahead of the pack.

"The company is well funded and the market has identified our value by its continuing support reflected in the share price and market cap."

Led by Jenn Chow, our team have developed over 25 cell therapies and have worked on 4 out of the 5 approved CAR T cell therapies in the world.

That's experience!

The year ahead will indeed be exciting.

PAUL HOPPER
CHAIRMAN AND FOUNDER

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