

# FRONT RUNNER IN CAR-T CELL THERAPY FOR CANCER PATIENTS

Investor Presentation, December 2021



### WHAT IS CAR-T CELL THERAPY?



- T cells that have receptors for specific binding to the antigens expressed on cancer cells.
- Developed and approved for the first time as a treatment method for acute leukemia in 2017 (KYMRIAH by Novartis).
- After being approved as a treatment for acute leukemia, indications are being expanded to other blood cancers.
- Most CAR-T cell therapies currently approved or under development are second-generation constructs that recognize the CD19 antigen.
- High remission rate for blood cancer. (CR, Complete remission).
- **Expensive treatment cost,** about CAD\$540,000 per treatment.



#### CANCER BREAKTHROUGH by CNN, 2017

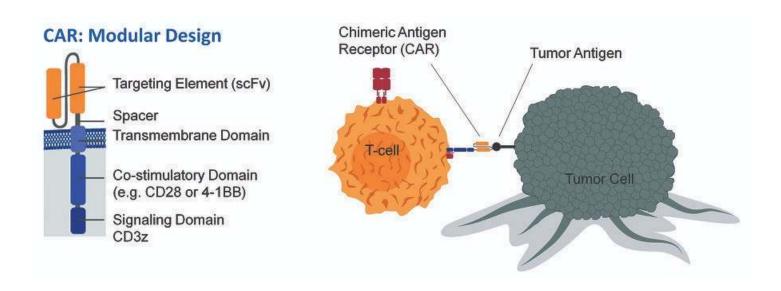
CAR-T therapy is a therapeutic agent that is challenging not only hematologic cancer but also incurable areas.

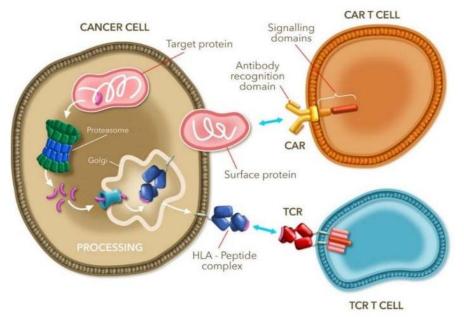


**High CR** for relapse and refractory patients with ALL who couldn't treat by existing drug.

# STRUCTURE AND PRINCIPLE OF CAR-T CELL







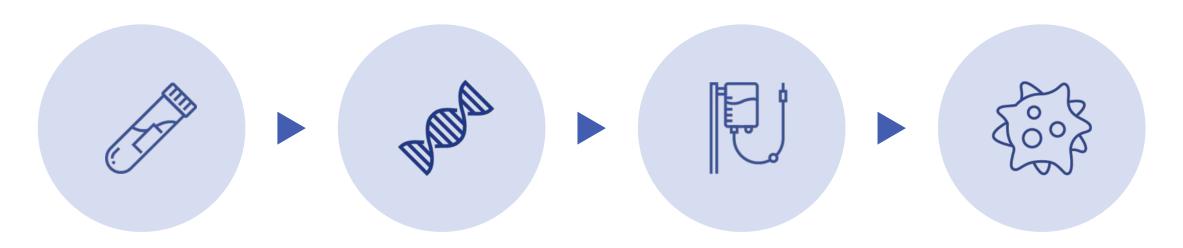
(Source: Genetic Engineering & Biotechnology News)

(Source: Adaptimmune IR Materials)

# **CAR-T CELL THERAPY MECHANISM**



Uses a patient's own immune system to fight certain types of cancer



Manufactured using T cells extracted from patient's blood.

Transduction of CAR
(Chimeric Antigen
Receptor) into T cells to
manufacture CAR-T cells
and cell culture.

Re-injection of CAR-T cells into the patient.

CAR-T cells recognize the CD19 antigen on the surface of cancer cells and induce cytotoxicity activation of T cells to kill cancer cells.



### FDA APPROVED CD19 CAR-T CELL THERAPY



- As of 2021, 4 types of CAR-T cells have been commercialized.
- All use Intravenous injection using autologous cells.
- The cost of one treatment Kymriah is about CAD\$540,000, which is an expensive high-tech biopharmaceutical.
  - Except for the recently approved ABECMA, all cells use the CD19 antigen as an indication for hematologic cancer.
  - After approval, indications are being expanded.

Product	Target	Indication	Manufacturer
(tisagenlecleucel) Suspension for IV infusion	CD19	ALL/DBCL	Novartis / UPENN
YESCARTA  (axicabtagene ciloleucel) terrindesin	CD19	ALL/DBCL	Gilead / KITE
Breyanzi	CD19	DBCL	BMS / Juno
Abecma (idecabtagene vicleucel) REPRINCESIN	ВСМА	Multiple myeloma	BMS / Blue Bird

# CLINICAL PROGRESS TREND FOR UPCOMING CAR-T CELL THERAPY



- The CD19 antigen is the most powerful antigen, and many clinical studies use the CD19 antigen.
- In the early stages of development, the biggest problem with CAR-T cell therapy was the side effects such as CRS.
- For this, various antigens, new processes, safety switch off, Engineered (allogeneic) T cell therapy, etc. were tried.
- Hematologic > multiple myeloma > Clinical trial for solid tumor is in progress.

Therapy	Target	Manufacturer	Stage	Indication
Kymriah® (tisagenlecleucel)	CD19	Novartis	FDA approved	ALL
Yescarta® (axicabtagene ciloleucel)	CD19	Gilead / KITE	FDA approved	Non-Hodgkin lymphoma
JCAR017 (lisocabtagene marealeucel)	CD19	BMS / Juno	Submission	Leukemia, lymphoma, NHL
BB2121 (idecabtagene ciclucel)	ВСМА	Celgene	Phase II	Multiple myeloma
AUTO-1	CD19	Autolus	Phase I/II	Leukemia, lymphoma
JCAR104	CD19	Juno	Phase I	NHL
UCART19	CD19	Cellectis / Servier / Allogene	Phase I	Leukemia, lymphoma

# BCP401: FIRST CAR-T CELL THERAPY BY BIOCURE PHARM



# Nonclinical Toxicity / Distribution

- Single to one toxicity
- Repeat permeability
- Immunotoxicity
- Carcinogenicity
- Reproductive toxicity
- Genetic toxicity
- Distribution test

#### **Nonclinical Efficacy**

- Physical chemistry and biological properties
  - Viability
  - Expansion fold
  - Phenotype
- CAR expression
- Gene copy number
- In vitro efficacy
  - Cytokine release
  - Cytotoxicity
- In vivo efficacy
  - Tumor regression
  - Survival rate

# Manufacturing in GMP / Specification and Assay

- Lenti virus
  - Genetic verification for vector
  - Construction of cell bank
  - Establishment of manufacturing process
  - Establishment of specification and assay
- CAR-T cell manufacturing
  - Establishment of manufacturing process
  - Stability test
  - Establishment of specification and assay

#### **IND Filing**

- Application
- Plan to clinical trial
- GMP documentation
- Self criteria and test method
- Document of stability and efficacy
  - Development plan
  - Introduction
  - CMC assay for clinical sample
  - Document of nonclinical results
  - Document for clinical trial applicant

#### **Documents to apply for clinical trial**

Nonclinical toxicity and distribution completed
Establishment of the specification and assay completed
Manufacturing in GMP is in process
CMC(Chemistry, Manufacturing and Control) completed

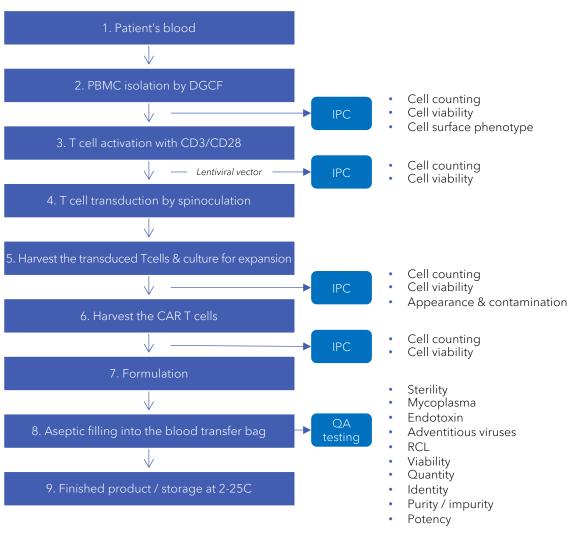
Choose the clinical center

Submit plan for trial

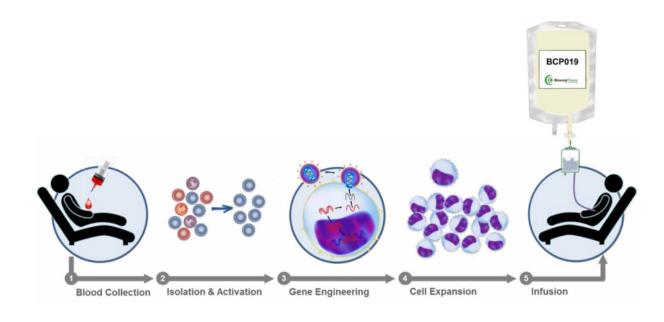
**Application for IND Status** 

# BCP401: MANUFACTURING PROCESS FOR BIOCURE PHARM DRUG PRODUCT



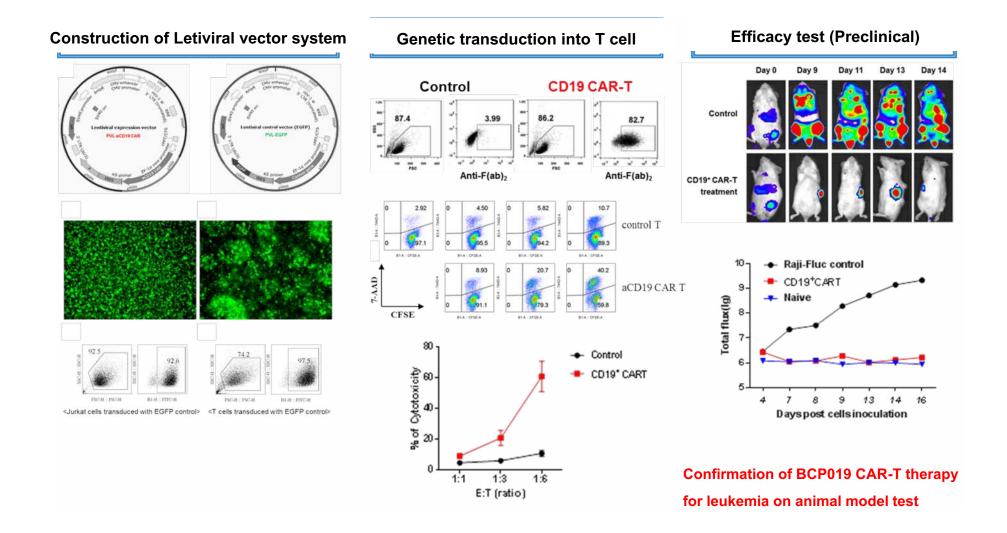


Re-injection into body to attack and kill a cancerous cells after making CAR-T cell, using the T cell extracted from patient's blood



# **BCP 401: NON-CLINICAL DEVELOPMENT**





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# BCP 401: RESULT FROM RESEARCH PURPOSE IIT CLINICAL TRIAL

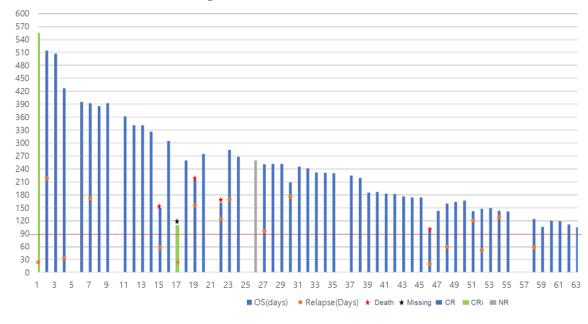


- Performed at People's Hospital, Beijing: 63 Subjects with relapse/refractory ALL (1~25 age)
- Primary Endpoint for the Efficacy Analysis
  - ORR evaluation within 3 mths after treatment. ORR confirmed through peripheral blood, bone marrow, cerebrospinal fluid analysis, and physical examination.
  - 7 of 63 are not allowed to be evaluated the efficacy
- ORR (overall response rate) was 55/56 (98.21%) as a result of the evaluated 56 subjects: CR (Complete Remission) \_53 (94.64%), CRi (Complete Remission with incomplete hematological response)\_2 (3.57%), NR\_1 (1.79%). Initial evaluation of CR or CRi was assessed from 28 days.
- Secondary Endpoint for the Efficacy Analysis
  - The percentage of CR and CRi in MRD negative patients.

#### Adverse Events

• Bridge treatment (Stem Cell Transplant, SCT): 35 (62.5%) of 56 subjects were carried out by HSCT and 21 (37.5%) did not undergo HSCT (due to cytokine/chemokine status).

#### Investgator Clinical trial for CAR-T in China



4 patients (#23, #32, #35, #48) was manufactured by the PBMC derived from their family(sister, brother, and father)

**Conclusion:** To treat r/r B cell ALL with CD19 positive, CAR-T program has good response with a single dose.

# BCP401: COMPARISON OF R/R B-ALL EFFICACIES OF CD19-TARGETED CAR-T IN VARIOUS TRIALS



Institution	# of Pts reported	Median age (range)	Disease-related outcomes
Children's Hospital of Philadelphia	30 (25 children, 5 adults)	Pediatric: ALL 11 (5-22) Adult: ALL 57 (36-60)	<ul> <li>CR: 90% (MRD-negative in 88% of those who achieved CR)</li> <li>6-month EFS: 67% / 6-month OS: 78%</li> </ul>
National Cancer Institute	20	Pediatric: ALL 15 (5-27)	<ul> <li>CR: 70% (MRD-negative in 60% of those who achieved CR)</li> <li>OS: 52% at 7.8 month / EFS: 79% at 4.8 month</li> <li>10 of 12 in MRD-negative CR underwent AlloHSCT</li> </ul>
National Cancer Institute	5	Adult: ALL	• <b>CR: 80%</b> (4/5, all MRD-negative)
Memorial Sloan Kettering Cancer Institute	51	Adult: ALL (22-74)	<ul> <li>CR: 82% (MRD-negative in 85% of those who achieved CR)</li> <li>16 of 41 in CR underwent AlloHSCT</li> <li>Median OS: 9 months (in patients with morphologic disease at CAR-T cell infusion), not reached (in patients with minimal disease at CAR-T cell infusion</li> </ul>
Fred Hutchinson Cancer Research Center	30	Adult: ALL 40 (20-73)	<ul> <li>MRD-negative CR: 10/12 among patients receiving Cy monotherapy; 16/17 among patients receiving Flu/Cy</li> </ul>
University of Pennsylvania	27	Adult: ALL 44 (21-72)	CR: 15/27 (across all cohorts)
Beijing People's Hospital	63	Pediatric: ALL (1-25)	<ul> <li>ORR 55/56 (98.21%): CR (94.64%), CRi (3.57%), NR (1.57%)</li> <li>7 of 63 are not allowed to be evaluated the efficacy(ND)</li> <li>35 of 56 in ORR underwent HSCT, 21 did not undergo HSCT</li> </ul>

- The CD19 technology used in BCP401 showed promising results with 94.6% of patients in complete remission
- However, the patent pathway for BCP401 was uncertain and BiocurePharm has taken the know-how accumulated to date to focus on its CLL CAR-T program BCP402.

Source: Current clinical applications of CAR modified T cell, Cytotherapy. 2016 November; 18(11):1393-1409

OS (Overall Survival), EFS (Event Free Survival), MRD (Minimal residual disease), ORR (Overall Response Rate), ND(Not determine)

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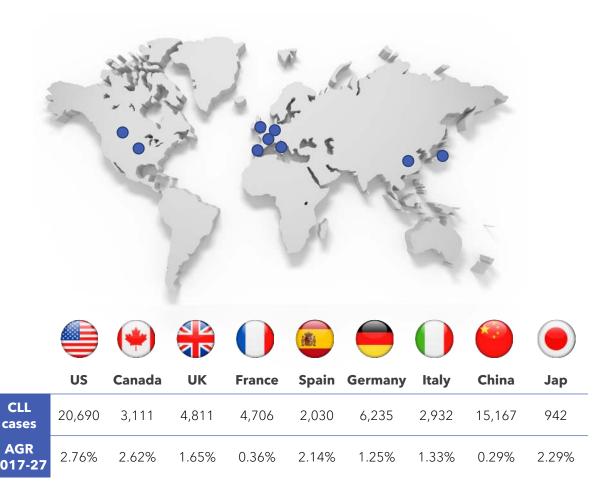


# **CLL (CHRONIC LYMPHOCYTIC LEUKEMIA)**



- Most common in adults and accounts for approximately 40% of all leukemia.
- The median age of diagnosis is 70 years, and twice as many men develop CLL compared to women.
- While no definitive cause of CLL has been established, targeted therapy regimens have proven to be efficacious treatments.
- Incidence of CLL patients in 2020 of major developed countries (Total 60,624).
- Biocure Pharm is focused on CLL CAR-T through its program BCP402.

#### **Incident cases of Chronic CLL in 2020**



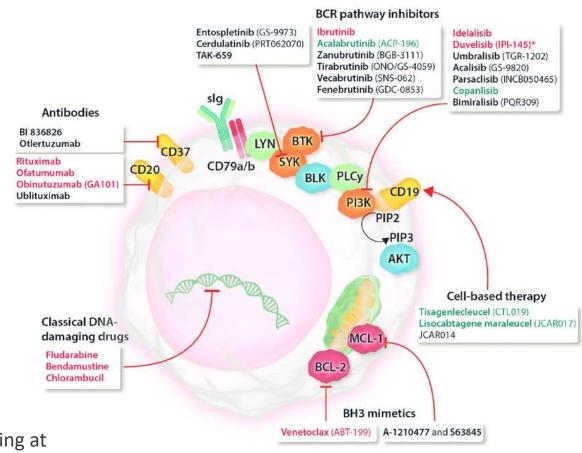
# **TOP-SELLING DRUGS OF TREATMENT FOR CLL**



Brand Name (generic name)	Company	Approval	Target	Global Sales (2019)
Imbruvica (ibrutinib)	AbbVie and Johnson & Johnson	2013	ВТК	\$7.24B
Rituxan (rituximab)	Biogen and Roche/ Genentech	1997	CD20 Monoclonal Antibody	\$6.62B
Venclexta (venetoclax)	AbbVie	2016	Bcl2 inhibitor	\$792M
Gazyva (obinutuzumab)	Roche/ Genentech	2013	CD20 Monoclonal Antibody	\$600M
Treanda (bendamustine)	Astellas Pharma	2008	DNA synthesis inhibitor	\$571M
Calquence (acalabrutinib)	AstraZeneca	2017	ВТК	\$164M

<sup>\*</sup>BTK (Bruton's tyrosine kinase); Bcl2 (B cell lymphoma antigen-2)

The global market for CLL is expected to reach \$12 billion by 2027, growing at CAGR 12.7% from 2021-27. (Source: (healthcareanalyst.com)

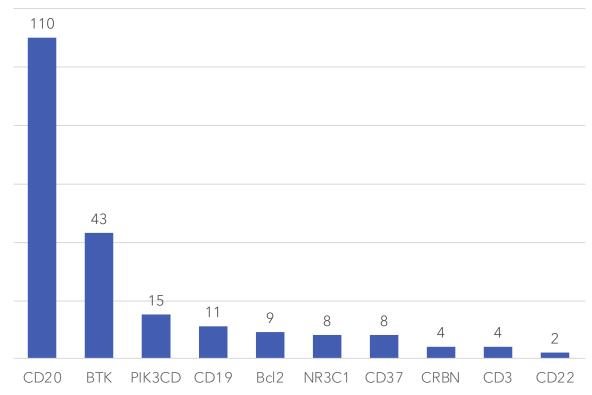


# TARGET OPTIONS OF TREATMENT FOR CLL UNDER DEVELOPMENT



- After CD20s, other promising targets under evaluation include BTK, PIK3CD, and Bcl2.
- CD37, CRBN and CD22 are targets being evaluated less in CLL drug development.





Source: GlobalData, Pharma Intelligence Center. Accessed April 2020.

# BCP402 AS TREATMENT FOR CHRONIC LEUKEMIA (CLL)



- ROR1 is a CLL-specific antigen, and its expression rate is very low in normal cells.
- It has high specificity and safety.
- The development of BCP402 can increase the response rate and reduce side effects.
- The use of ROR1 antigen can be expanded to solid cancers.



## **BCP'S CAR PLATFORM**



- Biocure demonstrated with the BCP401 (CD19 CAR-T) project the ability to design, create and develop effective and powerful CAR-T therapy.
- We are developing CAR-T for the therapy of CLL (BCP402) and solid tumors (BCP403).
- We are currently designing CAR-T of the next generation (already with BCP402, 403):
  - a) Bi-specific CAR-T, i.e. binding two instead of only one target molecule: increased specificity and efficacy.
  - b) Combination of CAR-T therapy with additional means to increase efficacy: e.g. increased function under certain ECM (Extracellular Matrix) conditions; combination with other therapy forms, e.g. RNAi and checkpoint therapy.
  - c) others.



### WHY INVEST?



### Accomplished Board

Biocure's has an extremely solid board of directors, advisory board and industry experts to enable it to execute on its growth strategy

### Established Track Record

Biocure boasts a proven track record of industry recognized research, development and intellectual property



#### Low valuation

At sub C\$20m market cap, huge upside potential exists for shareholders upon rerating of its shares

### Strong Partners and Talent

Biocure aligns itself with top-tier industry partners which enables it to attract top tier, world class talent

### Large Addressable Market

The market for Car-T Cancer therapies is massive and growing strongly year on year - Large Blue Sky potential exists across the Cancer therapy space

### Opportunistic Pipeline

Biocure has an extremely robust pipeline and numerous near-term drivers exist for the stock

### **CORE COMPETENCIES**



1. Possesses innovative
CAR-T development
capabilities based on CD19
CAR-T experience

2. R&D network established

3. Established 4. Overseas overseas clinical network network established

Established a first-class CAR-T pipeline targeting hematological and solid cancers.

For future second-generation CAR-T development, Y-Biologics and Theranotics core competency cooperation partnerships were established.

Planning for innovative CAR-T development and CLL clinical trials with a hematology group in Europe (BCP402).

Completion of local production and partnering infrastructure with headquarters in Canada and additional base in Germany.

Accumulated experience in preclinical and clinical practice.

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Based on bio-similar development capability, mass production base and smooth QC system are established.

Signed an agreement for BCP401 clinical trial with the University of Malaya, Malaysia.

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Signed an agreement with Bulgaria S&B Pharma for local production of CAR-T.

# **BUSINESS STRATEGY**



Productization strategy	Innovative CAR-T series development and patent application in the shortest time: chronic leukemia, solid tumors.
	Preparing for clinical development of BCP402 (ROR1 CAR-T) for the treatment of chronic leukemia (CLL) with a clinical expert team in Europe.
	Based on the case experience of CD19 CAR-T after preclinical progress of new solid cancer treatment CAR-T, clinical entry in the shortest time envisioned.
Commercialization strategy	Production and marketing in North America is being promoted from the Vancouver, Canada HQ.
	Product licensing, and technical cooperation with European partners from our offices in Frankfurt, Germany.
	Promoting clinical trials and production localization with Malaysia University of Malaya.
	Exploring EXIT plans through active cooperation with e.g. major pharmaceutical companies.

# PLANS FOR PRODUCT DEVELOPMENT AND COMMERCIALIZATION

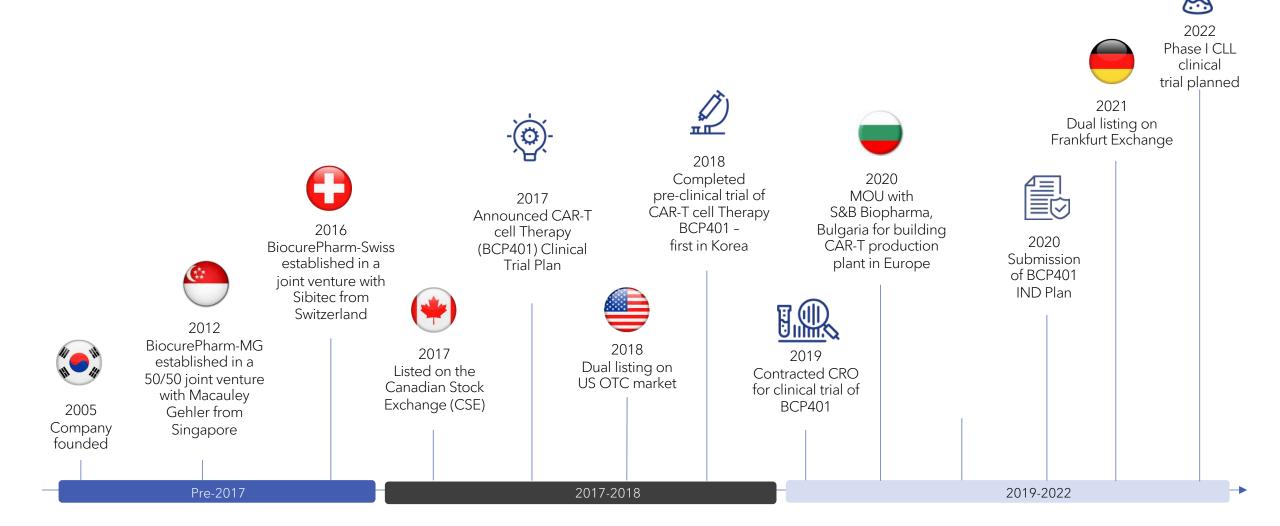


Program	Indication	2022	2023	2024	2025	2026
BCP402	CLL	<ul><li>Patent filed</li><li>Preclinical progress</li><li>IND application</li></ul>	<ul> <li>Phase 1 clinical trial (Europe)</li> </ul>	<ul> <li>Phase 2 clinical trial (Europe)</li> </ul>	*	
		- 1414				
BCP403	Solid cancer	<ul><li>Patent filed</li><li>Preclinical progress</li><li>IND application</li></ul>	<ul> <li>Phase 1 clinical trial (Korea)</li> </ul>		Phase 2 clinical trial (Korea)	*

# **CORPORATE HISTORY TO DATE**



Substantial investment and business progression made

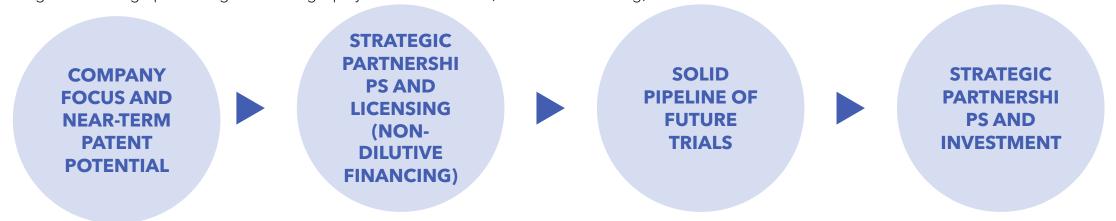


# 12 MONTH FOCUS & OUTLOOK



The Company continues to build financial value within Cancer Treatment through two ways;

- Development of it's own pipeline products with potential for the Company to secure a number of patents covering revolutionary Car-T bi-specific therapies in the near term.
- Building value through partnering with strategic players and licencees (non-dilutive funding).



The Company is currently focused on two kinds of innovative CAR-T pipelines covering;

- Chronic Lymphocytic Leukemia ("CLL") - Patent application expected to be lodged by the end of Q1, 2022.
- Lung and Ovarian cancer preclinical trials expected to begin in Q2, 2022.

- Strong interest received from Technology-based Industry experts and Academic institutes to develop multiple new therapies.
- Company is in advanced collaboration discussions with a number of Strategic Industry players in Europe and Korea regarding development of a new CAR-T form using nanobody and new immune regulation factors.
- Company is in cooperation with a number of academic institutes focused on further development of its CAR-T therapies.

The Company is in discussions with a number of groups regarding planned trials in the medium term (12 months) including;

- A clinical trial planned in Germany with a team of CLL specialists.
- A clinical trial in Korea targeting lung cancer including multi-national clinical trials in Australia and Singapore.

- The Company has received strong interest out of Europe and Korea from a number of groups regarding potential strategic partnership and investment to leverage the enormous potential value of these therapies.
- The company is currently evaluating these proposals and will further update the market as these discussions progress.

# HISTORIC VALUE ESTIMATION AND POTENTIAL



Company	Listed	IPO at Non-Clinical Stage (mUSD)	Current Market Cap (mUSD)	Current Stage
Autolus Therapeutics	NASDAQ	150	520	Ph 1
Adaptimmune Therapeutics	NASDAQ	191	950	Ph2
Cabaletta Bio	NASDAQ	75	270	Ph1
Kite Pharma	N/A	128	Acquired by Gilead for 12 bUSD	Approval
Neximmune	NASDAQ	126.5	325	Ph1/2

# **COMPARISON TO EARLY CLINICAL STAGE COMPANIES**

Company	Listed	Current SP (USD)	Market Cap (mUSD)	Stage (of Lead Program)*
CARsgen Therapeutics	HKG	5.75	3.260	Ph2
Fate Therapeutics	NASDAQ	54.52	5.333	Ph1
Poseida Therapeutics	NASDAQ	7.29	455	Ph1

<sup>\*</sup>stage of the development process/most advanced pipeline project

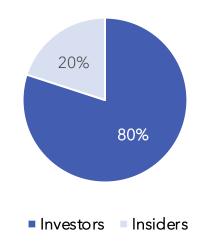
Biocure Technology	CSE	0.19	19	Ph1
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# **CAPITAL STRUCTURE**



Share Structure *as of Nov 5th 2021	
Outstanding Shares	106,621,158
Share Price	\$0.15
Warrants Outstanding	9,051,272
Options Outstanding	7,570,000
Market Capitalization	\$15,993,174

# **Outstanding Shares**



Options Outstanding					
	Expiry Date	Exercise Price	Amount of Options		
	Apr. 2022	\$0.38	300,000		
	Feb. 2024	\$0.30	6,020,000		
	Jul. 2024	\$0.30	1,250,000		
	Total		7,570,000		

warrants Outstanding		
Expiry Date	Exercise Price	Amount of Warrants
Oct. 2022	\$0.21	1,786,725
Jul. 2023	\$0.16	7,240,547
Total		9,027,272

Warrante Outstanding

# **BOARD OF DIRECTORS AND MANAGEMENT**



Experienced leadership team					
<b>Dr. Sang Mok Lee</b> CEO & Founder, Director	<b>Dr. Bjorn Cochlovius</b> President	<b>Mr. Konstantin Lichtenwald</b> CFO, Director	<b>Mr Collin (Sang Goo) Kim</b> Director	<b>Mr. Berkan Unal</b> Director	<b>Dr. Danny Joh</b> Director
<ul> <li>President and CEO of Biocure Technology since the inception in 2005</li> <li>Holds a PhD in microbiology from Busan National University in Korea and is currently an adjunct professor in microbiology at Chungnam National University</li> <li>A committee member for the hi-tech medical complex city in Daejon, Korea and a committee member of KOFST (the Korean Federation of Science and Technology Societies)</li> </ul>	<ul> <li>Bjoern Cochlovius, Ph.D,. is a Molecular Biologist and Associate Professor for Immunology at Heidelberg University, Heidelberg, Germany.</li> <li>Bjoern has held various leadership positions in biotech (e.g. Affitech, Oslo) and big pharma (amongst others at Roche, Basel; Abbvie, Singapore) in R&amp;D, BD&amp;L and strategic positions.</li> <li>Currently holds two chairmanships (Sapreme, Netherlands, and Karolinska Development, Sweden).</li> <li>Currently CEO at Medraxa Therapeutics, Heidelberg.</li> </ul>	<ul> <li>Over 15 years' finance and accounting experience, including corporate compliance, accounting and financial management and IPO, RTO services</li> <li>Extensive knowledge and know-how for companies in North America and German speaking parts of Europe</li> <li>A Chartered Professional Accountant (CPA, CGA) and Chartered Certified Accountant (ACCA), where he is a member of Chartered Professional Accountants of B.C. and Canada as well as a member of the Association of Chartered Certified Accountants of United Kingdom</li> </ul>	<ul> <li>30 plus years of experience in the petrochemical, coal and mineral industries and involved in various mineral projects bringing together Canadian and major Korean State-Owned Firms.</li> <li>Vice President for Columbia Capital since 2008 and a director of ArcPacific Resources Corp., a public Canadian junior exploration company since 2015</li> <li>Worked for Hanwha Corp., one of Koreas business conglomerates for 16 years including 5 years in Jakarta, Indonesia as a Chief Representative of Hanwha's Jakarta office.</li> <li>Bachelor's degree in Business Administration from Korea University in 1990.</li> <li>Communicates between Korean management and Canadian management cross the border with his vast knowledge and work experience</li> </ul>	<ul> <li>Over 10 years' experience in the biopharmaceutical industry in Germany and Switzerland and connections to global leaders in the biopharmaceutical sector</li> <li>Currently, acts as business development director for biologics, gene and cell therapy of GenScript Biotech, a global leading biotech company, and has been involved in the processes that provide end-to-end solutions from discovery to commercialization</li> <li>Studied bioprocess engineering and medical biotechnology at Berlin Technical University of Applied Sciences, Hamburg University of Technology and Imperial College London</li> </ul>	<ul> <li>20 years' biopharma product development and cross-functional program management experiences with Chiron, Genentech, Biomarin, Sangamo and other biotech companies</li> <li>Experience spans from early to late stage product development in various platforms, including biologics, small molecules, and gene therapy across many therapeutic areas, including cancer and rare genetic disorders</li> <li>PhD in Biochemistry at Texas A&amp;M university and an MBA at Rice University</li> </ul>



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