BioCure Technology Inc.

BCP CAR-T cell Therapy Program – BCP401

March, 2021

CSE: CURE I www.biocuretech.com
OTC: BICTF

Biocure Technology

Superior points of BiocurePharm's CAR-T cell therapy

1. **Front runner of Commercializing of CAR-T cell therapy in Korea**

2. **Experience of the investigated clinical trial in China**
   - Secure the data of efficacy and safety for CAR-T cell therapy

3. **Product Cost Competitiveness**
   - Empirical cost competitiveness based on manufacturing data

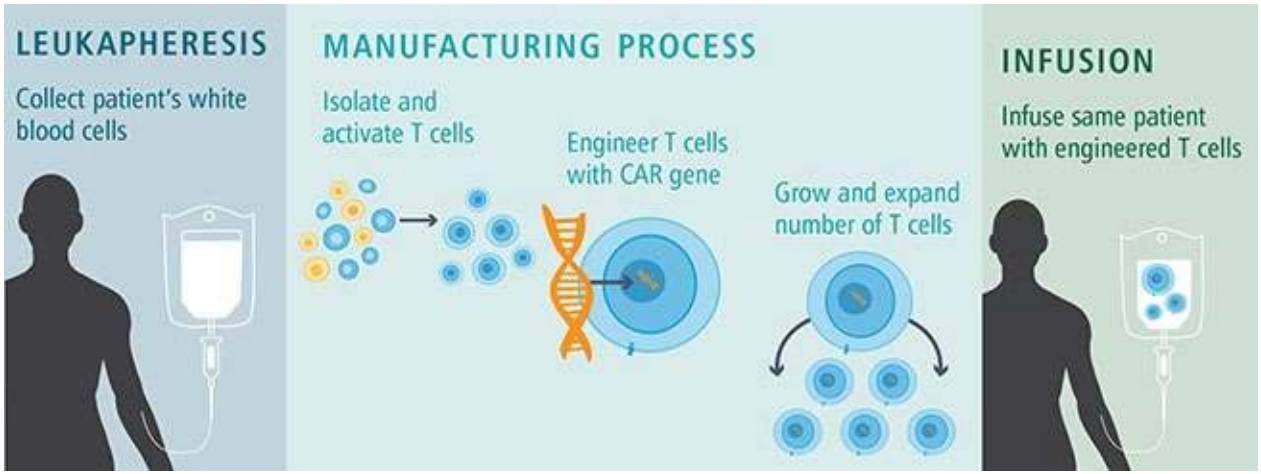
4. **Experience of CAR-T therapy in Korea**
   - **2 terminal stage ALL patient who being cared in Asan medical center transferred to Chinese hospital for operating BCP 401 CAR-T. Those 2 patients show CR (Complete Remission) after 1month of CAR-T therapy.**
   - **It is the first case of CAR-T therapy in Korea.**

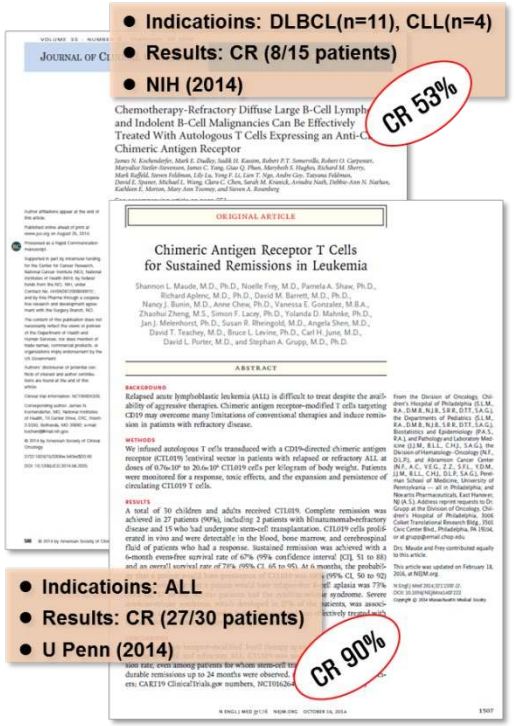
5. **Establishment of the bridge into a global market**
   - Establishment of CAR-T production factory in South-eastern Asian and Europe

6. **Improvement of manufacturing process of CAR-T cell therapy with localization**

Immuno-cell therapy : CAR-T cell therapy

- **Extract T cell from patient's blood, modify to recognize specific antigen on the surface of cancer, and re-injection of CAR-T cell into patient**
- **Competitive treatment individually customized for the blood cancer.**





– Emily Whitehead

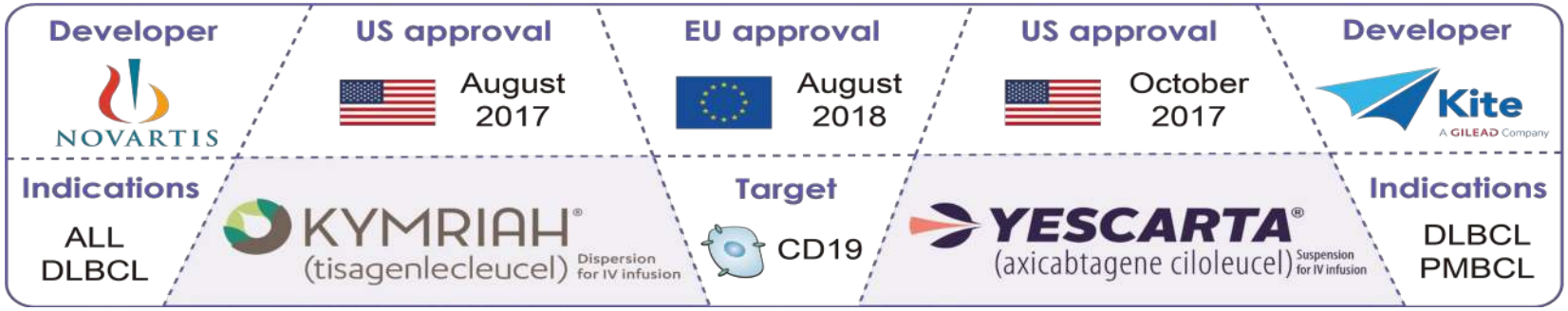
The 1ST child patient to be enrolled in clinical trial for CAR-T Cell immunotherapy
- April 2012, 7-year-old

She is 18 years old and recovered completely. She is living cancer free more than 5 years after treatment

FDA Approved CD19_CAR-T cell therapy

For autologous use only.

For intravenous use only.



At 10 to 20 mL per min injection

Max. 2.5 x 10^8

$475,000, per 1 dose

KYMRIAH is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of patients **up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL)** that is refractory or in second or later relapse.

Approximately 68 mL per patient

Max. 2.0 x 10^8

$373,000 per 1 dose

YESCARTA is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of **adult patients with relapsed or refractory large B-cell lymphoma** after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.

Forecast of CAR-T Cell therapy

Worldwide CAR-T cell Immune Therapeutics Market Size and forecast

(2021-2028, Unit: Million USD)

Coherent Market Insights, CAR-T Cell therapy market (2021.2)

- The 1st CAR-T Cell therapy Kymriah was launched in late 2021(USA) and 2021(EU) by Novartis
- The therapy is expected to benefit many leukemia patients – old and young
- According to the NIH report, more than 340,000 leukemia patients were reported in 2015 in the U.S. (corresponding to 0.1% of the population)
- Annual growth rate is expected to increase steadily to around 53.9% (2021-2028)
- The market value for CAR-T cell therapeutics is anticipated to grow significantly

Clinical trials of a competitive CAR-T cell products

- Many bio companies are seeking to enter the market by merging with global companies.
- CD19 is still the most powerful antigen of hematologic tumors in clinical trial.
- Many new attempts are being made using CAR-T cell therapy to treat solid cancer beyond hematologic cancer.
- Finding the specific antigen, combination therapy, safety switch off, engineered(Allogeneic) T cell etc..

Therapy Name	Target	Manufacturer	Stage	Indication
Tisagenlecleucel, Kymriah(CTL019)	CD19	Novartis	FDA Approved	relapsed/refractory ALL
Axicabtagene ciloleucel, Yescarta (KTE-C19, ZUMA-1)	CD19	Gilead (KITE)	FDA Approved	non-Hodgkin lymphoma
Lisocabtagene marealeucel (JCAR017)	CD19	BMS (Juno)	Submission	Leukemia, Lymphoma, NHL
Idecabtagene Ciclucel (BB2121)	BCMA	Celgene	Phase II	multiple myeloma
AUTO-1	CD19	Autolus Limited	Phase I/II	Leukemia, Lymphoma
JCAR014	CD19	Juno therapeutics	Phase I	NHL
UCART19	CD19	Cellectis (Servier/Allogene)	Phase I	Leukemia, Lymphoma

Currently stage of ‘BCP401’ for Clinical Trial

BCP401 IND filing

- Preclinical efficacy / toxicity test completed
- SOP and Specification for manufacturing on GMP facility
- CMC (Chemistry, Manufacturing and Control)

IND submission(Dec. 2020) and review for Clinical trial

Nonclinical Toxicity / Distribution

Single to one toxicity
~~Repeat permeability~~
~~Immunotoxicity~~
~~Carcinogenicity[Δ]~~
~~Reproductive toxicity~~
~~Genetic toxicity~~
Distribution test

Nonclinical Efficacy / CMC

Physical Chemistry and Biologcial properties
- Vialbility
- 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

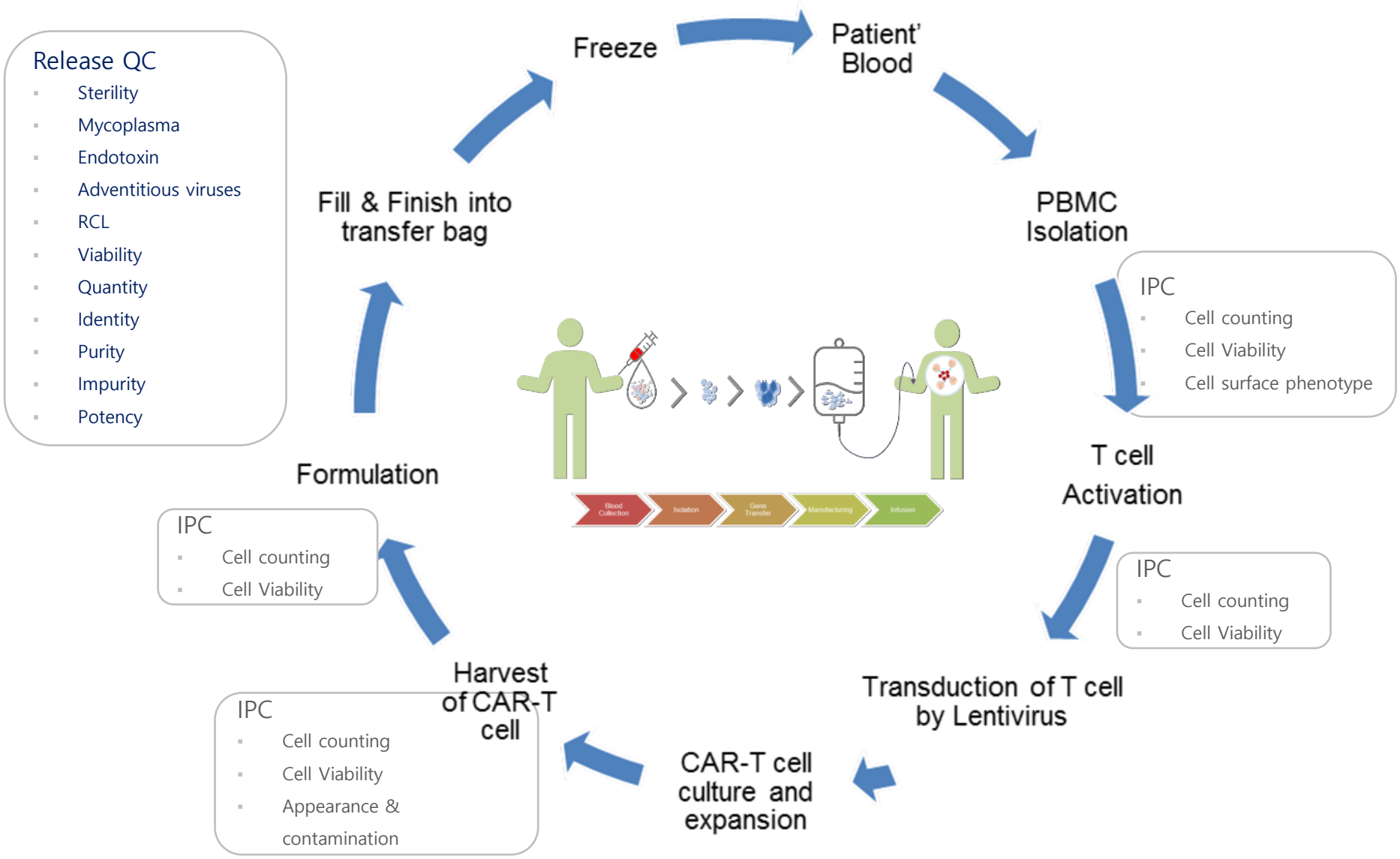
Lenti virus
- Genetic verification for Vector
- Construction of cell bank
- Establishment of manufacturing process
- Stability test
- Establishment of Specification and Assay

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

Manufacturing Process and QC Management



Safety Test for BCP401 in a Non-Clinical

	Toxicity test						
Efficacy	Distribution	Single to toxicity	Repeat to toxicity	Genetic toxicity	Carcinogenicity	Reproduction toxicity	Others
O	O	O	X	X	Δ	X	Δ(Local)

Single to toxicity

- Test Model: Balb/c nu/nu mice
- How to inject: Single administration, I.V.
- Dosing: Low, middle, High
- maximum dose considering safety
- Period: 28 days

Results :

There is not any specific toxicity to test, when the BCP401 injects individually single administration into immunodeficiency animal Balb/c nu/nu mouse. The NOAEL is maximum dose, $5x10^7$ cells/head.

Distribution

- Test Model: NSGA(NOD-Prkdc^{acid} IL2 Yg^{null}) with Raji-Fluc(lymphoblast)
- How to inject: Single administration, I.V.
- Dosing : maximum dose considering safety
- Test organs: Brain, Heart, Lung, Liver, Kidney, Spleen, Pancreas, Stomach, Intestine, Gonads, Mesentery lymph, BM, Blood, Tail injection
- **Detection for BD: qPCR by validated protocol**

Results :

BCP401 was identified in most samples of organs one hour after administration, most samples lost between 1st and 3rd days, and it was sporadically detected again at the day of 28. The highest concentration of BCP401 of test was in BM at 7th days. At 60th days, BCP401 did not detect in most tissues. That means BCP401 after injection were in all tissues to remove the Raji cells, and that was lost after a certain period.

Carcinogenicity

- The genomic DNA of CAR-T cell was analyzed to determine the insertion site and distribution of the lentivirus gene.
- RCL Assay of CAR-T cell was conducted.

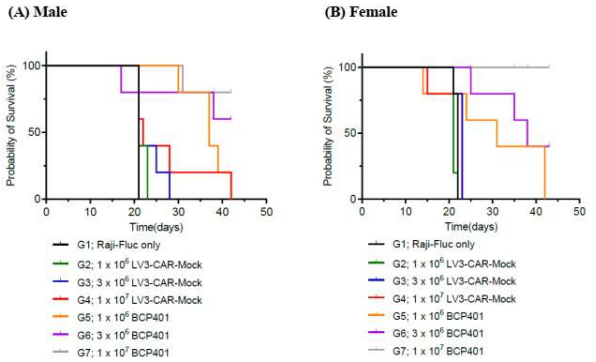
Results :

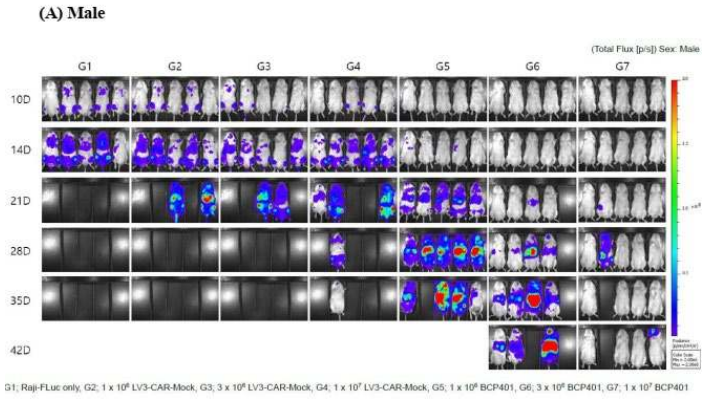
A total of 497 types of overlapping sites of BCP401 were identified, and Carcinogenic genes (GSK3A, CBL, MLL3, GNA13, FYN) were identified as Protein-coding Type genes, with a probability of 4.2±2.8%. It was found to be lower than the results of other studies(6.3% - 10.5%)

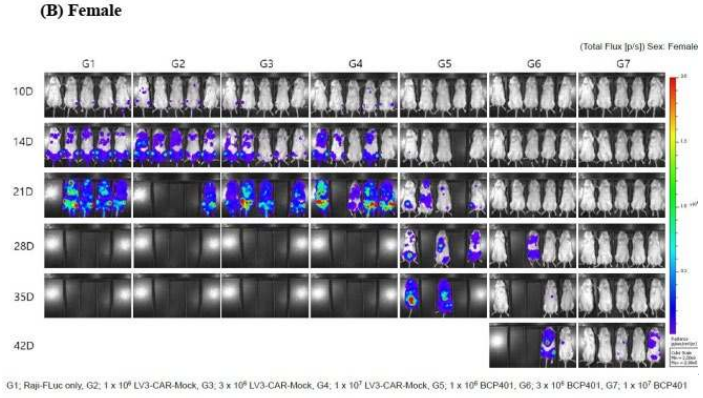
In addition, the RCL assay was negative to confirm the presence of lentivirus in BCP401.

BCP401 is considered to be less carcinogenic

Efficacy Test for BCP401 in a Non-Clinical







- Test Model: NSGA(NOD-Prkdc^{acid} IL2 Yg^{null}) with Raji-Fluc(lymphoblast)
- How to inject: Single administration, I.V.
- Sample : BCP401(CAR-T-19)
- Test dose condition
  - Raji-Fluc only(G1),
  - CAR-Mock(w/o CD3ζ & 4-1BB) 1 x 10^6 (G2), 3 x 10^6 (G3), 1 x 10^7 (G4),
  - BCP401(CD3ζ & 4-1BB) 1 x 10^6 (G5), 3 x 10^6 (G6), 1 x 10^7 (G7)

Results :

To investigate the efficacy of BCP401 in a non-clinical, Raji-Fluc cells was administrated to NSGA(NOD-Prkdc^{acid} IL2 Yg^{null}) to induce leukemia and BCP401 was injected by respectively concentration of cells to measure abnormal reactions, weight changes, and the expression of luciferase in mice. As a result of the test, most of the G1 died on the 14th, and the test group with CAR-Mock that did not contain signal domain and co-stimulation domain died owing to the disease. On the other hand, the group with BCP401 which contain 4-1BB and CD3ζ were found to have anti-cancer effects and the increasement of survival, and the results showed in dose-dependent.

Summary of Clinical Trial to BCP401 in Korea

Title	Multicenter, Single Arm, Open, Phase 1 Clinical Trial to Evaluate the Safety and Tolerability after Administration of BCP401 (CD19 recognition specific chimeric antigen receptor T cells) to Patients with CD19-Positive Recurrent B cell Precursor Acute Lymphocytic Leukemia under 25 years of Age
Substance	Autologous T cells introduced with lentiviral vectors expressing anti-CD19 scFv with CD3-ζ and 4-1BB signaling domains
Purpose	Assessing the Safety and Tolerability after BCP401(Autologous T Cells) with an Anti-CD19 Lentiviral Vector. **Primary**: Evaluation safety and tolerability after administration of BCP401 in patients with acute lymphocytic leukemia and establishing recommended dosages for subsequent clinical trials. **Secondary**: Investigation pharmacokinetics, cytokine change, disease response, immunogenicity, CAR-T cell persistence , and RCL etc.. after administration of BCP401 in patients with acute lymphocytic leukemia
Number of Tester	9-12 patients
Target Group for Patient	Patients with CD19-positive B-cell tumors and relapse and recurrent Acute lymphocytic leukemia Relapse : > 5% Blast, Relapse in bone marrow after anticancer therapy or SCT Recurrent : Not CR after 2 cycles of standard treatment for anti-cancer, Cases where CR has not been acquired with one or more standard treatment since relapse
Dosage and Administration	Low : 0.2 ~ 1 x 10^6/kg Middle : 1 ~ 2.5 x 10^6/kg High : 2.5 ~ 5 x 10^6/kg <2.5 x 10^8 CAR-positive viable T Cells, single dose, IV (20 minutes)
Indication	CD19 positive B - ALL

Plan for Clinical trial of BCP401

- Clinical hospital or institute
  - Korea : Asan Medical Center, Catholic University of Korea Seoul St. Mary's Hospital (In discussion and to be determined upon IND approval)
  - Europe : German and/or Bulgarian parties (In discussion)
- Korea IND submission
  - Dec. 28. 2020
- Expected date for clinical trial
  - Korea : 2Q 2021
  - Europe : 2022 (Korean IND documents to be submitted to EMEA)

Investigator Clinical Trial in China

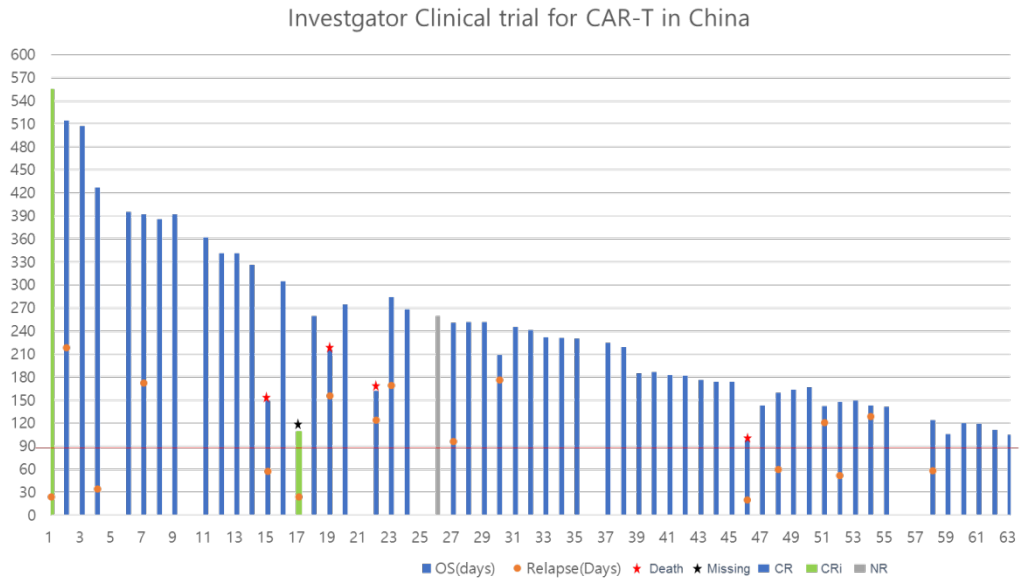
- **63 Subjects with relapse/refractory ALL (1~25 age)**
- **Primary Endpoint for the Efficacy Analysis**

  7 of 63 are not allowed to be evaluated the efficacy(ND_Not Determine),

  ORR(overall response rate) was 55/56(98.21%) as a result of the evaluated 56 subjects : **CR_53(94.64%)**, CRi_2(3.57%), NR_1(1.79%)

- **Management of CAR-T program**

  According to references of CAR-T cell therapy, it is known that the most adverse event by CAR-T cell occurred between 3 and 12 days after infusion. But, all patients were alive at 3 months.



➢ **Conclusion**

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

Evaluation Index : ORR

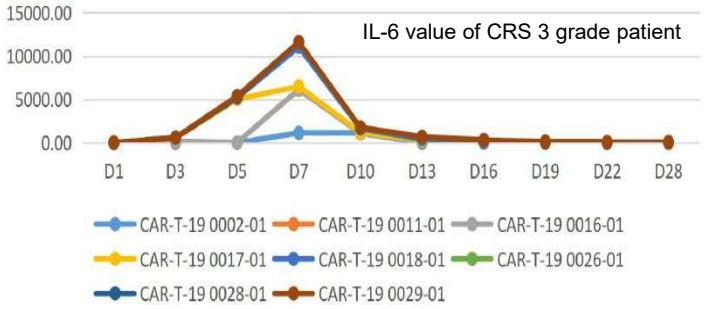
It was confirmed through peripheral blood, bone marrow, cerebrospinal fluid analysis, and physical examination. Initial evaluation of CR or CRi was assessed from 28 days.

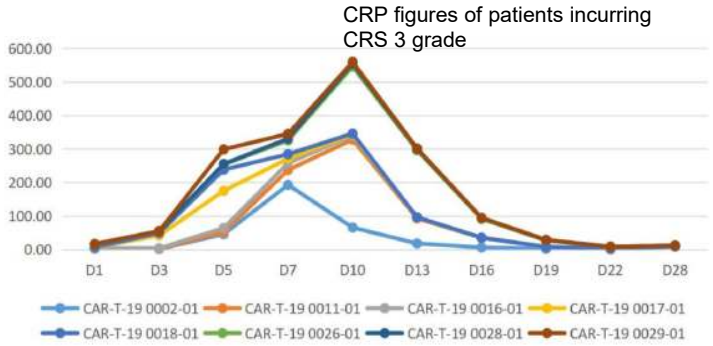
The product of 4 patients(#23, #32, #35, #48) was produced by PBMCs derived from sister, brother, and father.

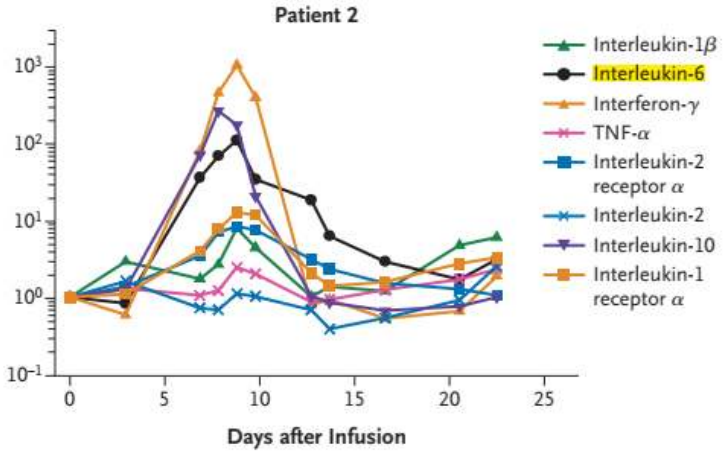
It was an investigated clinical trial to cure people in Beijing University Hospital in China by using CD 19 CAR-T Cell Therapy provided by Pharos Vaccine, a collaborative research and development company of BiocurePharm. This document requires confidentiality.

Investigator Clinical Trial in China : CRS

- Adverse events were immune responses related to CAR-T cell proliferation and cytokines release such as IFN gamma, IL-6, IL-10 etc..
- It was possible to control with IL-6 inhibitor and corticosteroid according to the level of IL-6 and CRP
- Evaluated with CTCAE(Common Adverse Event Terminology Standard) 4.03 of NCI.







CTL019(KYMRIAH) Patient in the early clinical trial - cytokines level *N Engl J Med 2013; 368:1509-1518*

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Investigator Clinical Trial in China : CRS

Classification	Number	Rate (%)
Fever	21	80.77
CRS (Cytokine Release Syndrome)	19	73.08
Hypotension	9	34.62
feel sick and vomit	6	23.08
Dizziness and headache	5	19.23
Coagulation abnormality	4	15.38
Edema	3	11.54
Oliguria	2	7.69
BNP increase	2	7.69
Blood oxygen decline	2	7.69
Sleepiness	2	7.69
Stomachache	1	3.85
Fatigue	1	3.85
BUN (Blood urea nitrogen)	1	3.85
Pulmonary infiltration	1	3.85
CRE increase	1	3.85
Involuntary speech	1	3.85

Classification	Number	Rate (%)
Twitch	1	3.85
Electrolyte disorder	1	3.85
Premature atrial contraction	1	3.85
Abnormal liver function	1	3.85
Dry cough, no blood o2 reduction	1	3.85
High blood sugar	1	3.85
Chill	1	3.85
Shortness of breath	1	3.85
Anorexia	1	3.85
Frequent urination	1	3.85
Parotid swelling	1	3.85
Upper limb jitter	1	3.85
Pleural effusion	1	3.85
Hand numb	1	3.85
Blurred vision	1	3.85
Tachycardia	1	3.85
Tremor	1	3.85

CRS Grade	No of adverse events	Rate (%)
No	7	26.92
Gr. 1	9	34.62
Gr. 2	2	7.69
Gr. 3	8	30.77

Adverse events after CAR-T shows similar results with Kymriah

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Comparison to other CAR-T cell therapy

Company	BiocurePhram	NOVARTIS	GILEAD
Product	BCP401	KYMRIAH	YESCARTA
scFv	CD19(FMC63)	CD19(FMC63)	CD19(FMC63)
Signal domain	4-1BB/CD3ζ	4-1BB/CD3ζ	CD28/CD3ζ
ORR	ALL(98.2%)	ALL(82.5%)	DLBCL(82%)
Response/patients	55/56	52/63	84/101
Other	-	DLBCL(50%)	ALL(CR 71%)
Source	IIT in Perking Univ.	FDA, JULIET(2018)	ZUMA-1(2017) ZUMA-3/4

- 7 of 63 patients was excluded for evaluating of response because their results could not determine whether CAR-T cell effect or lymphodepletion, but they was alive after these program.
- ORR(overall response rate) was evaluated at 3 months
- Results of OS at 3 months, Kymriah is 57/63(90.5%), versus BIOCURE is 63/63(100%).
- The rate of overall survival are 82.5%(52/63) in Kymriah and 93.7%(59/63) in BIOCURE.

OS	Kymriah	BIOCURE
*OS at 3 Month	57/63 (90.5%)	63/63 (100%)
*OS (Total Period)	52/63 (82.5%)	59/63 (93.7%)

OS, overall survival

Source : FDA Statistical Reviewer

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Further R&D planning on basis of the CAR-T therapy

➢ Targetable to Solid tumor

: Pancreatic cancer, Lung cancer, Ovarian cancer

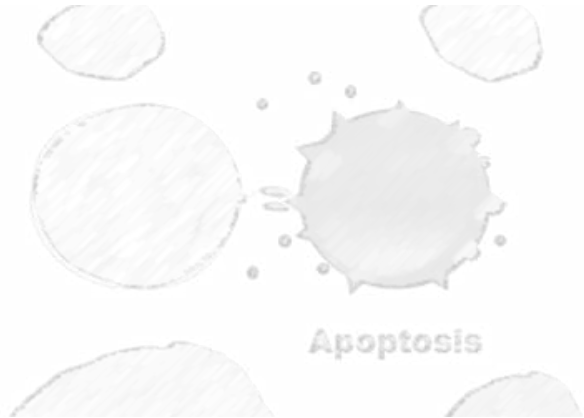
① Development of new treatment for solid cancers using antibody technology of Y biologics that have various libraries of antibody and developing techniques

② Development of treatment for solid cancers using combination injection with IL-2 and IL-7

➢ **The possibility of solid cancer target treatments using CAR-T cell is seen as likely and important**

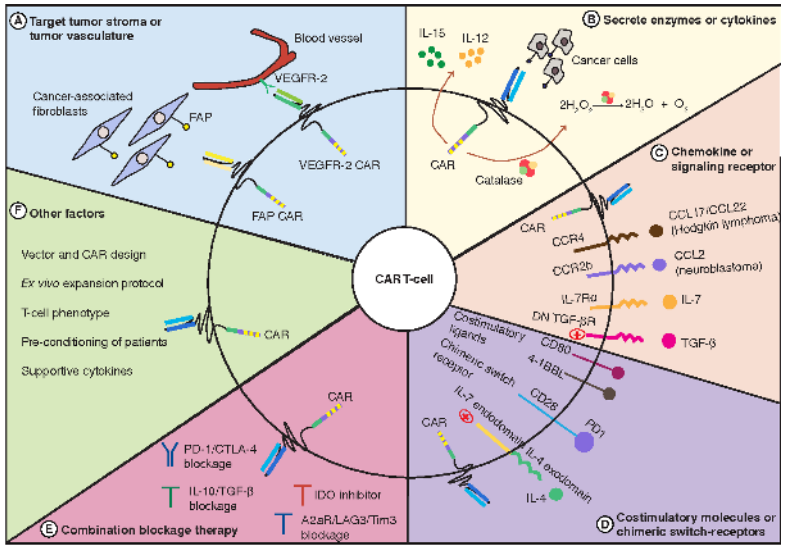
No CAR-T Cell treatment for solid tumor has been approved by the FDA yet

Several early clinical studies have indicated in roads to successful treatment in solid cancers



Overcoming Solid caner with next CAR-T cell

Hurdles	Cause	Challenges
Target antigen Heterogeneity	Antigen	Humanized scFv, Optimal antigen as on target & off tumor
Hostile Tumor microenvironment	Trafficking	Chemokine, signaling receptor(IL-7, CCL2, TGFβ etc..), CARs that degrade the extracellular matrix
	Immune-suppression	Combination blockage : PD-1/CTLA-4, IL-10/TGF-β, IDO inhibitor etc..), stimulating Treg by IL-7 and IL-21
Intrinsic regulatory mechanism	Others	CAR design, T cell phenotype, pre-conditioning of patients, manufacturing etc..



Immunotherapy (2016) 8(12), 1355–1361

Plans for Production GMP Facility and Advance for Global Market

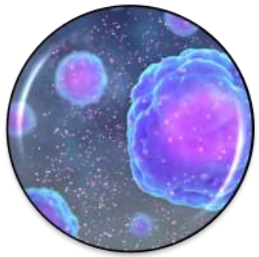
Area	Plan	Progress
Korea	It will be established in a Science business belt in Daejeon city on a site already owned by BiocurePharm	Design in 2021
Germany	To manufacturing and commercializing a CAR-T cell therapy based ROR1 scFv for a CLL,	MOU has been executed Establishment of JV 'Oncocart'
Bulgaria	JV to be set up for clinical trial and local GMP facility.	MOU has been executed
Asia	Compassionate clinical trial in Malaysia with Univ. of Malaya	MOU has been executed

- **If existing facilities and production systems are available, it will be advantageous for the business to proceed.**

- **Compassionate clinical trial with Malaysian Hospital may start in 2021 subject to fund availability.**

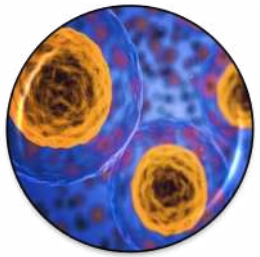
Main Business Category

➢ Leading company to commercializing **CAR-T cell therapy**



BIOPHAMACEUTICAL

COSMETICS



IMMUNOCELL THERAPY

- Clinical trial Scheduled for early 2021
- IND for clinical submitted in 2020
- CAR-T Cell therapy preclinical completed in 2018

GENETIC ENGINEERING

BiocurePharm's technology is based on genetic engineering, and developed with collaborators in various fields

Company Roadmap

Classification	Pipeline	Indication	2021	2022	2023	2024
IMMUNOCELL THERPEUTICS	BCP401	ALL	Clinical trial		Launching	
	BCP402	CLL	Development and Pre-clinical		Clinical trial	
	BCP403	Solid tumor	Development and Pre-clinical		Clinical trial	
BIOPHARMACEUTICAL	BCP101	MS		Clinical	Launching	

	2021	2021	2022	2023
Overseas network	Malaysia	Germany, Bulgaria	Italy, France, UK and EU	

BCP401 is 2nd generation CAR-T with anti-CD19 scFv

BCP403 is developing for solid tumor with advanced CAR-T platform

Share Structure

Biocure Technology Inc. (CSE: CURE)

• Outstanding Shares	108,045,358
• Outstanding Options	6,320,000
• Outstanding Warrants	1,810,725
• Insiders' Holdings	25.42%

BiocurePharm Corp. (Korean Subsidiary)

• Outstanding Shares	3,808,197
• CURE Ownership	3,591,832 (94.32%)
• Outstanding Options / Warrants	Nil

The Team

- **Sang-Mok Lee, CEO & President, Director**

  Dr. Lee has been a President and CEO since the inception in 2005. Dr. Lee holds a PhD in microbiology from Busan National University in Korea and is currently an adjunct professor in microbiology at Chungnam National University. Dr. Lee is a committee member for the hi-tech medical complex city in Daejeon, Korea and a committee member of KOFST (the Korean Federation of Science and Technology Societies).

- **Konstantin Lichtenwald, CFO, Director**

  Mr. Lichtenwald has over ten years of finance and accounting experience, including corporate compliance, accounting and financial manag ement and IPO, RTO services. Mr. Lichtenwald offers extensive knowledge and know-how for companies in two key financial jurisdictions, North America and German speaking parts of Europe. His accounting, financial skills offer a multi-faceted hands on approach to strategic m anagement and problem solving. Mr. Lichtenwald earned his bachelor of business administration degree from Pforzheim University, Germa ny, and holds the professional designation of 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 Cer tified Accountants of United Kingdom.

- **Collin (Sang-Goo) Kim, Director**

  Mr. Kim holds a bachelor degree of business administration from Korea University, Seoul, Korea. Mr. Kim came to Vancouver, Canada in 2006 after working for Hanwha Corp., one of Korean business conglomerates for 16 years, where he was dedicated to International trading business for various industrial products. He has been working as a Vice President for Columbia Capital since 2008 and a director of ArcPac ific Resources Corp., a public Canadian junior exploration company, since 2015. He is imperative in the communication between Korean m anagement and Canadian management cross the border with his vast knowledge and work experience.

The Team

- **Danny Joh – Director**

  After completing a PhD in Biochemistry at Texas A&M university and an MBA at Rice University, Danny Joh moved to the San Francisco area to build a career in the biopharma industry. For twenty years, he has expanded his biopharma product development and cross-functional program management experiences while working for major biopharma companies, including Chiron, Genentech, Biomarin, Sangamo and other biotech companies in the San Francisco area. His 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. He joins the Board of Directors of Biocure Technologies in March 2021.

- **Berkan Unal – Director**

  Mr. Berkan has over 10 years of experience in the biopharmaceutical industry and has solid connections to the global leaders in the bio-/pharmaceutical sector. As the strategic business advisor, he will support Oncocart to build and strengthen their business development activities. Berkan studied bioprocess engineering and medical biotechnology at Berlin Technical University of Applied Sciences, Hamburg University of Technology and Imperial College London.

  Currently, he is acting as Business Development Director for Biologics, Gene and Cell Therapy of GenScript Biotech, a global leading biotech company which provides end-to-end solutions from discovery to commercialization. Before joining GenScript Biotech, he worked for biotech companies in Switzerland and Germany.

  In 2021, Oncocart is going to additionally hire an assistant who will be supporting the management team. For the areas of accounting, taxes, legal and IP Oncocart will use external service providers in order to minimize fixed costs.

The Team

- **Hans Frykman – Consultant**

  Dr. Hans Frykman is the current medical director of Neurocode Labs in Vancouver and UBC Diagnostic Services Lab. Neurocode is world leading in the field of neurogenetics accepting difficult adult and pediatric neurology cases from Asia, North America and Europe. It is Canada's first and only clinical whole exome sequencing laboratory. Also, Neurocode has a best in class software product linking genotype to phenotype in the area of neurogenetics. UBC Diagnostic Services Lab is Canada's leading clinical Neuroimmunology laboratory servicing all provinces with this highly complex testing. Under Dr. Frykman's guidance, the UBC Diagnostic Services lab has expanded fourfold. Dr. Frykman has a medical degree from Karolinska Institute in Stockholm, a PhD in Biocatalysis at Royal Institute of Technology, and post graduate medical training from Karolinska University Hospital Solna Campus, Mayo Clinic, University of Minnesota, Memorial Sloan Kettering and University of British Columbia in the areas of internal medicine, oncology, clinical pathology, molecular genetics and medical biochemistry. Dr. Frykman held reaearch positions with the US Government, Astra Zeneca, Akzo Nobel and Novo Nordisk. Early in his career he was part of the discovery teams around Victoza and Losec(Prilosec). He is licensed to practice medicine in Sweden and British Columbia.

- **The Company also has a very strong Advisory Board comprised of Medical Professionals that have key industry contacts and alliances. For their full Bio's and Summary of expertise please refer to our website.**

Biosimilar and Biopharmaceuticals by BiocurePharm

- "…**Biosimilars will provide access to important therapies for patients who need them…**"FDA Commissioner Margaret A. Hamburg M.D.

- **BCP101(Interferon β) : Multiple Sclerosis Treatment**
- **BCP102(Filgrastim) : Combine therapy for Anti cancer and blood disease**
- **BCP104(Ranibizumab) : Macular Degeneration Treatment**

BiocurePharm had already developed of cell bank, manufacturing process, CMC , and QC for Interferon β, Filgrastim and ranibizumab those are blockbuster bio-s imilar. BiocurePharm can offer you the technical know-hows to be a product at th e earliest time with a competitive price.

Tel : +1 604 609 7146
E-mail : info@biocuretech.com

Thank you.

Revision – Sep. 2021

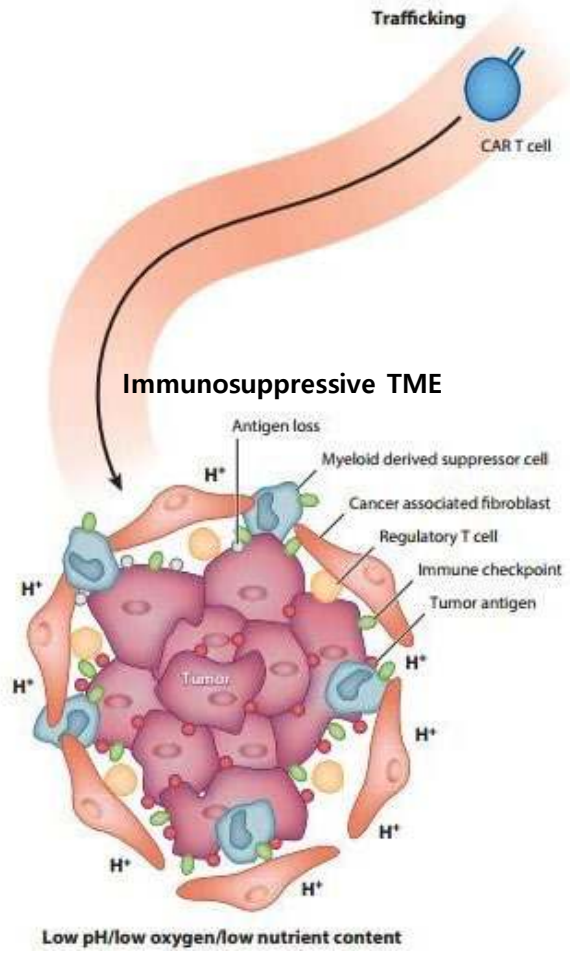
Biocure Technology

Hurdles of CAR-T cell therapy in Solid tumor

2nd CAR-T cell therapy showed outstanding response rate in hematological malignancies. The results of treatment for non-hematological malignancies, especially solid tumors, seems to be restricted. A lot of researchers are studying various try on the basis of hypothesis and mechanisms.

Major challenges followed as :

- **Target antigen heterogeneity**
- **Trafficking**
- **Hostile Tumor microenvironments**
  - **physical barriers, low pH, low oxygen, low nutrient**
  - **Immunosuppressive immune cells**
- **Intrinsic regulatory mechanisms of T cells**

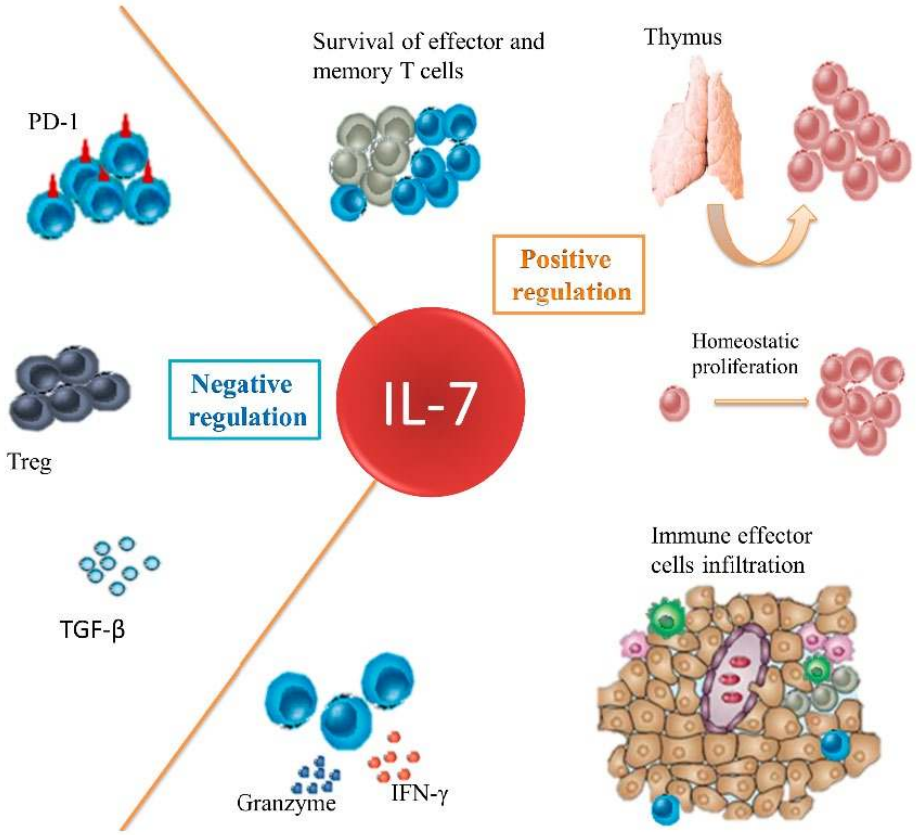


Ann. Rev. Med. 2021.68:139-152

Interleukin-7

Proliferation of immature T cell stimulated by IL-7 results in expansion.

IL-7 guides more CTLs and other immune effectors cells infiltration with better survival and upregulated killing activities. It fights against the immunosuppressive network to improve immune function on cancer cells



Int. J.Mol. Sci. 2015

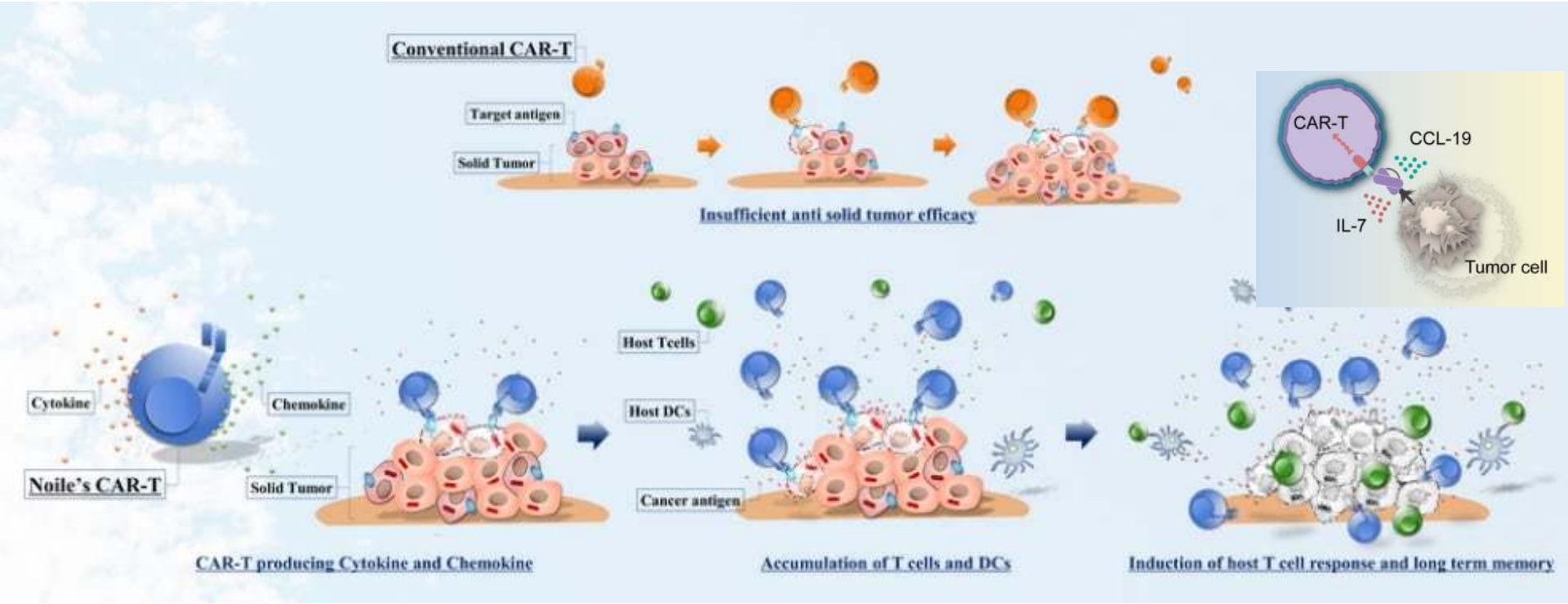
PRIME CAR-T cell(IL-7 and CCL19)

- NOILE Immune tech.(Japan) cooperates with LEGEND BIO.(china) and J&J

PRIME(proliferation-inducing and migration-enhancing) : IL-7 and CCL19 secretion with proliferation of CAR-T cell

IL-7 and CCL19 helps to infiltration and survival on T-zone fibroblastic reticular cell of tumor

IL-7 increases T cell proliferation and CCL19 induces T cell and DC as a chemoattractant

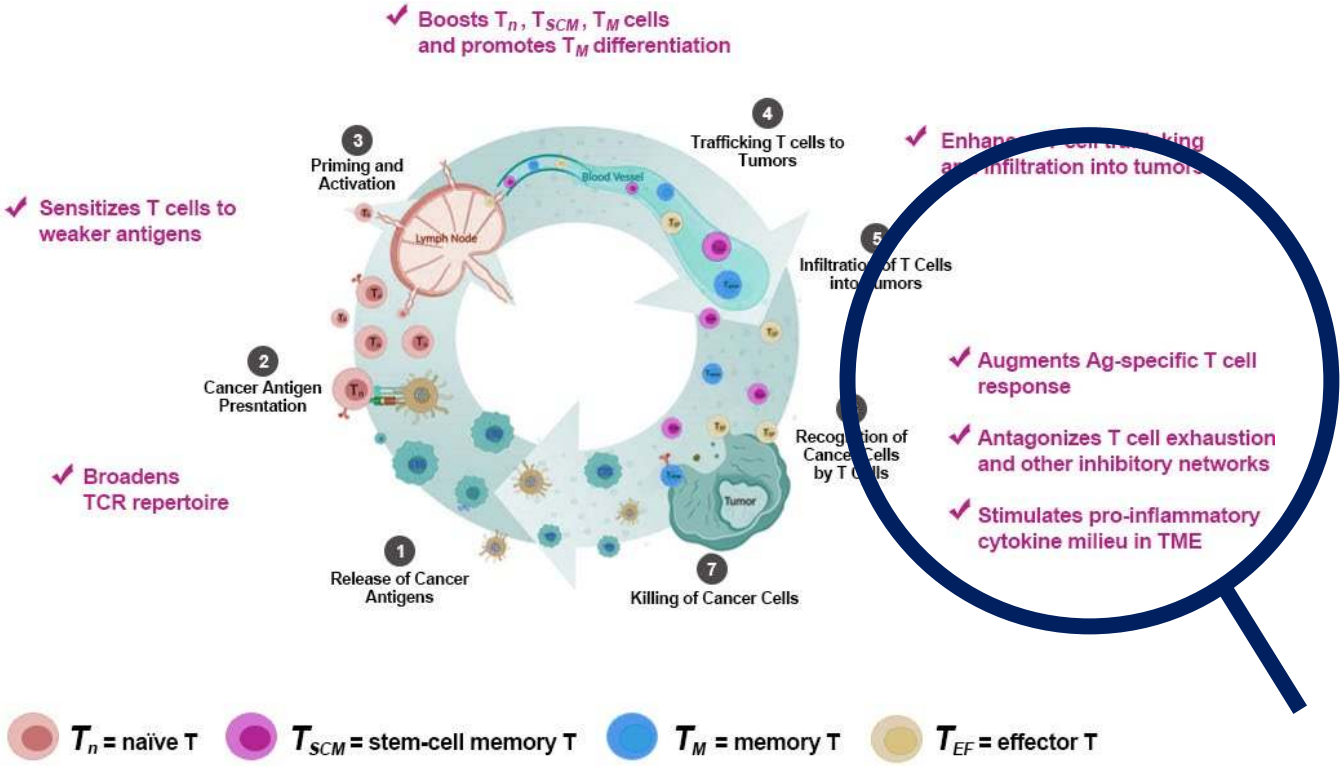


Combination therapy with Hyleukin-7

✓ Interleukin-7 enhances T cell trafficking and infiltration into tumors.

✓ Antagonizes T cell exhaustion

Possible to be more positive results of treatment for solid cancers by the combination of BCP-CAR-T and safety Hyleukin-7 that could use a high dose than others.



Source: NeoImmue Tech

Y Biologics – Biocurepharm 'ICI+CAR-T Combined Therapy' Development of Anticancer Treatment for Solid Tumors

Anti PD-1 Mono Clonal Antibody YBL-006 & Anti-CD-19 CAR-T Combined Therapy Development

The purpose of this agreement is to research the effectiveness of combined treatment of Immune Checkpoint Inhibitor PD-1 (Programmed Cell Death Protein-1)developed by YB and anti-CD19 CAR T-Cell Therapy developed by BPK.

Next Generation Anticancer Treatment for Solid Tumors.

Reporter Jong Won Chang at Biospecdata on January 8, 2021