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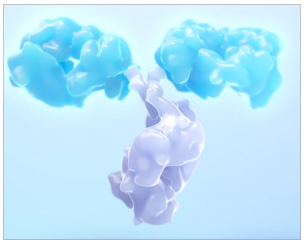


SAFA (anti-Serum Albumin Fab Associated) platform technology

Developer(s)

AprilBio

Originator

http://www.aprilbio.com/

South Korea

AprilBio is a South Korean biopharmaceutical company that is based at Gangwon University, developing specialized biologics and antibody drugs for rare diseases, oncology, autoimmune and inflammatory diseases. Their focus areas include rare diseases, oncology, autoimmune and inflammatory diseases.

Sponsor(s)

Yuvan, USA

https://www.yuhan-usa.com/

Partnerships

Evoimmune

https://www.evommune.com/

Lundbeck

https://www.lundbeck.com/uk

Technology information

Type of technology

Fusion of a therapeutic protein with a human antibody engineered to bind albumin.

Administration route

Intravenous

Development state and regulatory approval

Active Pharmaceutical Ingredient (API)

APB-A1 (anti-CD40L agent)

Development Stage

Phase I

Regulatory Approval

Not provided

Description

SAFA (anti-Serum Albumin Fab-Associated) is a novel technology that modifies antiserum albumin Fab fragments to create long-acting therapeutic proteins. This modified fab can be fused with antibody fragments and/or recombinant proteins. These fused constructs, termed SAFAbodies, exhibit high affinity binding to natural serum proteins. At the cellular level, these SAFAbodies bind to neonatal Fc Receptor (FcRn) to avoid degradation. This FcRn binding mechanism results in the prolonged action of the SAFA formulation i.e., prolonged half-life and targeted site of action.

Technology highlight

1) Prolonged Half-Life 2) Targeted Site of Action 3) No chemical conjugated with PEG or any other polymer 4) Flexibility in choosing protein expression system 6) Less immunogenic side effects due to no/low Fc gamma receptor (FcgR) interaction.

Technology main components

1) Genetically Modified Albumin Fusion protein 2) API 3) FcRN4 4) Excipients such as fillers, antiagglutinating agents, lubricating agents, wetting agents, flavoring agents, emulsifiers, and preservatives are added based on the API.

Information on the raw materials sourcing, availability and anticipated price

Not provided

Delivery device(s)

No delivery device

APIs compatibility profile

API desired features

Proteins

Therapeutic proteins such as Monoclonal Antibodies, Interleukins, CD-40, Granulocyte Colony-Stimulating Factor (G-CSF) analogues, Human Growth Hormone (HGH), IFN-β (Interferon Beta), checkpoint inhibitors, Follicle-Stimulating Hormone (FSH) analogues, and GLP-2 (Glucagon-Like Peptide-2) are targeted

Additional solubility data

Not provided

Additional stability data

Not provided

API loading: Maximum drug quantity to be loaded

75-90 wt%

API co-administration

1 single API :

LogP

Not provided

Scale-up and manufacturing prospects

Scale-up prospects

Not provided

Tentative equipment list for manufacturing

Not provided

Manufacturing

The manufacturing process of the SAFA formulation involves the following key steps: • Generation of SL33X-API Fusion Constructs: This step is performed using polymerase chain reaction (PCR) amplification followed by cloning techniques to produce the desired constructs. • Preparation of Soluble Fab Fragments and SL33X-API Fusion Proteins: Soluble Fab fragments and fusion proteins are synthesized and purified as part of the formulation process. Note: The complete manufacturing process for the finalized product remains undisclosed.

Specific analytical instrument required for characterization of formulation

• Differential scanning calorimeter (DSC) • Enzyme-linked immunosorbent assay (ELISA) • In vitro bioactivity assay • UV Spectrometer (Bio-Rad) • Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis (SDS-PAGE) and Western Blot analyses (using Coomassie Blue staining)

Clinical trials

APB-R3-101

Identifier

NCT05715736

Link

https://clinicaltrials.gov/study/NCT05715736

Phase

Phase I

Status

Completed

Sponsor

Syneos Health

More details

This will be a single centre, Phase 1, First-In-Human, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Single Ascending Dose of APB-R3 in Healthy Participants.

Purpose

Assessment of Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of APB-R3

Interventions

Intervention 1

APB-R3

Intervention 2

Placebo

Countries

Australia

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2023-03-08

Anticipated Date of Last Follow-up

2024-01-04

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2023-12-19

Actual Completion Date

2023-12-19

Studied populations

Age Cohort

- Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

Yes

Comments about the studied populations

Inclusion Criteria: 1. Male or female, non-smoker, 18 to 60 years of age (both inclusive), 2. Healthy as defined by: 1. the absence of clinically significant illness and surgery within 4 weeks prior to study drug administration in the opinion of the investigator. 2. the absence of clinically significant history of neurological, endocrine, cardiovascular, respiratory, hematological, immunological, psychiatric, gastrointestinal, renal, hepatic, and metabolic disease in the opinion of the investigator. Exclusion Criteria: 1. Abnormal finding at physical examination 2. Evidence of clinical significant hepatic or renal impairment 3. Clinically significant abnormal laboratory test results or positive serology test results for HBsAg, HCV antibody, or HIV antigen and antibody.

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

31

Allocation

Randomized

Intervention model

Sequential assignment

Intervention model description

Not provided

Masking

Quadruple-blind masking

Masking description

Not provided

Frequency of administration

Other : "Single dose "

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intravenous

Use case

Treatment

Key results

Not provided

20119A

Identifier

NCT05136053

Link

https://clinicaltrials.gov/study/NCT05136053

Phase

Phase I

Status

Completed

Sponsor

H. Lundbeck A/S

More details

The main goal of this study is to learn more about the safety of a drug called Lu AG22515. During the trial, healthy adult participants will receive a single dose of Lu AG22515 or a placebo (normal saline solution).

Purpose

A Study Investigating Lu AG22515 in Healthy Adults

Interventions

Intervention 1

Lu AG22515

Intervention 2

Placebo

Intervention 3

Immune System Activator

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2022-03-18

Anticipated Date of Last Follow-up

2023-08-24

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2023-08-05

Actual Completion Date

2023-08-05

Studied populations

Age Cohort

Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

Yes

Comments about the studied populations

Inclusion Criteria: * Body mass index (BMI) ≥18.0 and ≤32.0 kilograms (kg)/square meter (m\^2) and weight between 55 and 110 kg (both inclusive) at screening. * Fully vaccinated against COVID-19, as evidenced by presentation of a vaccine card. The last administration of the COVID-19 vaccination must be received a minimum of 30 days and maximum 6 month prior to dosing in this study. * Medically healthy with no clinically significant medical history, physical examination and neurological assessment, laboratory profiles, vital signs, or electrocardiograms (ECGs), as deemed by the principal investigator (PI) or designee.

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

58

Allocation

Randomized

Intervention model

Sequential assignment

Intervention model description

Not provided

Masking

Double-blind masking

Masking description

Not provided

Frequency of administration

Other : "Single dose "

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intravenous

Use case

Treatment

Key results

Not provided

Excipients

Proprietary excipients used

No proprietary excipient used

Novel excipients or existing excipients at a concentration above Inactive Ingredients Database (IID) for the specified route of administration

No novel excipient or existing excipient used

Residual solvents used

No residual solvent used

Additional features

Other features of the technology

- Room temperature storage
- At least 1 year shelf life
- Other(s)

  Drug release from the protein fragments at intercellular level

Release properties

The antigen-binding fragment (Fab) of the API specifically binds to albumin, enhancing protein binding and thereby extending the API’s half-life (~19 days), volume of distribution at steady state (Vss), and systemic clearance (CL). The prolonged release mechanism involves FcRn-mediated recycling of the Fab-albumin complex at the cellular level, resulting in the slow, sustained release of the API from the complex.

Injectability

SAFA injections are administered via subcutaneous route of administration using a standard 21-gauge needle or even thinner depending on the formulation characteristics.

Safety

Preclinical animal studies show that the 4-week repeated dose toxicity revealed no abnormal toxicological symptoms.

Stability

The shelf life of the SAFA is approximately one year, with a serum stability of the SAFA-coordinated complex lasting 16 days.

Storage conditions and cold-chain related features

Room temperature storage is possible.

Potential application(s)

Therapeutic area(s)

Other(s) : "Male infertility, Endocrine disorders, Auto-inflammatory disease , Still's disease and Obesity"
Oncology

Use case(s)

Treatment

Use of technology

Ease of administration

- Administered by a community health worker
- Administered by a nurse
- Administered by a specialty health worker

Frequency of administration

Weekly, Monthly

User acceptance

Not provided

Targeted user groups

Age Cohort

- Adults
- Older Adults

Genders

- All

Pregnant individuals

Unspecified

Lactating individuals

Unspecified

Healthy individuals

Unspecified

Comment

Not provided

Potential associated API(s)

Interleukins

Class(es)

IL-18 inhibitor

Development stage

Phase I

Clinical trial number(s)

NCT05715736

Foreseen/approved indication(s)

Auto-inflammatory diseases and Still's disease

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Cytokines agonists

Class(es)

Anticancerous agent

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Solid Tumors

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Interleukins

Class(es)

IL-2R inhibitor

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Autoimmune diseases

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Glucagon-like peptide-1 (GLP-1) analogues (GLP-1)

Class(es)

GLP-1R agonist (antiobesity agent)

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Obesity

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

APB-R6 (TSHR analog)

Class(es)

Anterior Pituitary Hormone receptor analogues

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Endocrine Disorders

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

APB-R2 (FSHR analog)

Class(es)

Anterior Pituitary Hormone Receptor analogues

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Male Infertility

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

APB-A1 (anti-CD40L agent)

Class(es)

Immunosuppressants

Development stage

Phase I

Clinical trial number(s)

NCT05136053

Foreseen/approved indication(s)

Autoimmune diseases, such as amyotrophic lateral sclerosis, systemic lupus erythematosus, Sjögren’s syndrome or organ transplantation

Foreseen user group

Not provided

Foreseen duration between application(s)

Every 2 to 4 weeks

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Patent info

Description

Anti - Serum Albumin Fab - Effector Moiety Fusion Construct And A Method Of Preparing The Construct

Brief description

The present invention relates to antigen-binding fragment (Fab) and a Fab-effector fusion protein or (poly)peptide comprising thereof. The Fab of the present invention specifically binds to serum albumin and thereby has extended in vivo half-life. The Fab of the present invention is characterized by not having cysteine residues that are responsible for the interchain disulfide bond in CH1 domain and CκL domain as well. The Fab-effector fusion protein or (poly)peptide of the present invention can be produced in periplasm of E. coli with high yield, and has increased in vivo half-life. Further, the present invention provides E. coli strain which produces various kinds of Fab-effector fusion proteins or (poly)peptides, pharmaceutical composition comprising the fab-effector fusion proteins.

Representative patent

US9879077B2

Category

Formulation

Patent holder

Aprilbio Co Ltd

Exclusivity

Not provided

Expiration date

August 29, 2034

Status

Anticipated expiration

Supporting material

Publications

** Kang, H. J., Kim, H. J., Jung, M. S., Han, J. K., & Cha, S. H. (2017). Optimal expression of a Fab-effector fusion protein in Escherichia coli by removing the cysteine residues responsible for an interchain disulfide bond of a Fab molecule. Immunology Letters, 184, 34-42. **

Development of novel bi-functional or even tri-functional Fab-effector fusion proteins would have a great potential in the biomedical sciences. However, the expression of Fab-effector fusion proteins in *Escherichia coli* is problematic especially when a eukaryotic effector moiety is genetically linked to a Fab due to the lack of proper chaperone proteins and an inappropriate physicochemical environment intrinsic to the microbial hosts. We previously reported that a human Fab molecule, referred to as SL335, reactive to human serum albumin has a prolonged *in vivo* serum half-life in rats. We, herein, tested six discrete SL335-human growth hormone (hGH) fusion constructs as a model system to define an optimal Fab-effector fusion format for *E. coli* expression. We found that one variant, referred to as HserG/Lser, outperformed the others in terms of a soluble expression yield and functionality in that HserG/Lser has a functional hGH bioactivity and possesses an serum albumin-binding affinity comparable to SL335. Our results clearly demonstrated that the genetic linkage of an effector domain to the C-terminus of Fd (VH + CH1) and the removal of cysteine (Cys) residues responsible for an interchain disulfide bond (IDB) ina Fab molecule optimize the periplasmic expression of a Fab-effector fusion protein in *E. coli*. We believe that our approach can contribute the development of diverse bi-functional Fab-effector fusion proteins by providing a simple strategy that enables the reliable expression of a functional fusion proteins in *E. coli*.

** Ji, S. I., Park, J. H., You, H. G., Chi, H.**

J., Bang, Y. W., & Cha, S. H. (2019). Intact bioactivities and improved pharmacokinetic of the SL335-IFN-?-1a fusion protein that created by genetic fusion of SL335, a human anti-serum albumin fab, and human interferon-?. Immunology Letters, 207, 46-55.</p>

Recombinant human interferon beta (rIFN-β) has long been used as a first-line treatment for multiple sclerosis (MS), and any attempt to develop a long-acting rIFN-β is desirable since only one pegylated version of long-acting rIFN-β-1a (Plegridy) is currently available in clinics. Previously, we reported that SL335, a human Fab molecule specific to serum albumin, exhibits an extended serum half-life *via* utilizing the FcRn recycling mechanism. With the ultimate goal of developing a long-acting rIFN-®, we generated a fusion construct by linking human IFN-β cDNA to the C-terminus of the SL335 H chain at the DNA level followed by expression of the fusion protein, referred to as SL335-IFN-β-1a, in Chinese hamster ovary-S (CHO-S) cells. In its N-linked glycosylated form, the resulting fusion protein was easily purified from the culture supernatant *via* a three-step chromatography process. *In vitro* functional assays revealed that the fusion protein retained its intrinsic binding capabilities to human serum albumin (HSA) and interferon α/β receptor (IFNAR) that were almost identical to those of parental SL335 and rIFN-β-1a (Rebif). In addition, the fusion protein possessed an antiviral potency and anti-proliferation activity comparable to those of Rebif. In pharmacokinetic (PK) analyses using Lewis rats and cynomolgus monkeys, SL335-IFN-β-1a exhibited at least a two-fold longer serum half-life and a significantly reduced renal clearance rate compared to those of Rebif. Finally, a four-week repeated dose toxicity study revealed no abnormal toxicological signs. In conclusion, our results clearly demonstrated that SL335-IFN-β-1a is worthy of further development as an alternative long-acting IFN-β therapeutic.

Additional documents

No documents were uploaded

Useful links

There are no additional links

Access principles

Collaborate for development

Consider on a case by case basis, collaborating on developing long acting products with potential significant public health impact, especially for low- and middle-income countries (LMICs), utilising the referred to long-acting technology

Not provided

Share technical information for match-making assessment

Provide necessary technical information to a potential partner, under confidentiality agreement, to enable preliminary assessment of whether specific medicines of public health importance in LMICs might be compatible with the referred to long-acting technology to achieve a public health benefit

Not provided

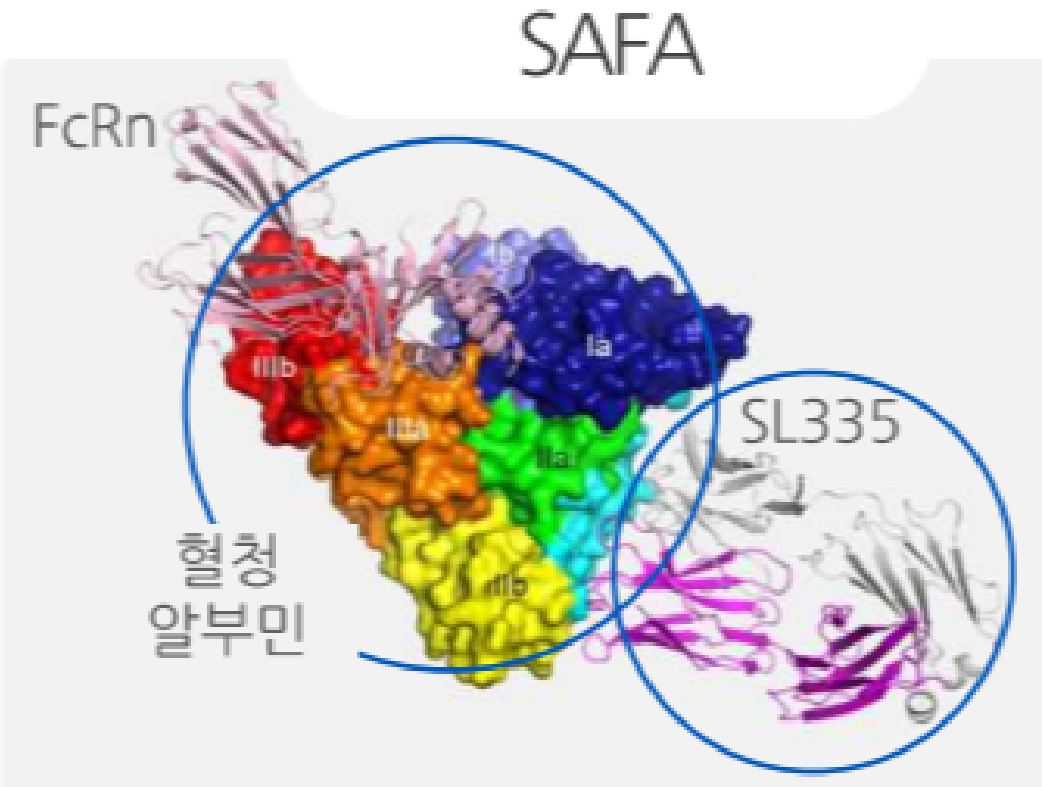
Work with MPP to expand access in LMICs

In the event that a product using the referred to long-acting technology is successfully developed, the technology IP holder(s) will work with the Medicines Patent Pool towards putting in place the most appropriate strategy for timely and affordable access in low and middle-income countries, including through licensing

Not provided

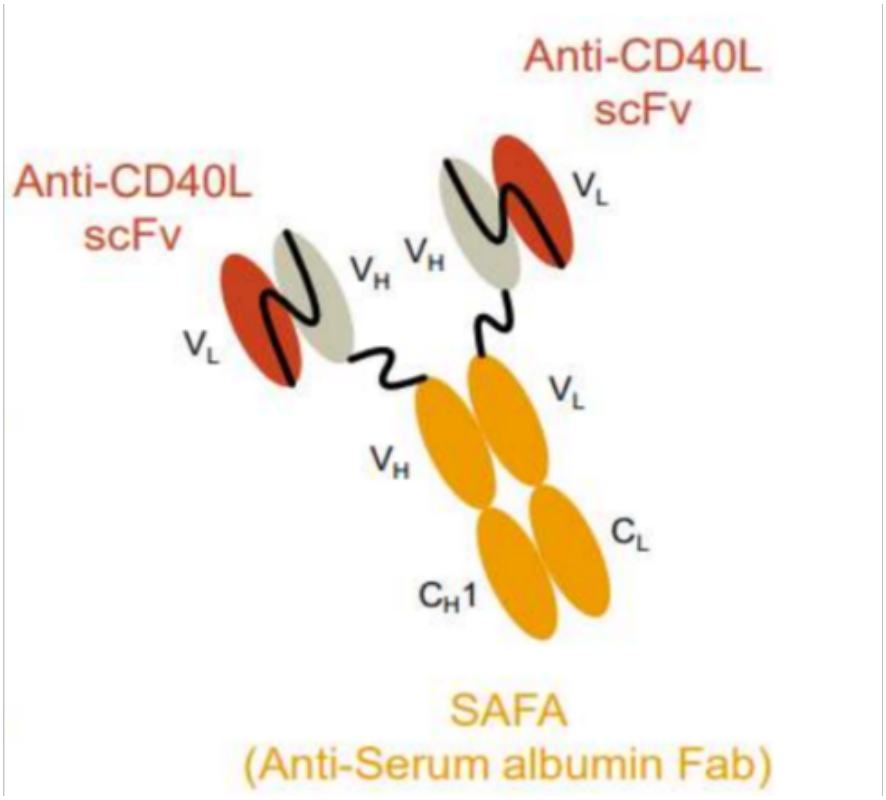
Comment & Information

Illustrations



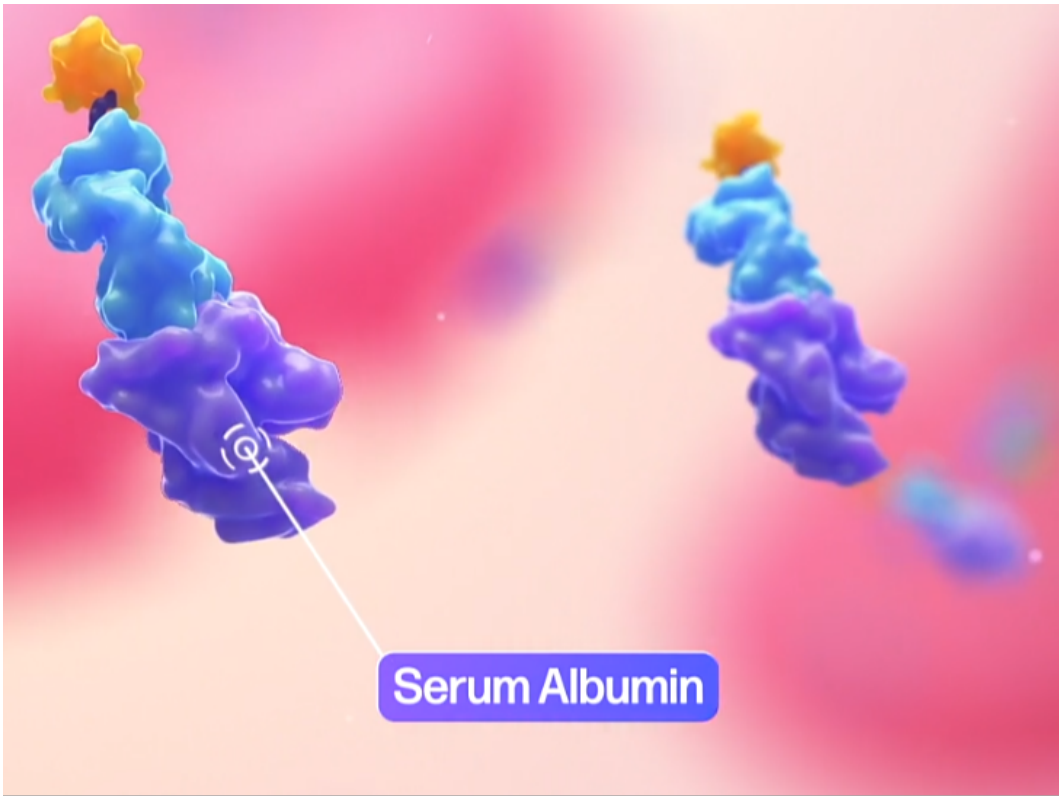
FcRn conjugated with SL335 (API protein)

Investor relations 2014 (no date) AprilBio. Available at: https://file.irgo.co.kr/data/PLAN/ATTACH_PDF/66dce57081c3650b509ae67ee6a245e4.pdf (Accessed: 28 November 2024).



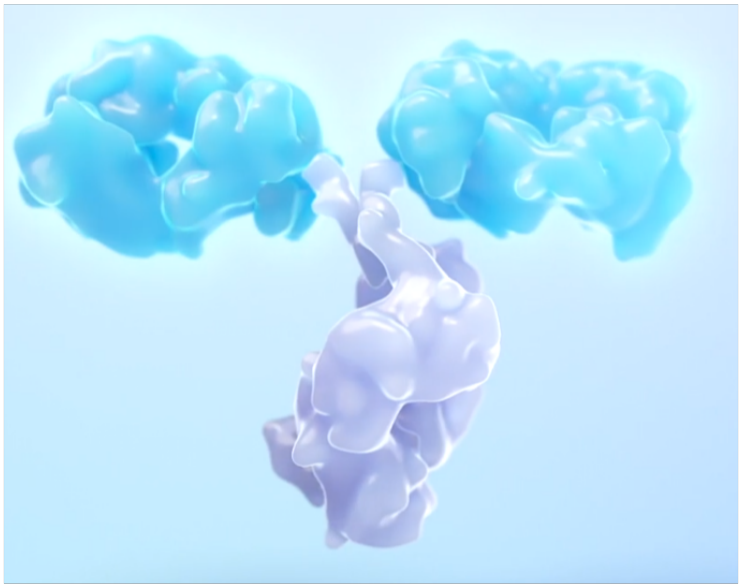
SAFA CD-40L inhibitor (Phase 1 completed)

Investor relations 2014 (no date) AprilBio. Available at: https://file.irgo.co.kr/data/PLAN/ATTACH_PDF/66dce57081c3650b509ae67ee6a245e4.pdf (Accessed: 28 November 2024).



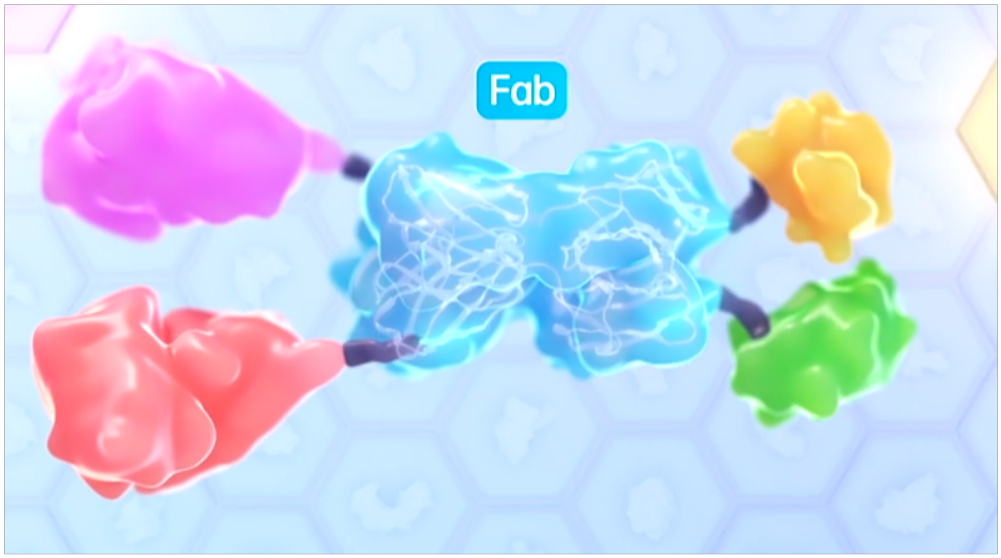
SAFA body conjugated with the serum albumin (protein binding)

AprilBio. (n.d.). AprilBio. AprilBio. Retrieved November 28, 2024, from http://www.aprilbio.com/



SAFA Body

AprilBio. (n.d.). AprilBio. AprilBio. Retrieved November 28, 2024, from http://www.aprilbio.com/



SAFA Body conjugated with therapeutic proteins

AprilBio. (n.d.). AprilBio. AprilBio. Retrieved November 28, 2024, from http://www.aprilbio.com/