# First-in-class Interleukin-15 Fusion Protein for the Treatment of Solid Tumors

## Overview

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| **Drug Name** | BioLink001 |
| **Description** | BioLink001 is a tumor-targeting interleukin-15 (IL-15) fusion protein and is in early clinical development for the treatment of locally advanced/metastatic or relapsed/refractory solid tumors. BioLink001 was granted orphan drug designation by the FDA. |
| **Target** | Interleukin 15 |
| **Drug Modality** | Fusion protein |
| **Indication** | Solid tumor |
| **Product Category** | Cancer immunotherapy |
| **Mechanism of Action** | Interleukin 15 replacements |
| **Status** | Phase I |
| **Patent** | Granted |

### Collaboration Opportunity

Protheragen Inc. is actively seeking partnership for BioLink001. Potential collaboration can be strategic alliance, licensing, or marketing agreement.
We look forward to hearing from you.

## Target

### Interleukin 15

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| **Introduction** | IL-15 is a cytokine expressed by monocytes, macrophages, dendritic cells (DC), keratinocytes, fibroblasts, and nerve cells. It binds to and signals through a |

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| | complex composed of the IL-2/IL-15 receptor beta chain (CD122) and the common gamma chain (CD132). IL-15 effects on many cells of the immune system and can promote the proliferation of B cells and the secretion of immunoglobulins. It is essential for the ontogeny of natural killer (NK) cells and CD8+ T cells, inducing the activation, proliferation, cytolytic activity and the production of cytokines such as interferon-γ (IFN-γ). IL-15 has no significant effects on regulatory T cells (Tregs), but plays an important role in supporting the long-term maintenance and high-affinity response of T cells to malignant cells by acting as a survival factor for memory CD8+ T cells.<br>In addition, IL-15 has pro-inflammatory potential. It is implicated in the pathogenesis of several autoimmune diseases, such as rheumatoid arthritis, psoriasis, and pulmonary inflammatory diseases. IL-15 is normally not secreted. However, viral infection can cause its secretion. |
| **Approved Name** | Interleukin 15 |
| **Official Symbol** | IL15 |
| **Gene Type** | Protein coding |
| **Synonyms** | IL-15; MGC9721 |
| **Ensembl** | ENSG00000164136 |
| **Gene ID** | 3600 |
| **mRNA Refseq** | NM_000585; NM_172175 |
| **Protein Refseq** | NP_000576; NP_751915 |
| **OMIM** | 600554 |
| **UniProt ID** | P40933 |
| **Chromosome Location** | 4q31.21 |

# Drug Modality

## Fusion Protein

BioLink001 is an IL-15 fusion protein developed with global intellectual property rights. It is composed of an integrin-binding arginylglycylaspartic acid (RGD)-4C motif, linked with a human IgG1 Fc, and a modified sushi domain of human IL-15Rα unit and a human IL-15. The RGD-4C motif of BioLink001 binds the αvβ3, αvβ5, and αvβ6 integrins, which are commonly overexpressed in solid tumors, leading to the tumor-targeting.

# Indication

## Solid Tumors

Solid tumors are abnormal masses of tissue that usually do not contain cysts or areas of fluid. Solid tumors may be benign or malignant. Different types of solid tumors are named for the cell type that forms them, such as sarcomas, carcinomas, and lymphomas. Solid tumors account for approximately 90% of cancers in adults and make up about 30% of all cancers in children. There were an estimated 18.1 million cancer cases worldwide in 2020. The most common cancers are breast, lung, colon, rectum, and prostate cancers. The most common type of solid tumor found in children is the brain tumor.
Cancer treatment usually includes surgery, radiotherapy, chemotherapy, hormonal treatments, and targeted biological therapies. Cancer treatment decisions should take into account the stage and biology of the tumor, risk and prognosis of planned therapy, and the economic costs associated with therapy. The global solid tumor cancer treatment market was estimated at $121.3 billion in 2018 and is projected to reach $424.6 billion by 2027, increasing to CAGR by 15.0% from 2019 to 2027.

# Mechanism of Action

## Interleukin 15 Replacements

IL-15 is essential in the growth, mobilization, and activation of immune cells such as NK cells, CD8+ T cells, γδ T cells and natural killer T (NKT) cells. IL-15 can also enhance the anti-tumor activity of immune cells, acts as a survival factor for CD8 memory T cells, and contributes to the long-term maintenance of high affinity T cell response to malignant cells. IL-15 is a promising immunotherapy agent due to its potent immune actions. BioLink001 is a tumor-targeting IL-15 fusion protein that is composed of an RGD-4C motif, a human IgG1 Fc, and a modified sushi domain of human IL-15Rα unit and a human IL-15. BioLink001 targets cancer cells that overexpress integrins such as αvβ3, αvβ5, and αvβ6 by the integrin-binding RGD-4C motif and stimulates anti-cancer immunity by its IL-15 motif. This design could enhance anticancer effects and reduce systemic toxicity

of BioLink001 by localizing the role of IL-15 in the tumor microenvironment.

## Status

### The Status of BioLink001

In the ongoing phase 1 clinical trial in adult patients with solid tumors, BioLink001 as a single agent or in combination with anti-PD-1/PD-L1 antibodies has demonstrated tolerable safety profiles, favorable PK/PD profiles, and encouraging preliminary efficacy results.