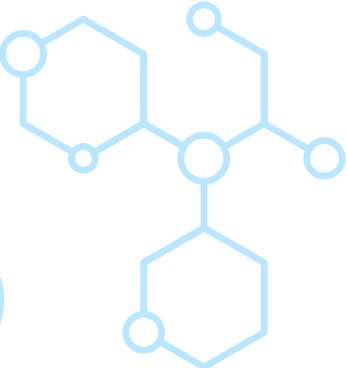
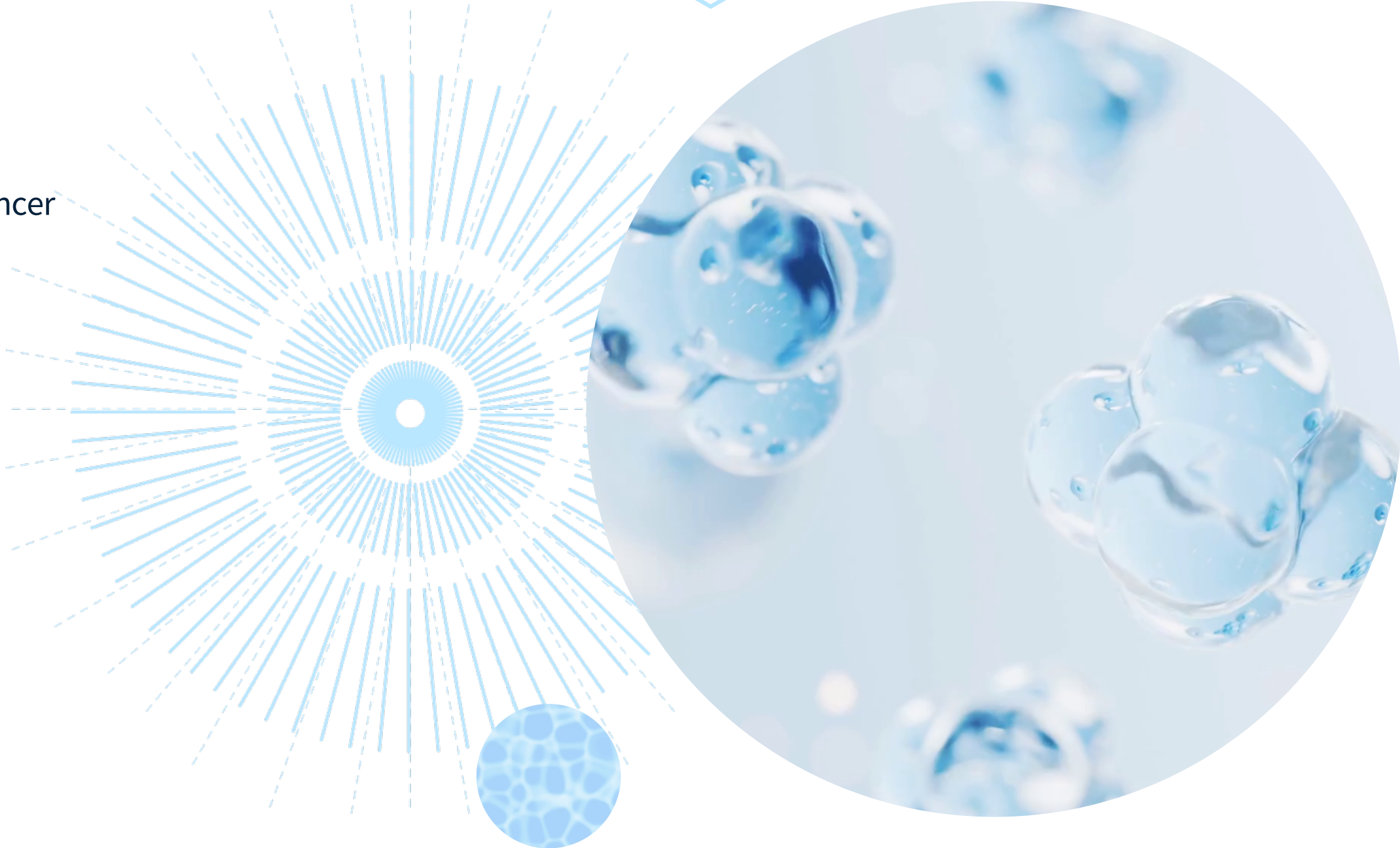


# In Vitro Abscopal Method

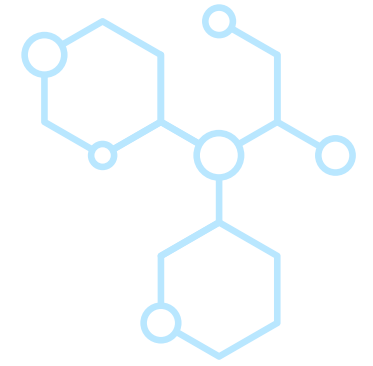
A novel tumor vaccine based treatment method for cancer



\*Patent pending

# Introducing The In Vitro Absopal Method (IVAM)

The In Vitro Absopal Method (IVAM) is a tumor cell vaccine-based cancer treatment that aims to induce immunogenic cell deaths (ICDs) by treating cancer tissue in vitro with radiation.



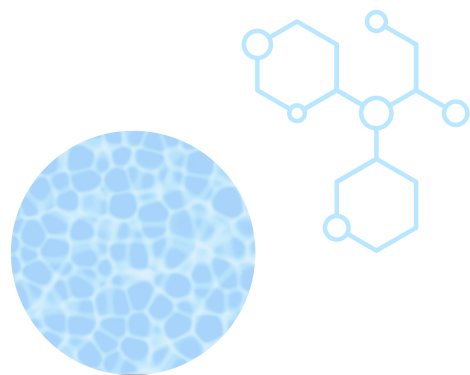
The IVAM is inspired by the "abscopal effect", which occurs when radiation therapy or other local cancer therapy not only impacts the targeted tumor but also shrinks other untreated tumors in the body.

IVAM can revolutionize cancer treatment by introducing a novel in vitro treatment method, that not only treats the primary tumor but distant metastases as well, also helping to prevent reoccurrence.

# Background

## The Abscopal Effect

The "abscopal effect" occurs when radiation therapy, or other local cancer therapy not only impact the targeted tumor but also, shrinks other untreated tumors in the body.



Recently, studies have shown that the administration of a vaccine (Flt3L) that inhibits TLR9 in early lymphoma and radiation therapy for certain areas of cancer showed a reduction in untreated remote areas. In addition, when the granulocyte macrophage-colony stimulating factor (GM-CSF) is administered with radiation therapy in patients with metastatic lung cancer, cancer in areas without radiation therapy may also show a reduced response.

.....

MHC, which is antigen presentation on cancer cells, causes CD8+ cytotoxic T lymphocytes to secrete interferon gamma, which promotes the creation of PD-1 ligand in tumor cells. This PD-1 ligand combines with the PD-1 of the T cell and worsens the activity of the T cell. Therefore, anti-PD-1 anti-body or basic T cell recruiting anti-ibodies (CD 133 × CD3 Ab) that can suppress this can be used in cancer treatment.

.....

Immune checkpoint inhibitors have been known to be effective in treating cancer through several research reports. Clinically, ipilimumab, which acts as an immune checkpoint inhibitor of cytotoxic T-Lymphocyte associated antigen-4 (CTLA-4), and nivolumab, which acts on programmed death-1 (PD-1), have been found to have increased survival rates in advanced melanoma patients. Pembrolizumab, also known as anti PD-1 Ab, was also effective in gastric cancer, nasopharyngeal cancer, and lung cancer.

# Problem

The abscopal effect remains uncommon its future possibilities remaining untapped and no way to effectively maximize the abscopal effect has yet been proposed.

The main reason the human body is unable to fight cancer is that it cannot recognize it. This is because cancer cells consist of the patient's own DNA, which the body's immune system recognizes as natural.

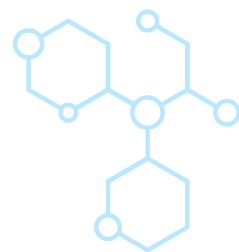
No large clinical trial has yet provided evidence to establish how radiation or other treatments should be delivered, and in what dosage, to elicit the abscopal effect with more efficacy.

The effectiveness of immunotherapy has been found to be limited to 10-30% with monotherapy.

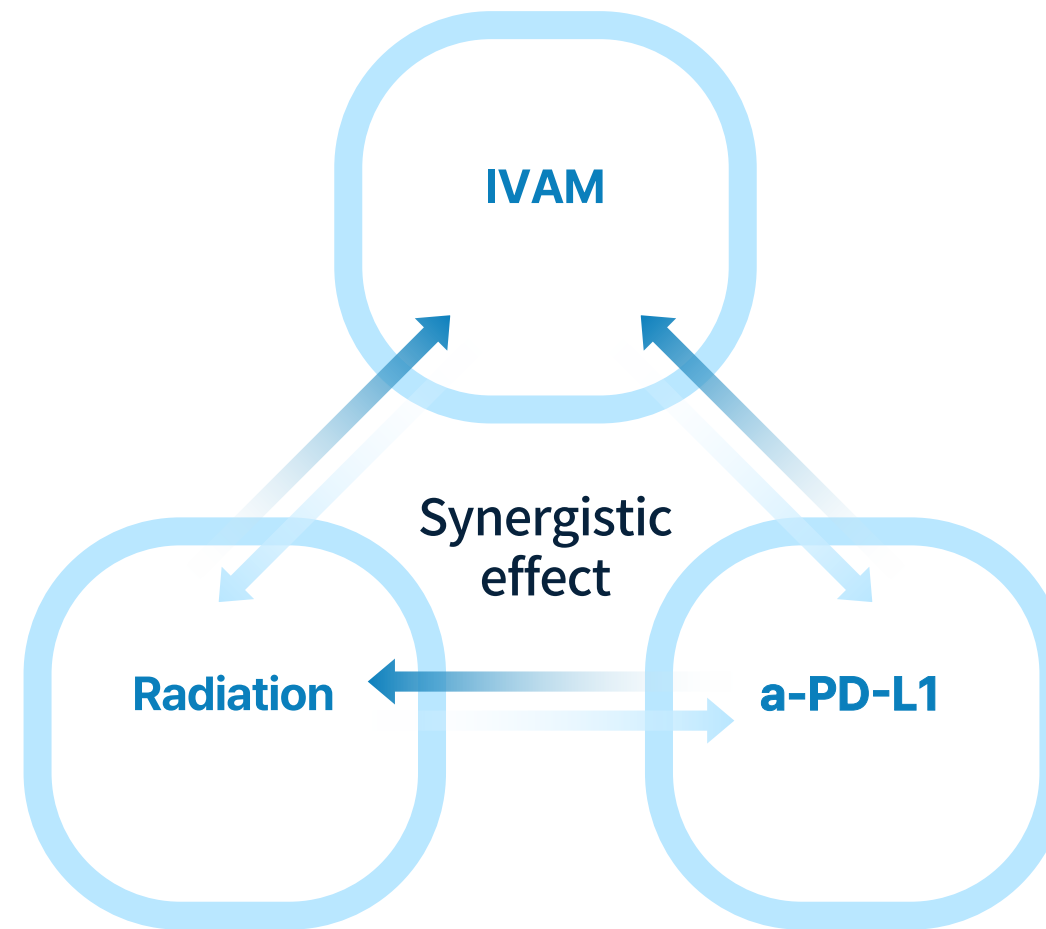
Cancer treatments such as radiation therapy cause damage, necrosis, or mutations to normal tissue causing patients to suffer and limiting treatment doses to minimize damage to healthy tissue.

# In Vitro Radiation Treatment

Our preclinical trials showed that cancer cells in which activity inhibition or death was induced through irradiation can magnify the abscopal effect when readministered.



The effectiveness of the proposed treatment method was given initial evidence using breast cancer animal models with low immunogenicity and immuno-suppressive tumor microenvironments.



The findings showed that when cancer cells in which attenuation or apoptosis is induced through in vitro irradiation are used together with radiation therapy and/or immunotherapy, the anticancer effect is maximized, anti-cancer immunity is enhanced, and a stronger abscopal effect can be achieved.

# IVAM Venture Team

Our managing team at EdgeX is working together with SNU Oncology department's team of doctors and researchers on the IVAM venture.



## EDGEX Co., Ltd

EdgeX is a privately owned startup company, located in Seoul South Korea, driving to overcome existing challenges and improve the lives of patients across the world.



M.D, Ph.D  
In Ah Kim

## SEOUL NATION UNIVERSITY BUNDANG HOSPITAL

Seoul National University and its Bundang Hospital and Healthcare Innovation Park, hospital-led convergence research complex, lead innovation in the healthcare industry in Korea and globally.



SEOUL NATIONAL UNIVERSITY  
BUNDANG HOSPITAL

# Pre-clinical trials

Two consecutive experiments were conducted to demonstrate whether the administration of irradiated tumor cells could activate anti-tumor immunity and induce the abscopal effect in breast cancer tumor animal models with low immunogenicity and immunoactive tumor microenvironment

The experiments were conducted by injecting 4T1 murine triple-negative breast cancer cells into the back legs and sides of immune-component mice.

The treatment groups, comprised of: only radiation treatment to the primary tumor (RT), a-PD-L1 immune checkpoint inhibitors only, IVAM only, and double and triple combination groups.

For the IVAM treatment, a second strand of tumor cells was irradiated in vitro. The treated cell suspension was injected subcutaneously after confirming the sensitization effect by the radiation.

Tumor volumes of the primary and secondary tumors of the mice pre and post-treatment and the ratio of mice spared from tumor formation were recorded.

\*All animal experiments were conducted in compliance with the animal ethics rules in accordance with the IACUC Animal Experiment Plan at Seoul National University Bundang Hospital.

## Primary findings

01

IVAM treatment alone significantly delayed the growth of the primary tumor, however, when RT and IVAM were used together, the synergic effect of delaying tumor growth was more substantial.

02

The growth of the secondary tumor that was not irradiated, was significantly inhibited by the combination of RT and IVAM, confirming the abscopal effect.

03

The tumor growth in the triple combination (IVAM + a-PD-L1 + radiation) group was significantly delayed in the primary tumor irradiated with radiation.

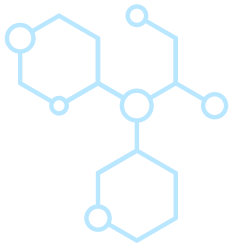
04

There was a significant delay in tumor growth in the triple combination group, showing an abscopal effect

05

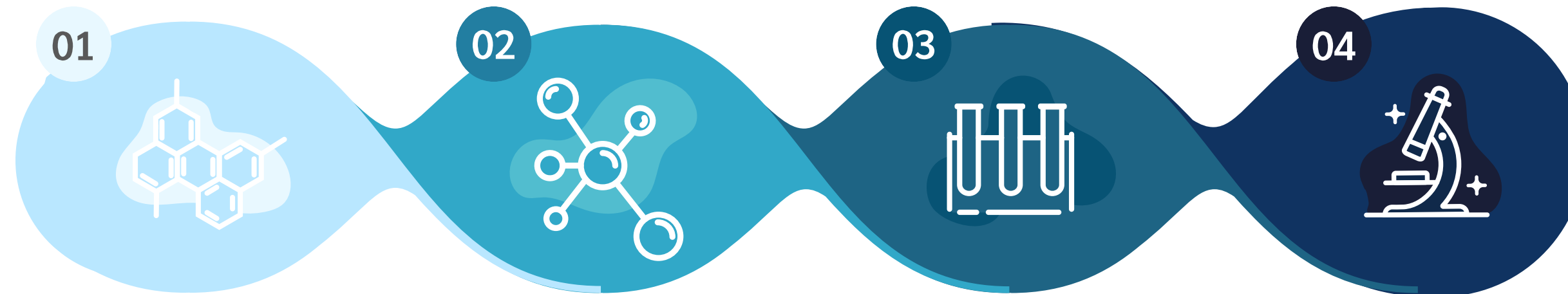
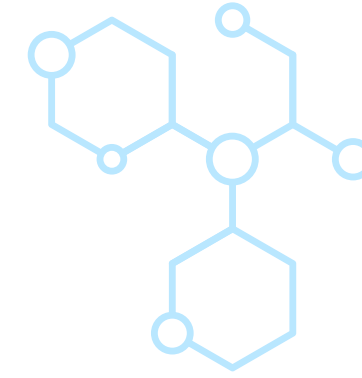
it was confirmed that even if only two or more of the three therapies of IVAM, RT, and a-PD-L1 were used together, the effect of inhibiting metastasis was increased, and in particular, if all of the above therapies were used together, synergistic metastasis inhibition effect appeared.

The delay in tumor growth could be explained by the anti-tumor immune effect of increased CD8+ T cells, CD8+ effector memory T cells, and lower Treg in the tumor microenvironment, which was most evident in the triple combination group. When measuring IFN- $\beta$  and IFN- $\gamma$  levels in Serum, it was observed that the level of IFN- $\gamma$ , which is important for anti-tumor immunity effects, increased significantly in the triple combination group which can be seen as an important clue to explaining the abscopal effect.



# Subsequent research plan

Following the promising initial data we have gathered we plan to proceed to conduct further research.



## 01 REPLICATION WITH HUMANIZED MICE

Repeats the previous experiments with humanized mice to validate the results. To be conducted with the Department of Radiation Oncology at Seoul National University.

## 02 IN VITRO THERMAL TREATMENT

To investigate whether similar results can be observed with thermal in vitro treatment methods.

## 03 COMBINATION WITH CHEMOTHERAPY

To introduce chemotherapy as additional combination treatment method with IVAM and to record the observed abscopal effects.

## 04 CLINICAL TRIALS

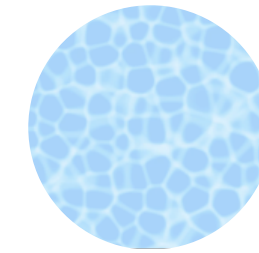
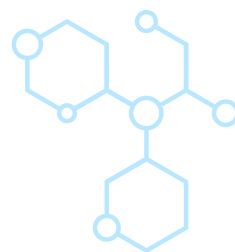
To observe the effectiveness of IVAM combination treatment and provide a personalised cancer treatment for patients.



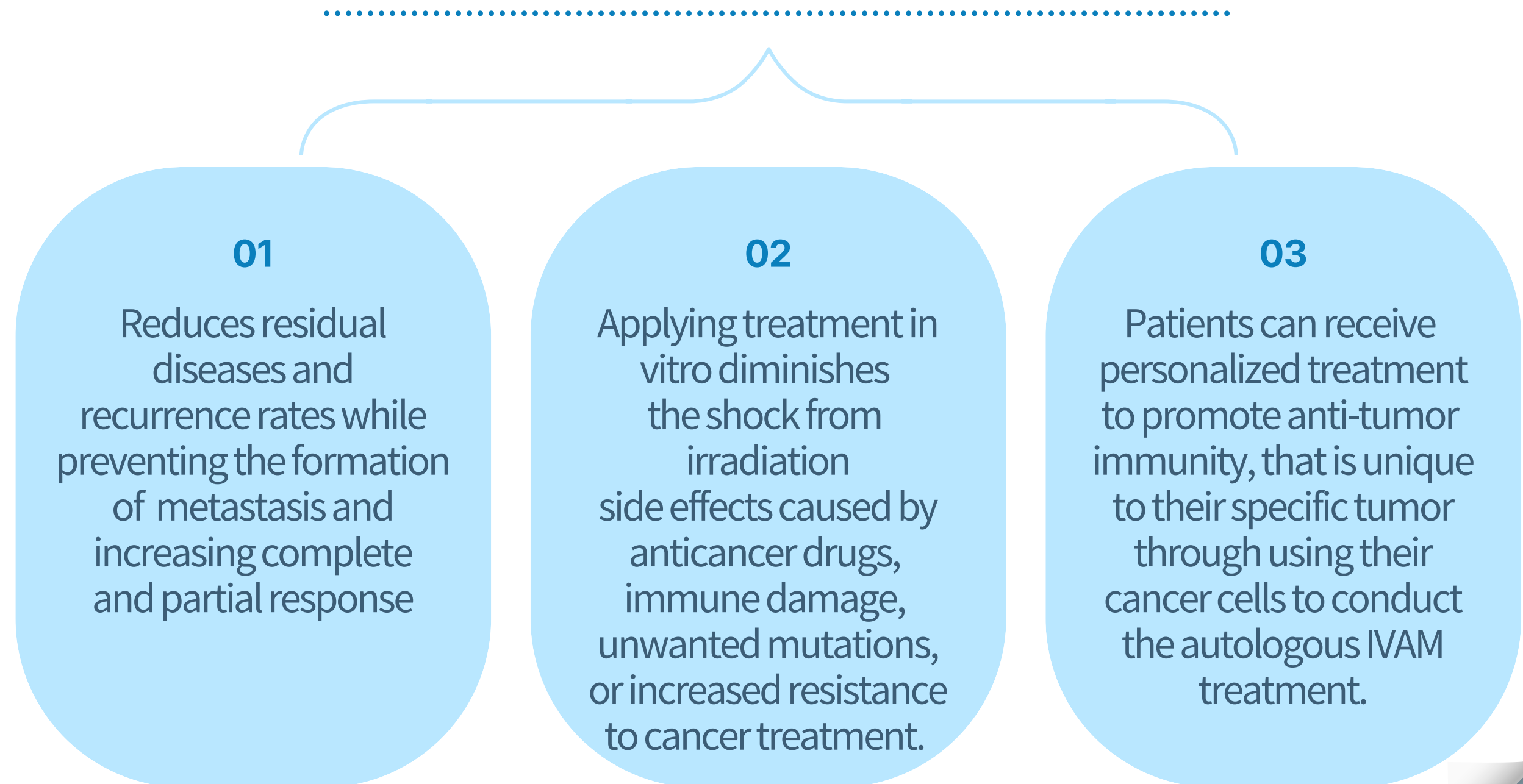


# Benefits

IVAM, used together with radiation therapy and/or immuno-cancer drugs, can not only more effectively suppress the growth of primary tumors but can also suppress the growth of secondary tumors through the abscopal effect, suppressing cancer metastasis.



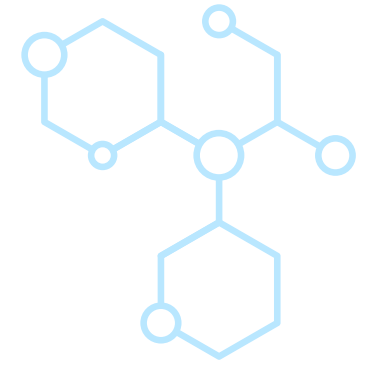
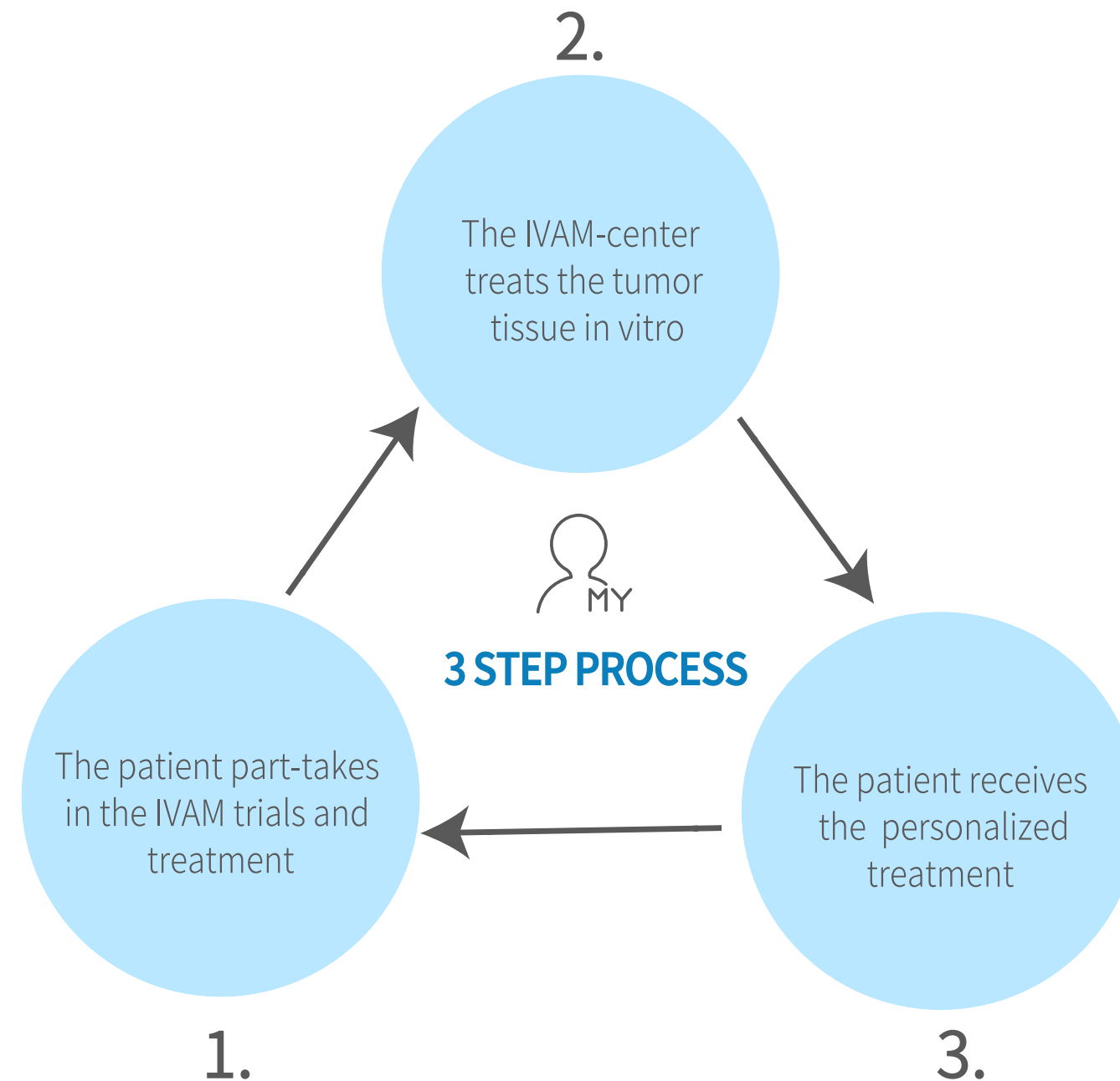
## What IVAM can help accomplish?



# Patient Impact

What if the tumor cells used to diagnose your cancer could also hold the cure for it?

1. The oncologist recommends the IVAM to the patient to receive personalized treatment after performing a tumor biopsy. With the patient's consent, the hospital does not dispose of the remaining biopsy but sends a tissue sample to the IVAM research center.
2. A combination of treatment methods is utilized to formulate the autologous therapeutic agent in vitro, based on existing knowledge to optimize the immunological effects of the treatment.
3. The patient receives their personalized treatment at their home hospital, while the IVAM center follows on its success storing the data for future research.

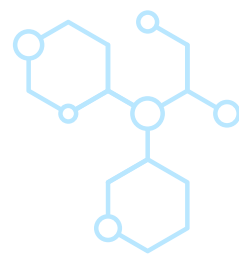


The research and clinical trials can be made accessible for patients while enabling large-scale information sharing and advances in cancer treatment.

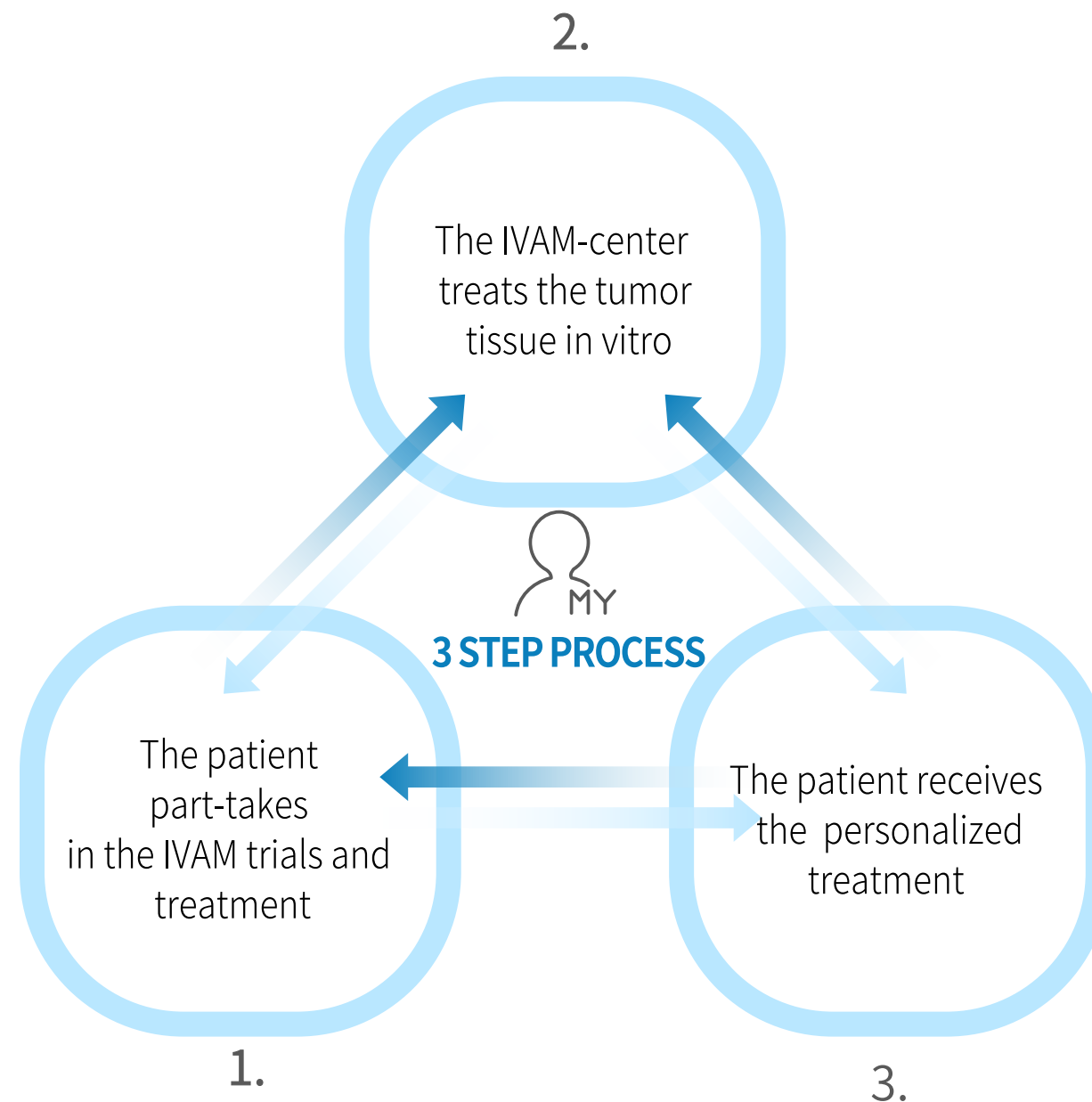
A public-private partnership of cancer research institutes, public hospitals, private hospitals, and pharmaceutical companies.

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The clinical trials can be made accessible for patients while enabling large-scale information sharing and advances in cancer treatment.

# Proposal for clinical trials

The IVAM center will store the tumor sample from patients enrolled in the trials, for the further development of in vitro therapies, offering value not only to the patients receiving personalized treatment, but also for the institutions and companies looking to research, develop and launch new cancer treatment therapies, with access to tumor sample data, and more cost-efficient, speedy clinical trials.

## Onchology Department



A biopsy is conducted to diagnose malignant tumors or for other purposes.

Afterwards, with the patients consent the tumor sample is sent to the IVAM center for treatment.

## IVAM center

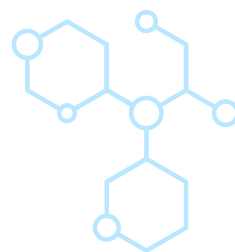


The IVAM center formulates an autologous treatment agent for the patient.

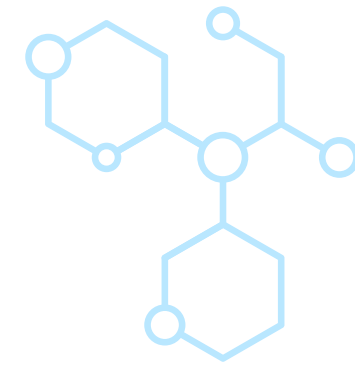
## Cancer patient



Does not require additional tumor samples or damaging treatments



# THANK YOU



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