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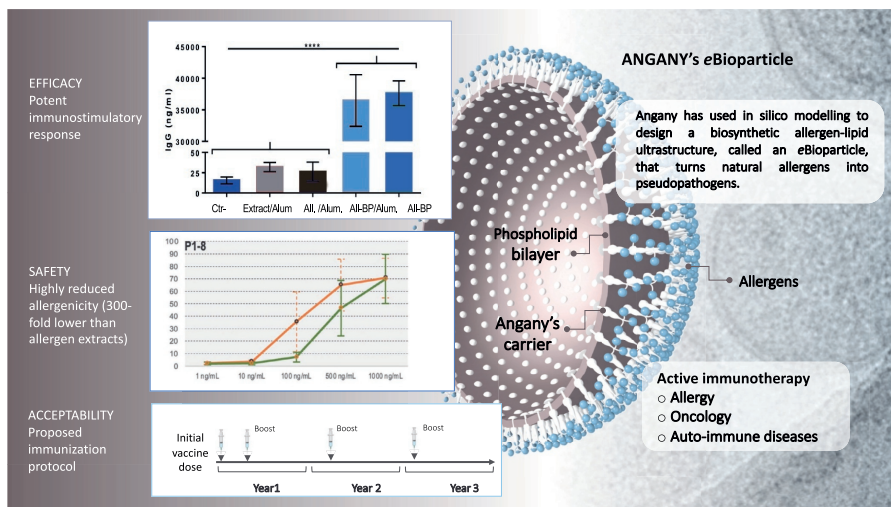
# Angany: a new generation of allergen immunotherapy

Targeting allergies and beyond, biotechnology company Angany is combining immunotherapy and anti-viral approaches for the development of innovative eBioparticles designed to increase immunogenicity and decrease allergenicity.

Allergy is at pandemic levels: currently ranked as the fourth global health threat by the World Health Organization, one in three individuals born after 1990 is allergic, at considerable cost to both patients and healthcare systems; prescription medications for just respiratory allergy amount to \$14 billion per year in the USA alone. Without new disease-modifying treatment approaches, 50% of the world's population will suffer from allergy by 2050.

Unfortunately, the three approaches currently used to manage or treat allergy are all suboptimal in different ways. The first, allergen avoidance by patients, is difficult to achieve effectively, and it is a permanent impediment. Failure of avoidance can be life-threatening, especially for food-allergic patients or those with severe asthma. The second option is to treat symptoms with short-acting meds, but these need to be taken lifelong, which can lead to poor compliance on the one hand and undesired side-effects on the other. Symptom medication neither alters the tendency of allergies to develop into poly-allergies nor inhibits the increased severity of disease phenotype—such as from hay fever to asthma. The third option is desensitization or allergen immunotherapy (AIT). This involves exposing patients to the offending allergen, starting at very low doses for safety reasons, and gradually increasing them until a tolerated maintenance dose is reached. Although AIT is the only disease-modifying treatment for allergy, in its current versions it comes with some major disadvantages. Allergic side-effects are common and can be life-threatening. For subcutaneous administration, aluminum salts are often used as an adjuvant. Furthermore, the treatment by monthly injections or daily sublingual tablets or drops has to be adhered to for 3–5 years to achieve sustained efficacy. This has been demonstrated for both subcutaneous and sublingual AIT for respiratory allergies; however, it has proven to be very difficult for oral AIT for food allergy.

Poised to overcome these drawbacks and offer patients a fourth treatment option is Angany, a private biotech company headquartered in Quebec City, Canada. Angany has combined recent findings and concepts of cancer immunotherapy and anti-viral vaccination with advances in metagenomics, in silico modelling, and protein engineering to design and develop a biosynthetic allergen-lipid ultrastructure, called an eBioparticle, which effectively turns natural allergens into pseudopathogens. These eBioparticles enable a fundamentally and drastically different approach to AIT and the treatment of other conditions.



**Fig. 1 | Structure and promising results of Angany's eBioparticle.** Panel 1 (efficacy): allergen-specific IgG response in mice immunized with either natural allergen, or with allergen exposed on eBioparticles. Panel 2 (safety): histamine release from sensitized basophil cells following exposure to either natural allergen or allergen exposed on eBioparticles. Panel 3 (patient acceptability): the short immunization protocol proposed by Angany for its eBioparticle-potentiated vaccines. All., allergen; Alum., aluminum hydroxide; BP, eBioparticle; Ctr, negative control; IgG, Immunoglobulin G.

## Angany's new allergen eBioparticles

The immune system in people with allergy is misguided: harmless allergens are mistakenly perceived as toxins—their reactivity far exceeds their immunogenicity—and exposure induces a problematic immunoglobulin E (IgE)-mediated response. “However, the immune system, if given appropriate signals, can be modulated towards providing an appropriate, efficacious, and lasting disease-modifying immunoglobulin G (IgG)-mediated response,” explained Angany's CEO Louis-Philippe Vézina. “eBioparticles are specifically designed to provide those signals.”

eBioparticles mimic viral pathogens in shape (spherical), dimension (~140 nm), and surface motifs. Although they resemble a virus, they do not contain infectious genetic material or viral immunogenic components; their complex molecular scaffold comprises a lipid-membrane envelope from which membrane-bound target allergen polymers (more than 1,000 copies) protrude.

Because dendritic and other antigen-presenting cells of the immune system recognize the three-dimensional (3D) structural patterns of a virus, attaching a small target antigen (like an allergen) to the surface of this highly organized structure causes them to initiate a strong anti-pathogenic

immune response. Consequently, antigen-laden eBioparticles trigger a strong and lasting allergen-specific IgG-based immune response, typical of the protective response mounted against a pathogen. As in cancer immunotherapy, this approach provides an efficacious and lasting disease-modifying response. But while the objective in cancer is to provide a T cell response against elusive tumor cells, the goal in allergy is to recognize and neutralize minute amounts of incoming allergens, and confer lasting protection.

“The 3D structure and membrane composition of eBioparticles strongly stimulate innate immune mechanisms without the need for adjuvants,” said Vézina, formerly the founder and CSO of Medicago Inc. Published research shows that a strong IgG-mediated immune response could be both neutralizing against incoming allergens and inhibitory to the programmed IgE-mediated activation of basophil cells involved in allergic reactions<sup>1</sup>. This suggests that Angany's allergen eBioparticle-potentiated immunization could suppress hypersensitivity responses in susceptible individuals.

Indeed, extensive preclinical studies performed by Angany show that exposing human dendritic cells to eBioparticles (comprising cat or dust-mite allergens) potentially increases immunogenicity while

significantly decreasing allergenicity compared to their natural counterparts. When presented with eBioparticles through vaccination (in animal models), the immune system reacts strongly and protectively, as if attacked by a pathogen, immediately releasing specific IgG antibodies that neutralize the allergens (Fig. 1).

“eBioparticles have the potential to establish a cell-based immune memory that will remain alert and ready to fight against any subsequent exposure to the offending allergen. They are 1,000 times more immunogenic but 150 times less allergenic than natural allergens, and the only immune response they will trigger is directed against the exposed allergen,” said Vézina. “This is a first-in-class allergen-bearing immunomodulatory vector that is a safe and highly immunogenic vaccinal ingredient.”

### Disease-modifying vaccines

Angany has developed candidate therapeutic vaccines consisting of a colloidal suspension of allergen-laden eBioparticles (API) for administration through a short prime-boost protocol and an annual maintenance injection. eBioparticles are stable in simple sterile saline formulations.

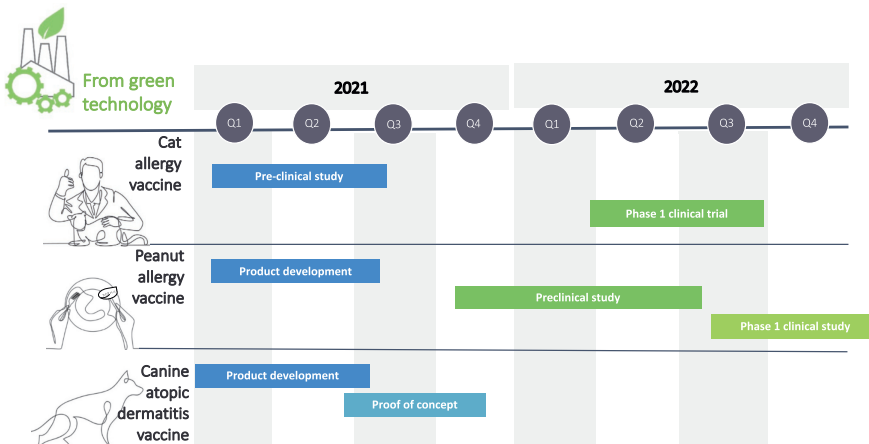
Animal studies have shown that immunization with vaccinal doses of allergen-laden eBioparticles can be performed safely in susceptible or sensitized subjects, and that the plateau of detectable IgG-mediated responses is reached after a simple prime-boost injection regimen and without adjuvants.

### Bio-manufacturing

If Angany's products are to make a difference to patients, they need to be reasonable in terms of both protocols and affordability. The company has tackled this challenge from different angles: its therapeutic approach is based on a single safe injectable biologic API, and it uses vaccinal dosages (in the micromolar range) and a short vaccinal protocol (two injections and an annual maintenance injection). In addition, Angany has opted for a bio-manufacturing system that is high yielding, easily scalable, fully current good manufacturing practice (cGMP) compliant and with remarkably low capital expense (CAPEX) and operational expense (OPEX). “Our products are true biologics, but in contrast to other modern efficacious immunotherapeutic products, ours benefit from both minimal clinical interventions and optimized cost of goods sold (COGS) for the API,” said Vézina.

### Product pipeline

Angany is initially developing therapeutic vaccines for first-line treatment of allergic rhinitis and asthma and for food allergy, administered through an initial prime-boost regimen, intradermally, with yearly or biannual maintenance vaccinations. The first candidate, for cat allergy, is scheduled to start first-in-human clinical trials at Imperial College London within the next 6 months. Angany's pipeline also includes a peanut allergy therapeutic, which is starting preclinical assessment at Massachusetts General Hospital (Fig. 2). “Our vaccines are simple, effective, safe and convenient treatments that have fewer complications than other allergy therapeutics, and our lead products target large unserved markets,” said Guy Tropper, VP of Medical and Corporate Affairs.



**Fig. 2 | Angany's innovative development product pipeline.** Timelines and milestones of the pre-clinical and clinical development of Angany's three allergy vaccine candidates. Q, fiscal quarter.

“As this new generation of allergy therapeutics is based on short vaccinal protocols, we expect their clinical development to be of far shorter duration than that of desensitization products.”

Allergy sensitization typically occurs at a very early age, and it has been suggested that vaccines could potentially be curative if used in early childhood. Successful pediatric treatment with eBioparticle vaccines would require the ability to diagnose specific allergies with a high level of accuracy, and simpler less-invasive alternatives to intradermal administration. To this end, the company has developed a portfolio of pure recombinant natural-like allergens for precocious non-biased allergen-specific diagnostics, and is initiating the development of formulations and administration protocols for oral immunization.

### Beyond allergy: eBioparticle-potentiated immunotherapy

Although its first applications are in allergy, Angany's immunotherapeutic eBioparticles can also be applied with great efficacy to other health conditions that require restoring adequate immune responses. “Our immunotherapy vectors possess the rare ability to turn elusive targets—such as cancer cell-surface markers, cytokines, or self-proteins—into strong immunogens, without adjuvants,” points out Véronique Gomord, Angany's CSO. “Because we have the potential to turn non-immunogenic components into strong immunogens, we are in a position to leverage the full potential of immunotherapy, including prophylactic applications.”

Indeed, the company is also involved in developing a complementary multi-product approach for the treatment of canine atopic dermatitis (CAD). As part of this, it has designed and produced an eBioparticle covered with a self-protein involved in the onset of itching in many pathologies. Angany will be using this eBioparticle as a vaccine in the treatment of CAD.

Angany has also developed, produced, and purified proprietary single-chain variable fragment (ScFv)-Fc monoclonal antibodies (mAbs) that are produced through the same basic bio-manufacturing approaches as eBioparticles. These antibodies have shown remarkable neutralizing potential towards difficult targets and are being developed as therapeutics for

specific conditions—undisclosed at this stage—that require a complementary approach to therapeutic vaccination.

### Partnering

Angany's team is strong in vaccinology, immunology, protein engineering, clinical allergology, and bio-manufacturing. Accordingly, Angany is developing as a fully integrated company for its allergy products, with the intent of commercializing its final finished or bulk products through collaboration with existing players in the industry.

Angany is also opening up to collaborative development for its eBioparticle vaccines and therapeutic mAb-based therapeutics outside of allergy. This dual approach to business development is already proving fruitful, with Angany on the verge of signing an agreement with a major player in the veterinary sector for the clinical and commercial development of its first CAD vaccine candidates. The company is seeking similar partnerships with strategic players for the development of therapeutic vaccinal applications in cancer immunotherapy and autoimmune diseases.

“We are disrupting the content, form, and potential outcome of allergy immunotherapy. Our new generation of eBioparticle-potentiated candidate vaccines are delivered through an effective, safe, and convenient schedule, offering a new disease-modifying treatment alternative for patients,” said Vézina. “We hope that this unique approach to reversing and protecting against allergy will help put an end to the ever-increasing incidence of this condition in our modern world and provide hope to those suffering from this debilitating and often life-threatening condition.”

1. Bachmann, M. F. et al. *Trends Mol. Med.* **26**, 357-368 (2020). <https://doi.org/10.1016/j.molmed.2020.01.007>

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