The Robert and Renée Belfer Center for Applied Cancer Science builds off of Dana-Farber Cancer Institute’s tradition of excellence in research and patient care by partnering with Institute and industry investigators to accelerate cancer drug discovery and development.

Under the scientific direction of Pasi Jänne, MD, PhD, and David Barbie, MD, the Belfer Center’s unique technologies and resources help academic and industry partners achieve preclinical success in developing and bringing to market novel therapeutics for cancer.

The Belfer Center works closely with the Belfer Office for Dana-Farber Innovations (BODFI) to facilitate the transfer of research discoveries from the laboratory to the clinic through timely commercialization. As just one example of the progress fueled, in part, by your philanthropy, XSphera Biosciences—a company co-founded by Dr. Barbie and Cloud Paweletz, PhD, based on the “tumor-on-a-chip” technology they developed at the Belfer Center—is in final stages of negotiation with BODFI to license the patent portfolio the researchers developed for this technology, known as patient-derived organotypic spheroids, or PDOTS (see page 5).

This annual report provides an overview of the range of scientific advances made possible due to your philanthropy. Thank you for your vision and generosity in making this important work possible.
Strengthening Industry Ties with Strategic Alliances

The Belfer Center’s strategic alliances with pharmaceutical and biotechnology companies connect academic research to industry-led drug development efforts to shepherd the most effective cancer therapies through Food and Drug Administration (FDA) approval and to market. In the past year, a number of these partnerships have tested novel single-agent and combination approaches to treat a variety of cancers, including:

**Array BioPharma:** The Belfer Center is helping Array BioPharma position two of its FDA-approved melanoma drugs, binimetinib and encorafenib, for clinical trials in non-small cell lung cancer, the most common type of lung cancer. Based on the Belfer Center’s work, Array is preparing an Investigational New Drug filing with the FDA for a proprietary small-molecule drug that blocks the activity of a protein that causes other molecules in a cell to become either active or inactive.

**AstraZeneca:** AstraZeneca and the Belfer Center are identifying new combinations with osimertinib to address next-generation treatments for EGFR-mutant cancers, including the development of patient-derived xenograft models.

**Daiichi Sankyo:** Belfer Center investigators are collaborating with Daiichi Sankyo on two antibody-drug conjugates (ADCs), which marry monoclonal antibodies with chemotherapy agents, to treat cancer. Based on work performed at the Belfer Center, one of these ADCs is being tested in a phase I clinical trial at Dana-Farber for patients with EGFR-mutated metastatic lung cancer.

**Eli Lilly and Company:** Belfer Center scientists are conducting further studies on a novel Lilly drug used in combination with an existing approved drug to treat breast and gynecologic cancers. Prior research has shown that these drugs, one of which manipulates cellular DNA repair mechanisms, work better together at treating these cancers than either does as a single agent.

Patient-derived xenografts, or PDXs, are surgical grafts of human tissue onto laboratory mice. These models mimic the genetic complexity of human cancers and offer a platform in which to test new therapeutic agents.
Strengthening Industry Ties with Strategic Alliances

(Continued)

Fujifilm:
The Belfer Center has conducted studies of Fujifilm’s investigational drug FF-10850 to test its safety and feasibility before use in patients. This formulation has shown superior anti-tumor effects compared with other similar drugs. Ursula Matulonis, MD, is planning a clinical trial of the drug for patients with ovarian cancer.

FF-10850 encapsulates topotecan, a common chemotherapy agent, in a liposome, a tiny, fat-like particle made in the laboratory. This approach may be more effective than using the drug alone and may result in fewer side effects.

Janssen Biotech:
The Belfer Center and Janssen Biotech have signed an agreement to develop a bispecific antibody that expands the power of immunotherapy. Unlike existing antibody drugs, which work by attaching to a single target, bispecific antibodies bind to two molecules at once, bringing both targets together to more efficiently destroy cancer cells.

Surface Oncology:
Belfer Center scientists have generated preclinical data on a Surface Oncology immunotherapy compound that has shown promise in several Belfer Center ovarian cancer laboratory models. Follow-up and combination studies of the compound are now being planned.

Syros Pharmaceuticals:
The Belfer Center has completed preclinical studies and provided basic data for Syros Pharmaceuticals to evaluate a drug it is developing that targets a cancer-driving protein. The drug is being tested in a phase I clinical trial at Dana-Farber as a single agent or in combination with standard-of-care therapies for breast and ovarian cancer.
Collaborating with Dana-Farber Laboratories

The Belfer Center’s 2015 move to the Longwood Center put it in closer proximity to many of Dana-Farber’s basic science laboratories, including its renowned chemical biology program. Partnerships with these laboratories help to strengthen the ties between Dana-Farber scientists and industry partners. These collaborations include:

- Testing, with Oliver Jonas, PhD, and Elizabeth Stover, MD, PhD, whether an implantable microdevice, inserted into ovarian tumors in animal models, can identify effective drugs or drug combinations to treat ovarian cancer. Developed in Dr. Jonas’ laboratory, the microdevice—smaller than a grain of rice—contains several minuscule reservoirs, each filled with a different drug. The device is inserted into Belfer Center PDX ovarian cancer models. After the drugs are released into the tumor, the device is removed along with surrounding tissue, and each region of the tumor is examined for evidence of tumor cell responses to the drugs.

- Using the Belfer Center’s PDOT technology to study the effectiveness of the immunotherapy drugs nivolumab and ipilimumab to treat thyroid cancer. Based on this work, Jochen Lorch, MD, MS, found that, while one of these drugs is effective at halting tumor growth, the other may be even more so. These preliminary results suggest that combining the two drugs may be a better way to halt the growth of these tumors.

- Developing a novel test to evaluate tumor DNA in both blood and saliva samples in human papillomavirus (HPV)-associated oropharyngeal cancer. Based on the Belfer Center’s plasma genotyping technology, this test measures cell-free DNA—types of DNA fragments that are shed by tumors into the bloodstream—to evaluate cancer levels, treatment response, and predict relapse in patients with HPV-positive oropharyngeal cancer. The Belfer Center and Glenn Hanna, MD, of Dana-Farber’s Head and Neck Oncology Program, published their results in the August 2019 Oral Oncology.

Grown from tissue samples, PDOTS are three-dimensional spheres that contain tumor cells and surrounding immune cells. These models, grown in a microfluidic chip, have broad implications for testing combination treatments in an accurate, rapid way.
**Sharing Results with the Broader Community**

**Publishing findings in scientific journals** is a key way for researchers to validate their work and share new developments with the broader community. In the past year, Belfer Center scientists have published their work in several of the world’s leading journals.

- In a study published in the July 2019 *British Journal of Haematology*, a team of Dana-Farber investigators compared the efficacy of clinically available anti-leukemia drugs with FDA-approved midostaurin in acute myeloid leukemia (AML) cells. As part of this study, Prafulla Gokhale, PhD, Head of In Vivo Pharmacology at the Belfer Center, performed studies in mice and found that a certain class of these inhibitors works better in specific AML subsets, while another class is more effective in others.

- Stephen Wang, a Senior Research Associate in the Belfer Center’s In Vivo Pharmacology group, co-authored a study published the July 2019 *Cancer Discovery*, which found that combining the FDA-approved drug osimertinib with an investigational compound may be effective for patients with EGFR-mutant lung cancer. Both of these drugs target the mutation, which is commonly found in lung cancer. Dr. Jänne, who led the study, was instrumental in developing osimertinib, the first targeted therapy for EGFR, which changed the landscape of lung cancer care.

- Belfer Center scientists and gynecologic oncologist Panagiotis Konstantinopoulos, MD, PhD, showed in a phase I study that combining the PARP inhibitor olaparib with alpelisib, an investigational drug, outperforms olaparib alone in patients with chemotherapy-resistant ovarian cancer. Alpelisib inhibits a protein that drives tumor cell growth. Studies at the Belfer Center showed that inhibiting this protein sensitizes cancer cells to the effects of PARP inhibitors, which hamstring tumor cells’ ability to repair damage to their DNA. The findings were published in the April 2019 *The Lancet Oncology*.  

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Dr. Konstantinopoulos (above) has proven that combining the PARP inhibitor olaparib with the investigational drug alpelisib is beneficial to patients with chemotherapy-resistant ovarian cancer.

Dr. Barbie recently led a study that uncovered why a key regulator of the body’s immune response is inactive in lung cancers with mutations in the KRAS gene.
■ In the April 2019 Annals of Oncology, the Belfer Center and thoracic oncologist Geoffrey Oxnard, MD, reported on the development of a technology that helps to illuminate lung cancer-driving genetic mutations in a patient’s tumor. Using the plasma genotyping test pioneered by Dr. Paweletz, the researchers were able to gather and study tumor DNA floating in the bloodstream. Strikingly, pathology tests had failed to identify any mutations that could be targeted with drugs, but the blood test revealed common lung cancer mutations, as well as drug resistance mechanisms.

■ In the January 2019 Cancer Discovery, Belfer Center investigators, led by Dr. Barbie, uncovered why a key regulator of the body’s immune response is inactive in lung cancers with mutations in the KRAS gene. The study provides the first evidence that this molecule is actively suppressed following the loss of a specific gene that controls the growth of KRAS-driven lung cancer.

■ Patrick Lizotte, PhD, Group Leader of the Human Tumor Profiling platform, and his colleagues developed a screening test to identify novel immunomodulatory drugs and other agents that might boost the efficacy of a range of immunotherapies. Their initial screen suggests that inhibiting EGFR might sensitize malignant cells to tumor-killing T cells. The findings were published in the December 2018 Clinical Cancer Research.

■ With the widespread use of osimertinib to treat lung cancers with EGFR mutations, acquired resistance has become a significant clinical challenge. A team of researchers, including Drs. Jänne, Oxnard, and Paweletz, used the Belfer Center’s plasma genotyping technology to study EGFR driver mutations and resistance mechanisms to osimertinib. The study, published in the November 2018 JAMA Oncology, found that drug resistance in some patients can arise from a variety of mutations, limiting the effectiveness of targeted therapies. The findings suggest that early intervention with combination targeted therapies may prevent the development of drug resistance.
Presenting Scientific Findings

**Presenting at medical conferences** is another way Belfer Center investigators share their findings with the broader scientific community and the public. A number of Belfer Center scientists presented at two of the largest oncology conferences in the past year, the American Society of Clinical Oncology (ASCO) meeting in June 2019 and the annual meeting of the American Association for Cancer Research (AACR) in April 2019.

- In a presentation at ASCO, Dr. Lizotte reported that a combination of two drugs, durvalumab and tremelimumab, enabled the immune system to recognize and attack malignant pleural mesothelioma (MPM) cells. He is now analyzing biomarkers of response to these drugs in patients with MPM, a rare cancer that affects the lining of the lungs and chest wall.

- Also at ASCO, Drs. Jänne and Paweletz revealed the results of a phase I study that combined osimertinib and necitumumab, both of which block the activity of mutant EGFR, in non-small cell lung cancer. They showed that patients whose tumors harbored a common resistance mutation showed some response to the drug combination.

- Belfer Center researchers presented three posters at the 2019 AACR meeting in Atlanta. Senior Research Associate Andrew Portell detailed a specialized technique in PDOTS that isolates individual cells in a sample to determine each cell’s function. Senior Research Associate Julianna Supplee’s poster highlighted how plasma genotyping can be used to detect the presence of a gene fusion—a gene made from joining parts of two different genes—in non-small cell lung cancer that can be targeted with drugs. Drs. Jänne and Paweletz collaborated with members of the Head and Neck Oncology Program on a poster that described a method of diagnosing HPV-induced head and neck cancers using a patient’s saliva (see page 5).

- Drs. Jänne and Paweletz spoke at the IASLC (International Association for the Study of Lung Cancer) World Conference on Lung Cancer in Barcelona, Spain, in September 2019. Dr. Jänne addressed KRAS mutations in lung cancer, while Dr. Paweletz discussed leveraging cell-free DNA genotyping for lung cancer care.

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Dr. Paweletz was one of several Dana-Farber physician-scientists who presented at ASCO this past year.

Drs. Jänne and Paweletz both spoke at this year’s IASLC World Conference on Lung Cancer, which attracted more than 7,000 delegates from more than 100 countries.
In September 2018, Dr. Jänne received two prestigious awards that recognize his scientific accomplishments. He received the National Cancer Institute Outstanding Investigator Award for his distinguished record of productivity in cancer research. The award includes funding of up to $600,000 for seven years. The European Society for Medical Oncology (ESMO) chose Dr. Jänne to receive the ESMO Translational Research Award for his co-discovery of EGFR mutations, which changed the treatment paradigm of lung cancer and led to FDA approval of the EGFR inhibitor osimertinib in April 2018.

Awarding Research Excellence

Dr. Jänne (second from left) receiving the ESMO Translational Research Award at a ceremony in 2018.
The Power of Philanthropy

For nearly two decades, the Robert and Renée Belfer Center for Applied Cancer Science has made incredible progress in transforming basic and preclinical discoveries into newer, more effective treatments for patients. Your philanthropic support is vital to furthering the Belfer Center’s objectives, which pave the way for the next generation of cancer treatments, and for bringing these treatments to market through the Belfer Office for Dana-Farber Innovations. Thank you for your commitment to Dana-Farber’s lifesaving mission.
Dana-Farber Cancer Institute has been the top ranked cancer hospital in New England by U.S. News and World Report for 19 consecutive years, and is ranked in the top 5 nationally for both adult and pediatric cancer programs.