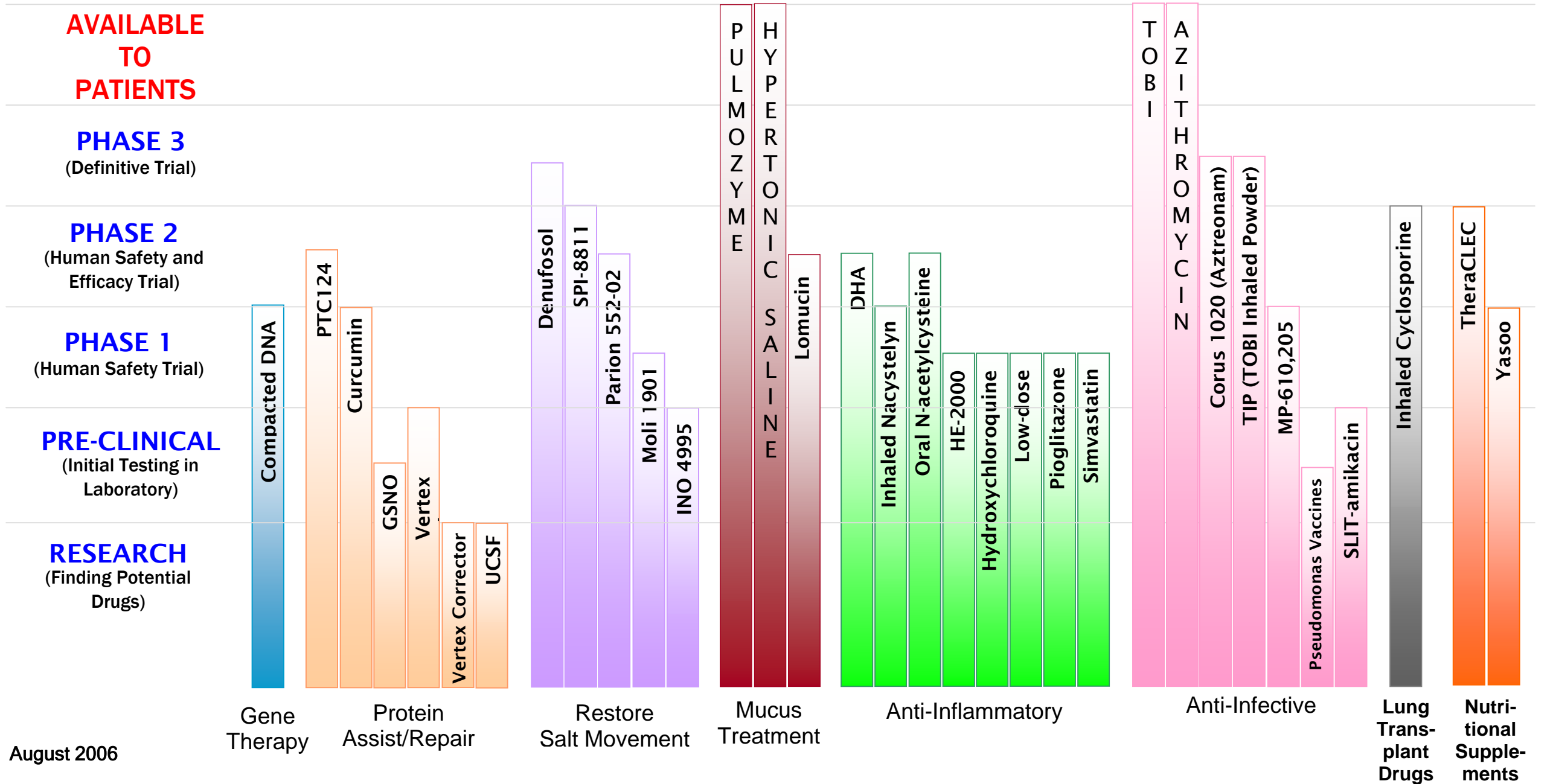


CYSTIC FIBROSIS FOUNDATION THERAPEUTICS PIPELINE



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GENE THERAPY

Because a faulty gene causes cystic fibrosis (CF), adding normal copies of the gene to cells should correct these cells and ultimately cure the disease.

- **Compacted DNA** (Copernicus Therapeutics, Inc.): An approach that delivers normal copies of the CF gene as tiny particles that can slip into CF cells.

PROTEIN ASSIST/REPAIR

This therapy is designed to correct the function of the defective CFTR protein made by the CF gene to allow chloride and sodium (salt) to move properly in cells lining the lungs and other organs.

- **PTC124**: (PTC Therapeutics, Inc.): PTC124 is designed to repair one type of CF gene mutation that causes the CFTR protein to stop being made in the cell before it is complete. These mutations are called “stop mutations” and about 6% of all people with CF have them.
- **Curcumin** (Seer Pharmaceuticals, LLC): An ingredient in curry spice, curcumin appears to have corrected the defective CFTR protein in mice with CF, but not yet in people. Studies in volunteers with CF are underway using higher doses.
- **GSNO Nitrox** (Nitrox LLC): A natural compound found in the airways, GSNO, helps to keep the airways open. In CF lungs, there is a reduced amount of this compound. Researchers are working on an inhaled form of GSNO to open airways and improve mucus clearance.
- **VX-770** (Vertex Pharmaceuticals, Inc.): This new compound is called a “potentiator” and it may help to open the defective chloride channel in CF cells by acting upon the CFTR protein.
- **Vertex Corrector & UCSF Corrector**: (no product names yet) These compounds, discovered through high-throughput screening, are being studied to see if they will help the defective CFTR move to its proper place in the cell where it should form a chloride channel.

RESTORE SALT MOVEMENT

The goal of this approach is to hydrate thick CF mucus in the lungs by correcting the amount of salt (sodium & chloride) along the cell surface.

- **Denufoso** (Inspire Pharmaceuticals, Inc.): This drug appears to activate a chloride channel other than the one associated with the CFTR protein. Denufoso was formerly called INS37217.
- **SPI-8811** (Sucampo Pharmaceuticals, Inc.): This drug also appears to correct the chloride channel transport problem in CF by activating a chloride channel other than that controlled by CFTR.
- **Parion 552-02** (Parion Sciences, Inc.): This inhaled drug decreases the over-absorption of sodium by CF cells, helping correct the salt imbalance in the airways.
- **Moli1901** (Lantibio, Inc.): Inhaled Moli1901 is designed to correct the chloride channel transport problem in CF cells.
- **INO 4995** (Inologic, Inc.): The drug appears to normalize the movement of both chloride and sodium across cells lining the airways. Correcting the salt balance in the airways will improve mucus clearance and help keep the lungs healthy.

MUCUS TREATMENT

The following studies are being evaluated for their effectiveness in thinning and clearing the thick mucus from the airways.

- **Pulmozyme** (Genentech): Pulmozyme was the first drug developed specifically for CF in 30 years and was approved by the FDA in 1993; it became available in 1994. It is used by thousands of people with CF worldwide.
- **Hypertonic Saline**: A CF Foundation-supported study in Australia showed hypertonic saline to be safe and effective in adults with CF, helping clear mucus and leading to better lung function. The drug is now being evaluated for safety and effectiveness in younger people with CF.
- **Lomucin** (Genarea Corp.): As an anti-inflammatory, Lomucin also may decrease the production of mucus and help clear the airways of people with CF.

ANTI-INFLAMMATORY

Anti-inflammatory drugs are being studied for their ability to reduce inflammation in CF lungs.

- **DHA**: People with CF appear to have lower than normal levels of DHA, a fatty acid that may be important to protecting the body against inflammation. A lack of DHA in people with CF may contribute to increased inflammation in the lungs. Researchers are evaluating a DHA-fortified infant formula to see if the increased DHA decreases lung disease in infants with CF.
- **Inhaled Nacystelyn** (Galephar Pharm. Research): The drug could thin both the thick mucus and fight inflammation in CF lungs.
- **Oral N-acetylcysteine** (BioAdvantex Pharma, Inc.): This drug may make mucus less sticky and easier to clear from the lungs, and could also replenish levels of glutathione, an antioxidant that is often low in the lungs of people with CF.
- **HE-2000** (Hollis-Eden Pharmaceuticals): A hormone that may help to regulate the immune system, which is in “overdrive” in CF lungs.
- **Hydroxychloroquine; Low-dose Methotrexate; & Pioglitazone**: These drugs, which are already approved to treat other diseases, are now being evaluated (individually) for their usefulness as anti-inflammatory treatments for CF.
- **Simvastatin** (Merck & Co., Inc.): Nitric oxide (NO), which fights bacteria and reduces inflammation in healthy lungs, is decreased in the lungs of people with CF. As a cholesterol-lowering drug, simvastatin (also known as Zocor) may increase NO levels in people with CF and improve lung function by decreasing inflammation and infection.

ANTI-INFECTIVE

The following drugs are being studied for their effectiveness in fighting lung infections for people with CF.

- **TOBI** (Novartis Pharmaceuticals): This aerosolized form of the antibiotic tobramycin is commonly used by older children and adults with CF. A Phase 4 study of TOBI is underway to help determine the most effective use of TOBI in very young children with CF.
- **Azithromycin** (Pfizer, Inc.): An extensive trial showed improved lung function and decreased hospital stays by people with CF who used azithromycin, which is an antibiotic and an anti-inflammatory. Two follow-up studies will help ensure the safety of long-term use and determine the most effective use of this drug.
- **Aztreonam Lysine for Inhalation** (Gilead Sciences): An aerosolized form of the intravenous antibiotic aztreonam is now being tested in people with Pseudomonas lung infections.
- **TIP** (TOBI Inhaled Powder) (Novartis Pharmaceuticals): A dry powder form of tobramycin is being tested to make inhaled tobramycin treatments faster and more convenient.
- **MP-610.205** (MPEX Pharmaceuticals, Inc.): An aerosolized drug that may help reverse or prevent antibiotic resistance of bacteria infecting CF lungs.
- **Pseudomonas Vaccines** (Berna Biotech): Vaccination against Pseudomonas bacteria may prevent or delay this infection in the lungs of people with CF. Vaccines are now being evaluated in Europe and studies in the United States are being planned.
- **SLIT-amikacin** (Transave, Inc.): This new inhaled formulation of the antibiotic amikacin contains lipids, or fatty particles, that help the drug attach and kill Pseudomonas bacteria better, thus reducing the amount of infection in the lungs of people with CF.

LUNG TRANSPLANT DRUGS

A lung transplant drug is currently being evaluated to help improve the chances of successful transplants.

- **Inhaled Cyclosporine** (Novartis Pharmaceuticals): This drug is used to suppress the immune system so that the body is less likely to reject “foreign” organs such as transplanted lungs. Researchers have made an inhaled version of the oral drug so that it can be delivered directly to the airways.

NUTRITIONAL SUPPLEMENTS

Nutritional supplements help improve the body’s ability to ward off the effects of CF.

- **TheraCLEC Total** (Altus Pharmaceuticals, Inc.): This novel pancreatic enzyme replacement is stable and highly concentrated, allowing people with CF to take fewer capsules with each meal.
- **Yasoo** (Yasoo Health, Inc.): This oral vitamin formulation is specifically designed to help provide the right balance of vitamins and antioxidants that are low in people with CF.