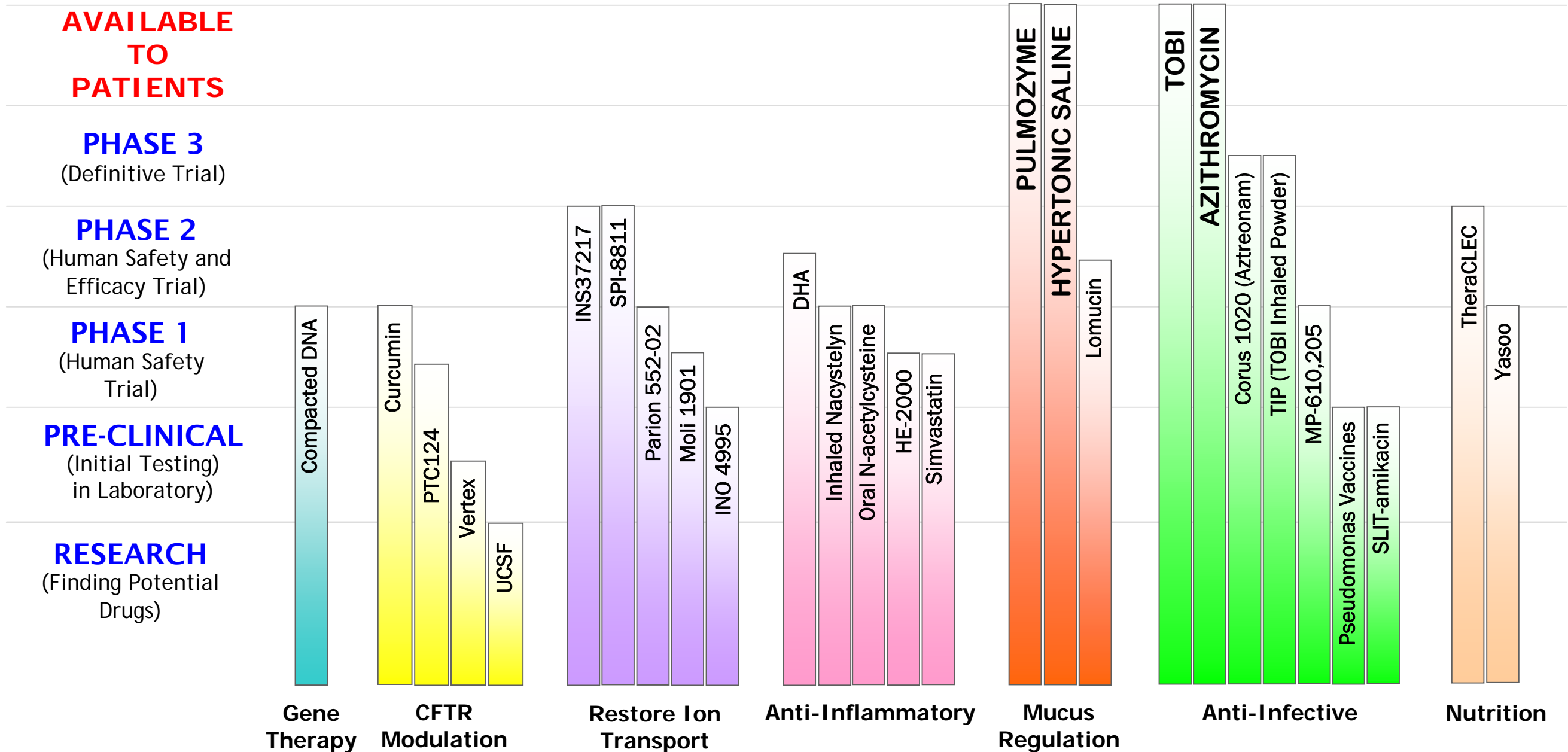


# CYSTIC FIBROSIS FOUNDATION THERAPEUTICS PIPELINE



## ACRONYM KEY

CFF: Cystic Fibrosis Foundation    CFFT: Cystic Fibrosis Foundation Therapeutics, Inc.    TDA: Therapeutics Development Award    CFTR: Cystic Fibrosis Transmembrane conductance Regulator    TDN: Therapeutics Development Network

### GENE THERAPY

- **Compacted DNA (PLASmin™)**: Copernicus Therapeutics, supported by a CFFT TDA and the TDN. Use compacted DNA (non-viral) to introduce normal copy of the gene into CF airways. Previous data suggested successful gene transfer. Planning a Phase 1b trial; number of patients to be recruited not determined.

### CFTR MODULATION

- **Curcumin**: Sponsored by Seer Pharmaceuticals and a CFFT TDA. Correct abnormal movement of CFTR in the cell. Two-site, Phase 1 safety trial planned for 2004 (one completed as of 9/04).
- **Vertex/UCSF**: CFFT-supported, high-throughput screening programs to identify correctors of the CFTR trafficking defect or potentiators of CFTR-mediated ion transport. The UCSF corrector and potentiator projects and the Vertex corrector projects are in the research phase, while the Vertex potentiator project is in the preclinical stage; a number of potential therapeutic compounds have been identified. It could be two years before any of these products are ready for clinical trials.
- **PTC124**: PTC Therapeutics - a novel, small molecule being, that promotes the read-through of premature truncation mutations in the CFTR RNA. It has been demonstrated to be safe, orally available and well tolerated in Phase 1 single dose trial in healthy volunteers.

### RESTORE ION TRANSPORT

- **INS37217**: Inspire Pharmaceuticals, supported by a CFFT TDA and the TDN. Correct the ion transport defect in CF. Recently completed Phase 2 trial to determine the effect of drug on pulmonary function in CF patients.
- **SPI-8811**: Sucampo Pharmaceuticals & the TDN. Oral agent believed to bypass transport defect of chloride ions. Initial Phase 2a trial evaluating safety and efficacy. Thirty patients recruited; expect study results late 2004 or early 2005.
- **Moli 1901**: Lantibio, Inc., supported by a CFFT TDA and the TDN. Thought to affect the ion transport defect in CF patients. Phase 1 trial demonstrated safety.
- **INO 4995**: Inologic, Inc., supported by a CFFT TDA, to be conducted in the TDN. Thought to correct the ion transport defect by acting on both the abnormal chloride and sodium transport. Early stage clinical trials evaluating safety are expected to begin in 2005/2006.
- **Parion 552-02**: Parion Sciences, supported by a CFFT TDA. Thought to correct the CF ion transport defect by acting primarily on abnormal sodium reabsorption. Single dose, Phase 1 in normal volunteers complete and plans to begin TDN trials in 2005.

### ANTI-INFLAMMATORY

- **Inhaled Nacystelyn**: Galephar Pharmaceutical Research, conducted in the TDN. Thought to act as a mucolytic and an anti-inflammatory. Phase 1 evaluation of safety and tolerability has been completed.
- **Oral N-acetylcysteine**: BioAdventix, Inc. - antioxidant that has been used as an inhaled mucolytic. Delivered in high doses, oral N-acetylcysteine replenishes glutathione levels in neutrophils. Has undergone pilot, 4-week dose ranging study at Stanford Univ. A placebo-controlled, 12-week study is planned.
- **DHA**: University of Massachusetts, CFFT-supported as clinical research grant. Pilot study to examine effect of infant formula with DHA on pathogenesis of CF in 120 newly diagnosed patients at 16 centers began in 2003.
- **HE-2000**: Hollis-Eden Pharmaceuticals, supported by a CFFT TDA. Examine an oral immune-regulating hormone to determine safety, tolerability & possible efficacy in CF patients. A single site Phase 1 study is planned to begin in 2005.
- **Simvastatin (Zocor™)**: A HMG-CoA reductase inhibitor that increases nitric oxide (NO) production in cultured CF epithelial cells. Investigators are evaluating, in a CFFT-funded trial, whether simvastatin increases exhaled NO production in CF patients, synthesis of pro-inflammatory cytokines and whether measures of inflammation in the upper respiratory tract correlate with those from the lower respiratory tract.

### MUCUS REGULATION

- **Pulmozyme®**: Genentech, approved in 1994 and currently being used by more than 18,000 U.S. patients. Clinical trials were conducted in the CFF's care center network.
- **Lomucin™**: Genaera Corporation, with support from a CFFT TDA. A Phase 2a clinical trial conducted in Ireland did not reveal any safety concerns. A larger trial to assess efficacy will begin in 2005.
- **Hypertonic Saline**: A CFFT-funded, Phase 3 trial in Australia was shown to have beneficial effects on pulmonary health in CF patients. A working group of CF clinicians is evaluating the data and will make recommendations regarding the use of hypertonic saline in the U.S.

### ANTI-INFECTIVE

- **TOBI®**: This CFF/Children's Hospital, Seattle-developed aerosol antibiotic was licensed to Chiron and received FDA approval in 1998. Currently being used by more than 15,000 patients worldwide. Benefit at first sign(s) of Pseudomonas infection will be evaluated in Phase 3 EPIC study to begin in 4<sup>th</sup> quarter of 2004.
- **Azithromycin**: A large-scale, CFFT-conceived and supported, TDN-coordinated trial completed in 2002. In patients with chronic *P. aeruginosa*, this oral antibiotic improved lung function and weight gain, and decreased hospitalization rate. One follow up study is in progress and several others are being planned.
- **Corus 1020 (Aztreonam Lysinate for Inhalation)**: Corus Pharma, supported by a CFFT TDA and conducted in the TDN. Phase 3 studies of the aerosolized form of aztreonam, a widely used IV antibiotic in CF, are underway; drug may be ready for market in 2006.
- **TIP** (TOBI Inhaled Powder): Chiron is developing TOBI as a powder to enable a faster, more convenient dosing regimen. Dosing of TIP will take a fraction of the time of liquid TOBI.
- **Pseudomonas vaccines**: CFFT is investigating development and use of several anti-pseudomonal vaccines. Clinical trials in Europe.
- **MP-610,205**: Mpx Pharmaceuticals, Inc., CFFT-supported. A bacterial efflux pump inhibitor that may increase the effectiveness of antibiotics in the treatment of chronic and acute bacterial respiratory infections in CF. A single-center Phase 1b clinical trial is planned to study tolerance of the aerosolized product in CF patients.
- **SLIT-amikacin**: Transave, Inc.; a liposomal formulation of the antibiotic amikacin. Animal model studies have shown it to decrease the *P. aeruginosa* burden in the lung. SLIT-amikacin is in a Phase I/II trial in Europe with filing of a U.S. IND planned for 2005.

### NUTRITION

- **TheraCLEC™**: Altus Pharmaceuticals, supported by a CFFT TDA, conducted in the TDN. Non-porcine pancreatic enzyme replacement. Phase 1 studies have not identified safety concerns. A Phase 2 trial began in the 3<sup>rd</sup> quarter of 2004.
- **Yasoo**: Yasoo Health is conducting a single site, pharmacokinetic trial, funded by CFFT, of an oral antioxidant formulation in CF patients.