TCDC Test Assets

# Asthma

## Approved

1. **Inhaled Corticosteroids (ICS):**
   * **Fluticasone (Flovent, Arnuity Ellipta)**
   * **Budesonide (Pulmicort)**
   * **Beclomethasone (QVAR)**
2. **Short-Acting Beta-Agonists (SABAs):**
   * **Albuterol (ProAir HFA, Ventolin HFA)**
   * **Levalbuterol (Xopenex)**
3. **Long-Acting Beta-Agonists (LABAs):**
   * **Formoterol (Foradil)**
   * **Salmeterol (Serevent)**
4. **Combination Inhalers (ICS/LABA):**
   * **Fluticasone/Salmeterol (Advair Diskus, Advair HFA)**
   * **Budesonide/Formoterol (Symbicort)**
5. **Leukotriene Modifiers:**
   * **Montelukast (Singulair)**
   * **Zafirlukast (Accolate)**
6. **Biologics:**
   * **Omalizumab (Xolair)** - Targets IgE
   * **Mepolizumab (Nucala)** - Targets IL-5
   * **Benralizumab (Fasenra)** - Targets IL-5 receptor
   * **Dupilumab (Dupixent)** - Targets IL-4 and IL-13
7. **Theophylline:**
   * **Theophylline (Theo-24, Uniphyl)**

## Clinical trials

1. **Janus Kinase (JAK) Inhibitors:** These drugs target specific enzymes involved in inflammation.
   * **Upadacitinib:** It's in trials for asthma.
2. **Thymic Stromal Lymphopoietin (TSLP) Inhibitors:** TSLP is involved in initiating allergic responses in the airways.
   * **Tezepelumab:** This monoclonal antibody is in trials for severe asthma.
3. **Prostaglandin D2 Receptor Antagonists:** These drugs aim to block receptors involved in inflammation.
   * **Fevipiprant:** It's being studied for its potential in asthma treatment.
4. **IL-33 Inhibitors:** Targeting IL-33, a protein involved in allergic responses.
   * **Anti-ST2 (GSK3772847):** This drug is in trials to assess its effects on asthma.
5. **Sphingosine-1-Phosphate (S1P) Receptor Modulators:** These medications regulate immune cell movement.
   * **Ponesimod:** Investigated for its potential in asthma management.
6. **Dual Bronchodilator Therapies:** Combining different types of bronchodilators.
   * **LAMA/LABA Combinations:** Long-acting muscarinic antagonists (LAMAs) with long-acting beta-agonists (LABAs) are being studied for efficacy in asthma.

# Cystic fibrosis

## Approved

1. **CFTR Modulators:**
   * **Ivacaftor (Kalydeco):** Approved for specific mutations.
   * **Lumacaftor/ivacaftor (Orkambi):** Designed for patients with specific CF mutations.
   * **Tezacaftor/ivacaftor (Symdeko/Symkevi):** For certain mutations in the CFTR gene.
   * **Elexacaftor/tezacaftor/ivacaftor (Trikafta/Kaftrio):** Approved for a broader range of mutations, including the most common.
2. **Mucolytics:**
   * **Dornase alfa (Pulmozyme):** A medication that helps to thin mucus, making it easier to clear from the lungs.

## Clinical trials

1. **Next-generation CFTR Modulators:**
   * **VX-121/VX-561:** Vertex Pharmaceuticals was developing these next-generation modulators, aiming to expand the number of CF mutations targeted.
2. **Correctors and Potentiators:**
   * **PTI-808:** Developed by Proteostasis Therapeutics, this corrector aimed to enhance the folding and function of the CFTR protein.
   * **ELX-02:** An experimental drug designed to enable the CFTR protein to overcome premature stop codons, being developed by Eloxx Pharmaceuticals.
3. **Anti-Inflammatory Agents:**
   * **AZD9668:** A potential anti-inflammatory drug being studied by AstraZeneca to reduce inflammation in the lungs of CF patients.
   * **Danirixin:** Investigated by GlaxoSmithKline, this drug targets the CXCR2 receptor involved in neutrophil recruitment, aiming to reduce inflammation.
4. **Antibiotics and Antimicrobial Agents:**
   * **Ciprofloxacin Dry Powder for Inhalation (DPI):** In a trial phase, this was intended as an antibiotic for CF-related lung infections.
   * **ALX-009:** A novel antimicrobial peptide being researched by Alaxia, designed to combat bacterial infections in CF patients.
5. **Gene Therapy:**
   * **AGEN-001:** A gene therapy candidate aimed at delivering a functional CFTR gene into lung cells, developed by 4D Molecular Therapeutics.
   * **AAV-CFTR:** Various trials exploring different adeno-associated virus (AAV) vectors to deliver the CFTR gene.

# Primary ciliary dyskinesia

## Off-label use

1. **Antibiotics:**
   * **Azithromycin (Zithromax):** Used in some cases for its anti-inflammatory and antibacterial properties.
   * **Amoxicillin/Clavulanate (Augmentin):** An antibiotic combination often used to treat respiratory infections.
   * **Ciprofloxacin (Cipro):** May be prescribed in specific cases of severe infections.
2. **Mucolytics:**
   * **Hypertonic Saline:** A solution used to help thin mucus and improve airway clearance.
   * **Recombinant DNAse (Dornase alfa/Pulmozyme):** Designed to break down DNA in mucus, aiding in its clearance.
3. **Bronchodilators:**
   * **Albuterol (Ventolin):** A common short-acting bronchodilator that helps open the airways for easier breathing.
   * **Salmeterol (Serevent):** A long-acting bronchodilator used for maintenance treatment of airflow obstruction.
4. **Anti-inflammatory Medications:**
   * **Inhaled Corticosteroids (Fluticasone, Budesonide):** These medications reduce inflammation in the airways and may help prevent lung damage.
5. **Nasal Irrigation Solutions:**
   * **Saline Nasal Sprays or Washes:** Simple saline solutions used to alleviate sinus congestion and help maintain nasal health.

## Clinical trials

1. **Mucus Clearance Agents:**
   * **Mannitol:** Inhaled mannitol was being studied to evaluate its effectiveness in improving mucus clearance and lung function in individuals with PCD.
2. **Anti-inflammatory Medications:**
   * **Montelukast:** This leukotriene receptor antagonist was under investigation for its potential to reduce airway inflammation and improve symptoms in PCD.
3. **Cilia-Stimulating Agents:**
   * **RPL554 (also known as Ensifentrine):** An investigational drug that acts as a dual phosphodiesterase 3 and 4 inhibitor, aimed at increasing ciliary beat frequency.
4. **Anti-Infective Therapies:**
   * **Colistin:** Trials were exploring the use of inhaled colistin, an antibiotic, to manage chronic respiratory infections in PCD.
5. **Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulators:**
   * **Ivacaftor:** Investigated in individuals with PCD who have specific CFTR mutations to assess its potential efficacy.
6. **Macrolide Antibiotics:**
   * **Clarithromycin:** Studies were investigating the use of macrolide antibiotics like clarithromycin for their anti-inflammatory effects and potential benefits in managing respiratory symptoms in PCD.
7. **Anti-inflammatory Approaches:**
   * **Inhaled Corticosteroids:** Some trials were assessing the use of inhaled corticosteroids to reduce airway inflammation in PCD.

# Idiopathic bronchiectasis

## Approved

1. **Mucolytics:**
   * **Dornase alfa (Pulmozyme):** This medication is approved for use in cystic fibrosis and can also be used off-label in some cases of bronchiectasis. It helps break down mucus, aiding in its clearance from the airways.
2. **Antibiotics:**
   * **Azithromycin:** While primarily an antibiotic, in some cases, it's prescribed for its anti-inflammatory properties in bronchiectasis to reduce exacerbations.
   * **Erythromycin:** Similar to azithromycin, it might be used for its anti-inflammatory effects rather than solely for its antibacterial properties.
3. **Bronchodilators:**
   * **Beta-2 Agonists (e.g., Albuterol):** These bronchodilators help open the airways, making breathing easier for individuals with bronchiectasis.
4. **Anti-inflammatory Medications:**
   * **Inhaled Corticosteroids:** In some cases, these medications may be prescribed to reduce airway inflammation and potentially decrease exacerbations.
5. **Mucokinetics:**
   * **Hypertonic Saline:** Similar to its use in cystic fibrosis, hypertonic saline might be used in bronchiectasis to help thin mucus, aiding in its clearance.

## Clinical trials

1. **Mucolytics:**
   * **Hypertonic Saline Solutions:** Different concentrations or formulations of hypertonic saline might be under investigation, such as 3%, 5%, or nebulized forms, to aid in mucus clearance and improve lung function.
2. **Antibiotics:**
   * **Azithromycin (e.g., Zithromax):** A macrolide antibiotic that might be used for its anti-inflammatory properties to reduce exacerbations and improve symptoms in bronchiectasis.
   * **Erythromycin:** Another macrolide antibiotic studied for its potential anti-inflammatory effects in bronchiectasis.
3. **Bronchodilators:**
   * **Albuterol (Salbutamol):** A common short-acting bronchodilator that might be explored to improve airway function and ease breathing difficulties in bronchiectasis patients.
4. **Anti-inflammatory Agents:**
   * **Inhaled Corticosteroids:** Medications like fluticasone or budesonide might be used in trials to reduce airway inflammation and prevent lung damage.
5. **Mucokinetics:**
   * **Acetylcysteine (Mucomyst):** While more commonly used in conditions like chronic obstructive pulmonary disease (COPD), acetylcysteine might be investigated for its mucolytic properties in bronchiectasis to help thin mucus.
6. **Immunomodulators:**
   * **Anti-TNF Biologics:** Drugs targeting tumor necrosis factor (TNF) such as infliximab might be studied to modulate inflammation in bronchiectasis.
7. **Anti-infective Therapies:**
   * **Levofloxacin:** A fluoroquinolone antibiotic that could be explored in trials for its effectiveness against bacterial infections in bronchiectasis.
8. **Mucus Clearance Aids:**
   * **High-frequency Chest Wall Oscillation (HFCWO) devices:** Devices that use oscillations to assist in airway clearance might be evaluated for their efficacy in improving mucus clearance and lung function.

# **L**ymphangioleiomyomatosis

## Off-label

1. **Sirolimus (Rapamune or Rapamycin):** This medication, an immunosuppressant, has shown efficacy in slowing the progression of LAM by inhibiting the abnormal cell growth associated with the disease. It's often considered the primary treatment for LAM.
2. **Everolimus (Afinitor):** Similar to sirolimus, everolimus is also an mTOR inhibitor and is sometimes used as an alternative treatment option for LAM.
3. **Bronchodilators:** These medications help relax the muscles around the airways, making breathing easier. While they don't treat the underlying cause of LAM, they can help manage symptoms like shortness of breath.

## Clinical trials

1. **Statins:**
   * **Simvastatin:** Commonly used to lower cholesterol levels, it was being studied for its potential in targeting cellular pathways involved in LAM progression.
2. **mTORC1 Inhibitors:**
   * **Temsirolimus:** Another mTOR inhibitor similar to sirolimus and everolimus, studied to assess its efficacy in slowing LAM progression.
   * **Ridaforolimus:** Also an mTOR inhibitor investigated in clinical trials for its potential role in treating LAM.
3. **Estrogen Modulators:**
   * **Tamoxifen:** A selective estrogen receptor modulator (SERM) studied for its impact on estrogen-related pathways in LAM.
   * **Letrozole:** An aromatase inhibitor explored due to its ability to reduce estrogen production, potentially affecting LAM progression.
4. **Anti-inflammatory Agents:**
   * **Prednisone:** A corticosteroid with anti-inflammatory properties, sometimes studied to assess its role in managing LAM-related inflammation.
5. **Immunosuppressants and Immunomodulators:**
   * **Mycophenolate Mofetil:** An immunosuppressant investigated for its potential effects on the immune system in LAM.
   * **Azathioprine:** Another immunosuppressive agent that might have an impact on the progression of LAM.
6. **Antiangiogenic Agents:**
   * **Bevacizumab:** An antiangiogenic drug targeting blood vessel formation, explored in clinical trials for its potential role in managing lung complications associated with LAM.

# Idiopathic pulmonary fibrosis

## Approved

1. **Pirfenidone (Esbriet):** This medication is an antifibrotic drug that helps reduce lung scarring by inhibiting the production of certain growth factors involved in fibrosis. It's one of the first approved drugs specifically for IPF.
2. **Nintedanib (Ofev):** Another antifibrotic medication, nintedanib, works by targeting multiple signaling pathways involved in fibrosis to slow down the progression of lung scarring in IPF.

## Clinical trials

1. **Tyrosine Kinase Inhibitors:**
   * **Fostamatinib:** A tyrosine kinase inhibitor targeting spleen tyrosine kinase (SYK), studied for its potential to reduce fibrosis and inflammation in the lungs of individuals with IPF.
2. **Galectin Inhibitors:**
   * **GB0139:** This is a galectin-3 inhibitor assessed to determine its impact on fibrosis progression in IPF. Galectin-3 is involved in inflammation and fibrosis processes.
3. **Autotaxin Inhibitors:**
   * **GLPG1690:** An autotaxin inhibitor studied in clinical trials to evaluate its effects on IPF progression. Inhibiting autotaxin may reduce the production of lysophosphatidic acid (LPA), implicated in fibrosis.
4. **Pirfenidone/Nintedanib Variants or Combinations:**
   * Various formulations, combinations, or modified versions of pirfenidone and nintedanib were being studied to assess potential improvements in efficacy, tolerability, or reduced side effects.
5. **Anti-inflammatory Agents:**
   * **Cenicriviroc:** An investigational drug targeting specific receptors involved in inflammation, assessed for its potential in reducing lung inflammation and fibrosis in IPF.
6. **Stem Cell Therapies:**
   * Different stem cell-based therapies were in clinical trials, exploring the potential of stem cells to regenerate lung tissue and modulate the immune response in IPF.
7. **Anti-fibrotic Agents:**
   * **Bardoxolone Methyl:** An antioxidant inflammation modulator (AIM) that has shown potential anti-fibrotic effects, undergoing trials for its impact on IPF progression.