



## **Vertex Pharmaceuticals** **[NASDAQ: VRTX]**

**Jacob Hirth**

*Committee Head*

**Matthew Gaines**

*Lead Analyst*

**Michael Mancuso**

*Analyst*

**Brie Rive**

*Analyst*

**Forrest Roy**

*Analyst*

**William Coleman**

*Analyst*

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# **I. Executive Summary**

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- Vertex is a pharmaceutical drug manufacturer
- Product portfolio consisting of 4 drugs that treat the underlying causes of cystic fibrosis
- Pipeline consisting of 15+ opportunities to expand their reach into other orphan disease areas
- VRTX trading about 30% down on the year due to bad trial results provides an opportunity for CIMG
- **BUY, Fair Value: \$268, Upside: 54%**

| Rates         |       |
|---------------|-------|
| Discount Rate | 8.00% |
| LTGR          | 0.00% |

| Valuation 10YR             |               |
|----------------------------|---------------|
| Sum FCF                    | \$ 29,272,293 |
| PV of TV                   | \$ 39,583,246 |
| Enterprise Value           | \$ 68,855,539 |
| (+) Cash                   | \$ 6,275,698  |
| (+) Investments            | \$ 685,187    |
| (-) Debt                   | \$ 876,800    |
| Equity Value               | \$ 74,939,624 |
| Diluted Shares Outstanding | 258,988       |
| Value Per Share            | \$ 289.36     |
| Current Share Price        | \$ 188.25     |
| P/V                        | 0.65          |
| Upside                     | 53.71%        |



## II. Company Overview

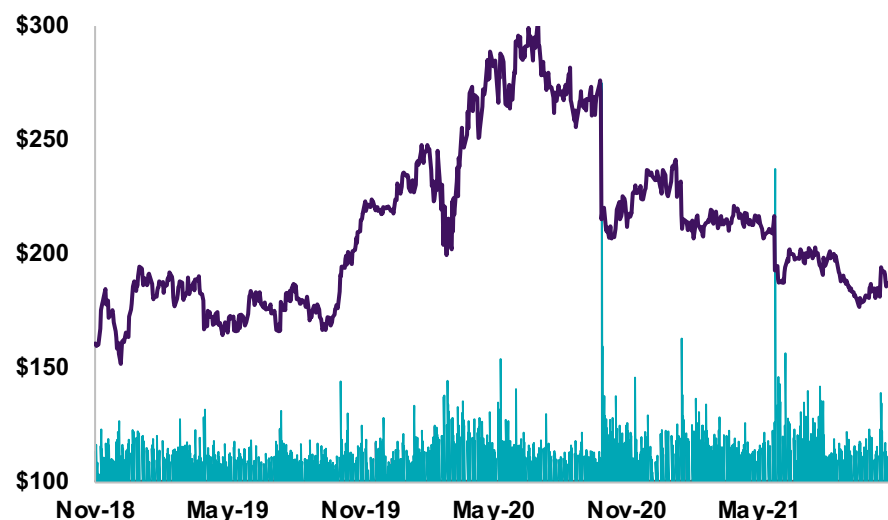
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# Financial Overview

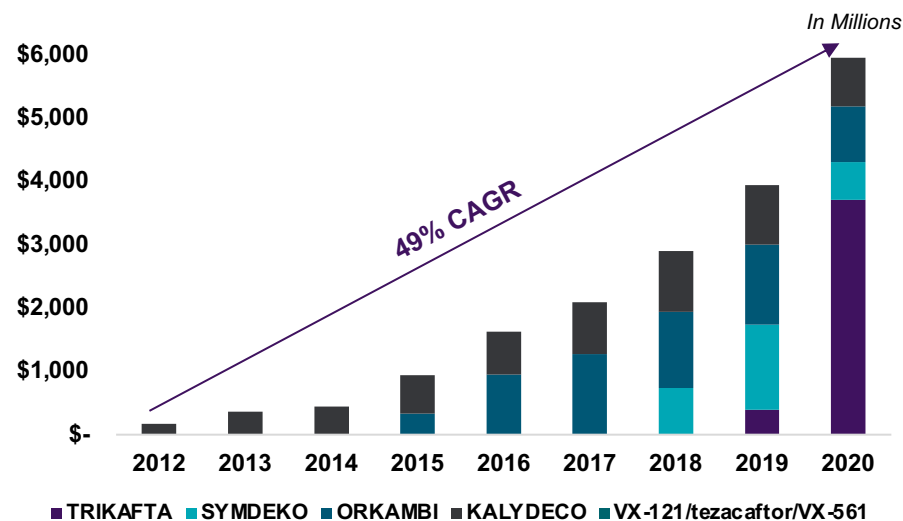


**NASDAQ: VRTX**

Recent Stock History



Total Revenue



Financial Snapshot

| Financial Snapshot |    |        |
|--------------------|----|--------|
| Price              | \$ | 188.25 |
| Market Cap         |    | 47.88B |
| EV                 |    | 41.79B |
| LTM EV/EBITDA      |    | 15.00x |
| NTM EV/EBITDA      |    | 8.63x  |
| 52 Week High       | \$ | 242.99 |
| 52 Week Low        | \$ | 176.36 |

| (In Millions)        | FY'16     | FY'17     | FY'18     | FY'19     | FY'20     |
|----------------------|-----------|-----------|-----------|-----------|-----------|
| <b>Top-Line</b>      |           |           |           |           |           |
| Rev                  | 1,702,177 | 2,488,652 | 3,047,597 | 4,162,821 | 6,205,683 |
| YoY Growth           |           | 46%       | 22%       | 37%       | 49%       |
| <b>Expenses</b>      |           |           |           |           |           |
| COGS                 | 12%       | 11%       | 13%       | 13%       | 12%       |
| R&D                  | 62%       | 53%       | 46%       | 42%       | 29%       |
| <b>Profitability</b> |           |           |           |           |           |
| Gross Margin         | 88%       | 89%       | 87%       | 87%       | 88%       |
| EBITDA Margin        | 1%        | 5%        | 21%       | 29%       | 46%       |
| Profit Margin        | -5%       | 4%        | 68%       | 28%       | 44%       |
| <b>Return</b>        |           |           |           |           |           |
| RORC                 | 113%      | 167%      | 186%      | 206%      | 299%      |
| ROE                  | -6%       | 4%        | 47%       | 14%       | 31%       |

# Company Overview



## Vertex dominates the cystic fibrosis pharmaceutical space

### What is Cystic Fibrosis?



Causes fluid build up in organs and tissues



Caused by a **mutation of the CFTR gene**



Treatable population **~83,000 people<sup>(1)</sup>**



Average lifespan with treatment is **53 years**

### Rational vs. Conventional Drug Design

Identify Relevant  
Enzyme/Receptor



Elucidate  
Structure/Function



Design Drug that  
Interacts Beneficially

Chemical Substance



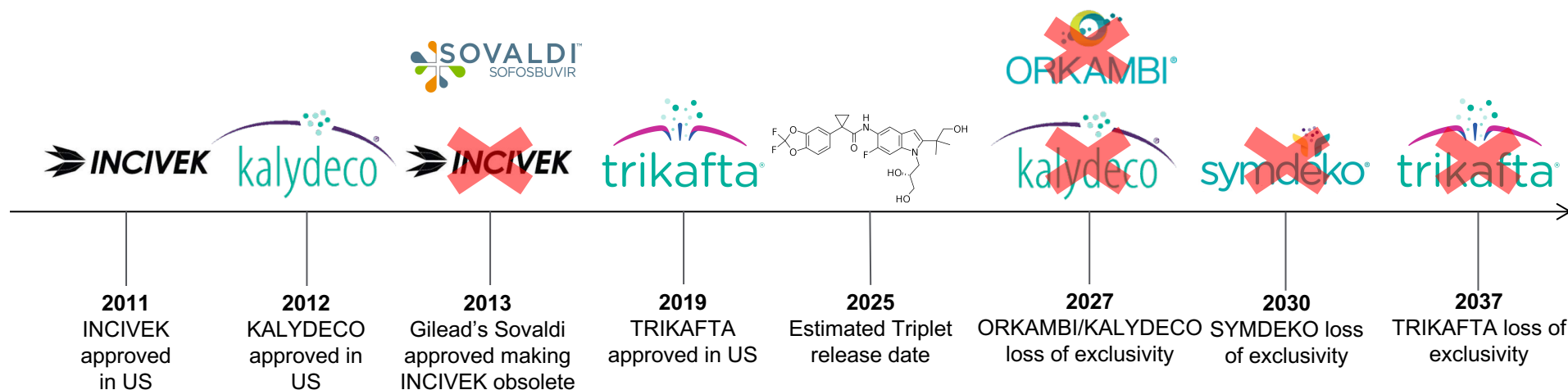
Test on Animals or  
Cells



Repeat (Trial and  
Error)

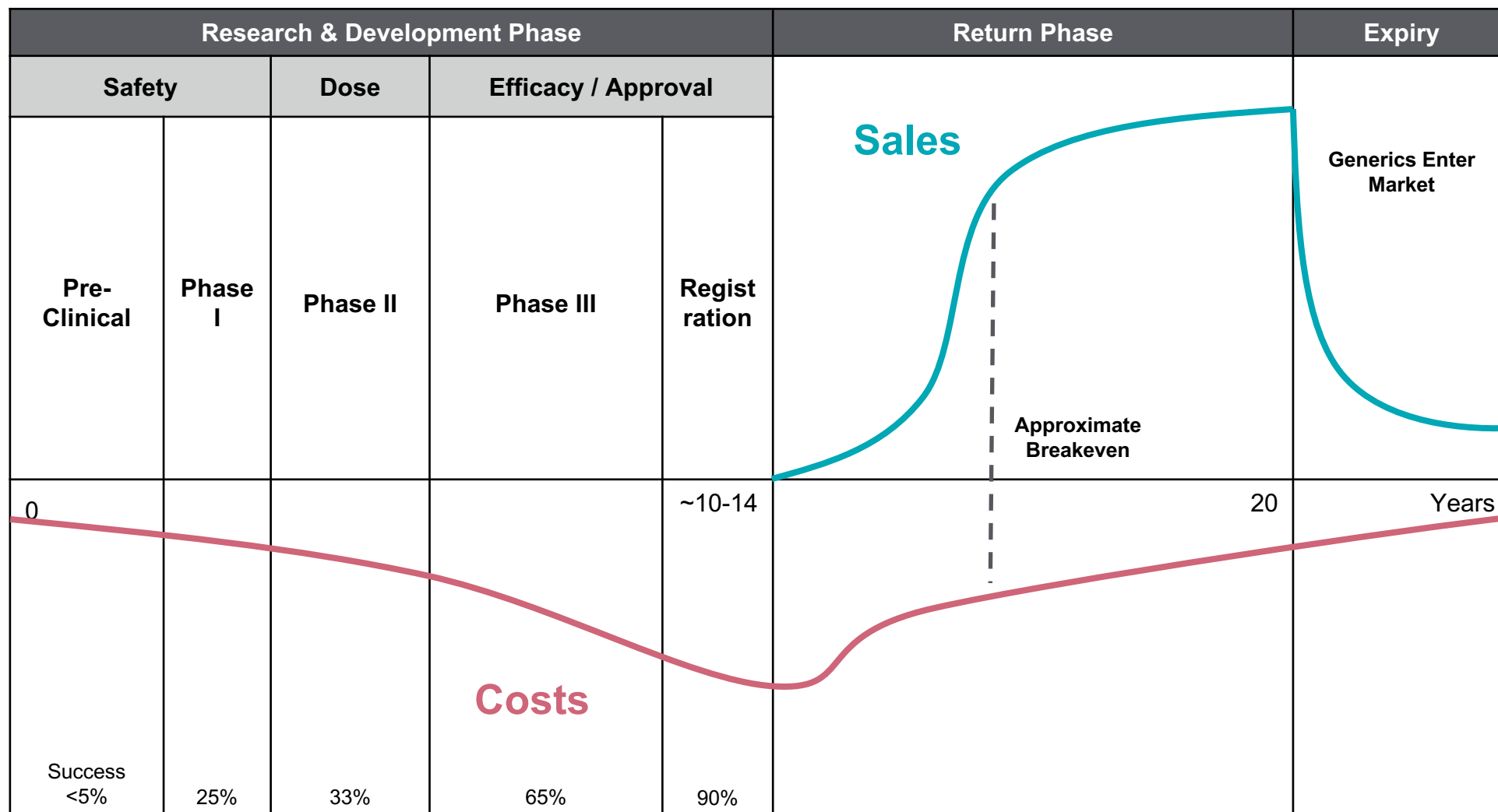
vs.

### Company Timeline



(1) Population in US, Canada, Europe, and Australia

# Pharmaceutical Drug Life Cycle



## III. Industry Overview

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# Industry Overview

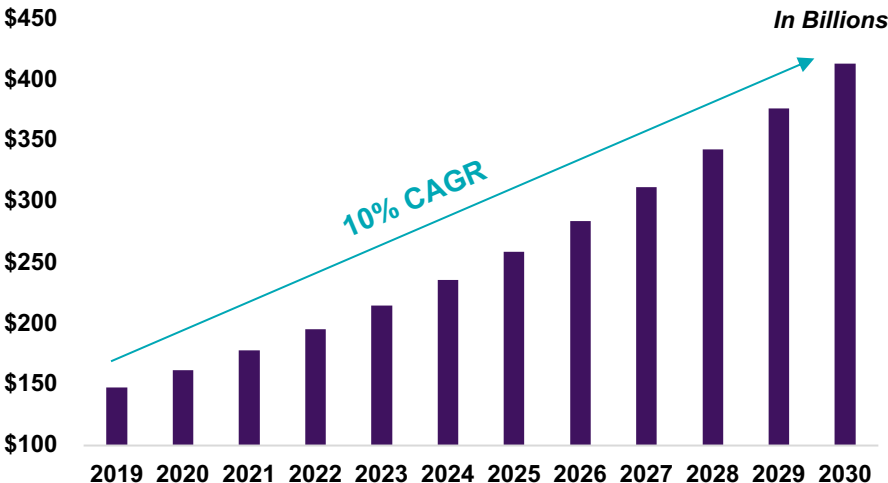


## Vertex's niche market within the pharmaceutical industry

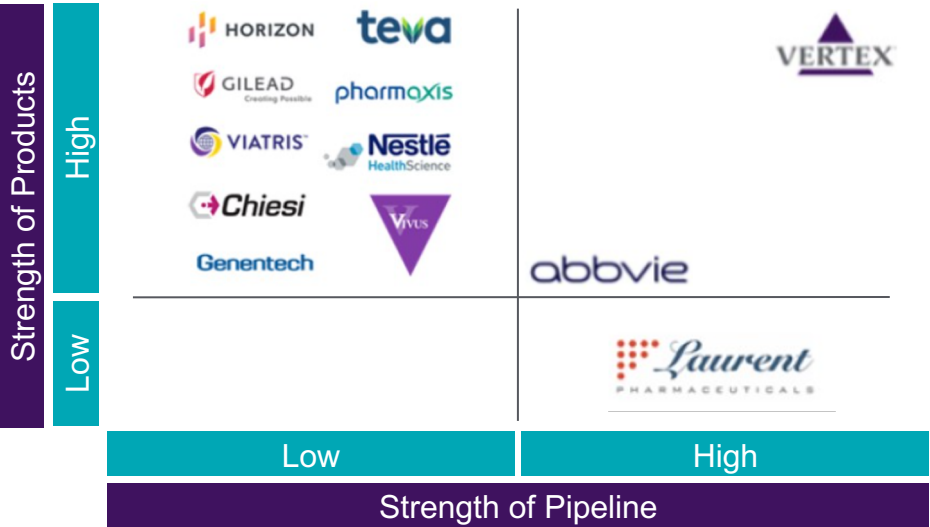
### Orphan Drug Designation

- Disease affects **<200,000 people in the US**
- 25-30m people** suffer from orphan disease in US
- 25% tax credit** given for the cost of trials
- 95%** of rare diseases still **have no treatment**

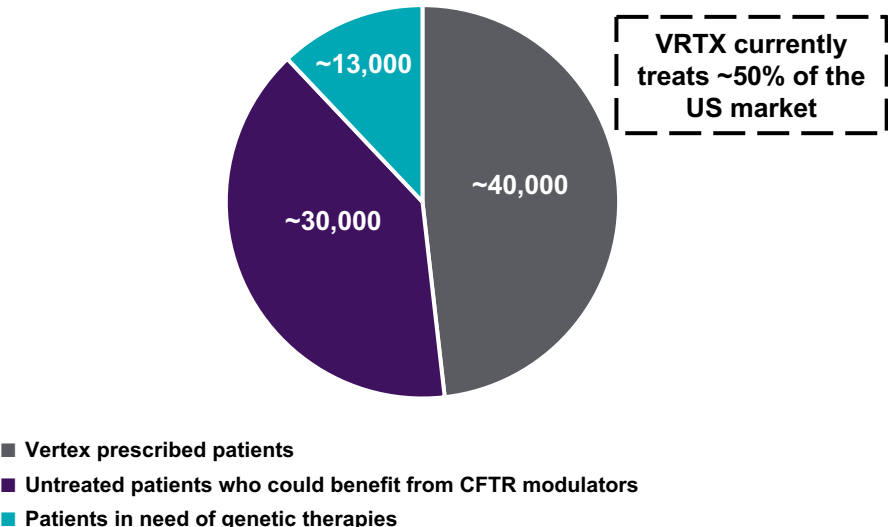
### Total Revenue of Orphan Drug Industry <sup>(1)</sup>



### Cystic Fibrosis Competitors



### Treatable Population <sup>(2)</sup>



(1) insightSLICE (2) Company Filings



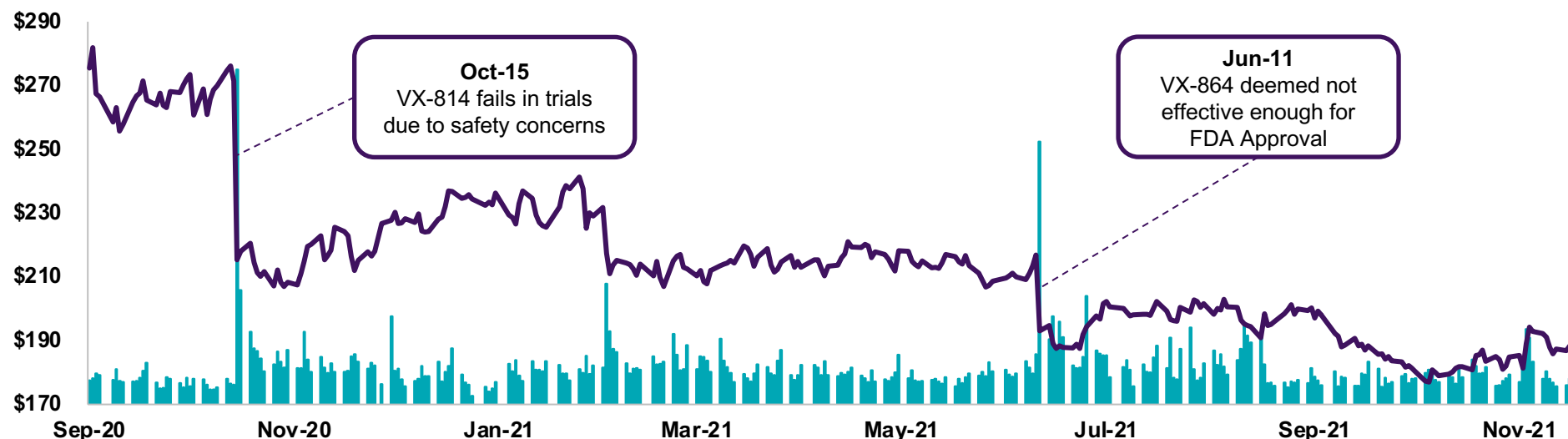
## IV. Investment Thesis

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# Mispricing Due to Recent Pipeline Failures

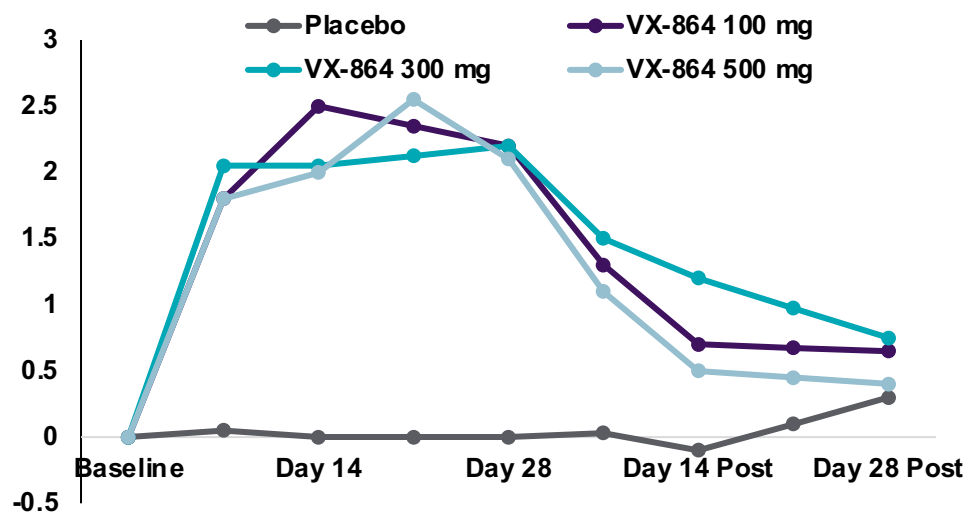


## Failure of AATD drugs creates value opportunity for investors



### VX-864 Shows Proof of Mechanism<sup>(1)</sup>

Change of AAT Levels in Patients Using VX-864 (micromolar)



### Upcoming Catalysts<sup>(2)</sup>

| Product    | Indication | Event  | Timing  | Impact |
|------------|------------|--|---------|--------|
| VX-147     | Kidney     | Ph2 proof-of-concept data                            | 2H21    | H      |
| CTX001     | BT/SCD     | Ph1/2 update from CLIMB-111 and CLIMB-121            | 2H21    | M      |
| CF triple  | CF         | Initiation of Ph3 non-inferiority study vs. Trikafta | 2H21    | L      |
| VX-548     | Pain       | Ph2 bunionectomy study data                          | 1Q22    | M      |
| VX-880     | T1D        | Ph1/2 initial data                                   | 2022    | M      |
| small mol. | AATD       | Enter clinic   | 2022    | L      |
| CTX001     | BT/SCD     | Filing for approval                                  | 1Q-3Q23 | L      |

(1) Company Filings (2) Barclays Equity Research

# Monopoly in the Cystic Fibrosis Market

## Dominant CF portfolio with room to expand

### Patients NEED Trikafta...



Average life span of untreated cystic fibrosis patient: 44 years

Treatment increases patient life span by 21% to 53 years

Decreases severe cases by 60%

Decreases mild cases by 18%

### ... and Vertex has made the drug obtainable

Approved in 32 countries

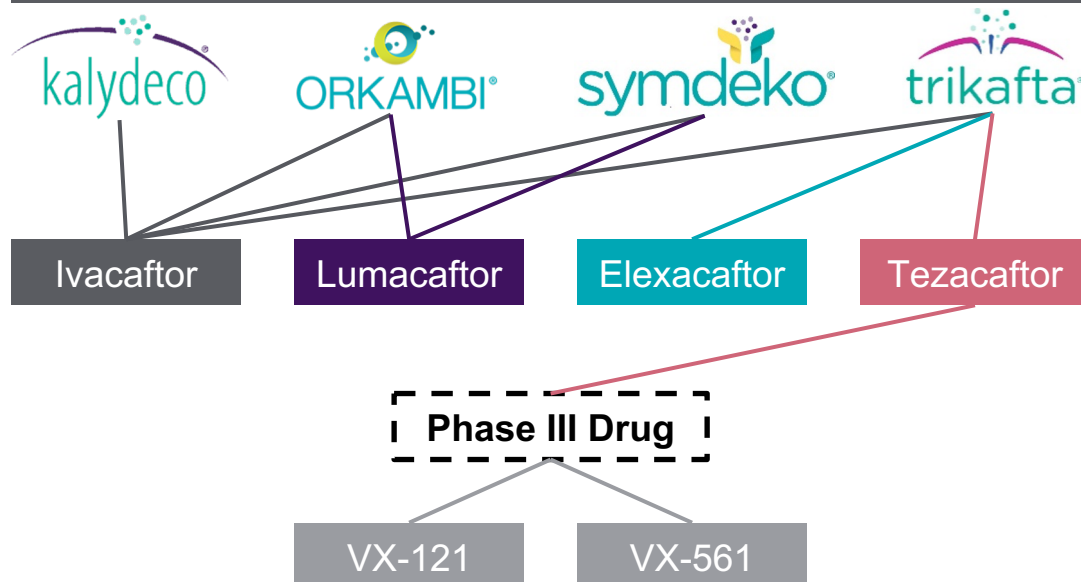
Reimbursement agreements in 25+ countries

30,000 patients eligible to be prescribed

40,000 Vertex prescribed patients

>\$10bn unpenetrated market opportunity annually

### CF Drug Composition



### Advantage over Abbvie

#### Effectiveness

"not expected to greatly improve efficacy and safety"<sup>(1)</sup>

#### Treatable Population

"agents are not expected to treat new mutations"<sup>(1)</sup>

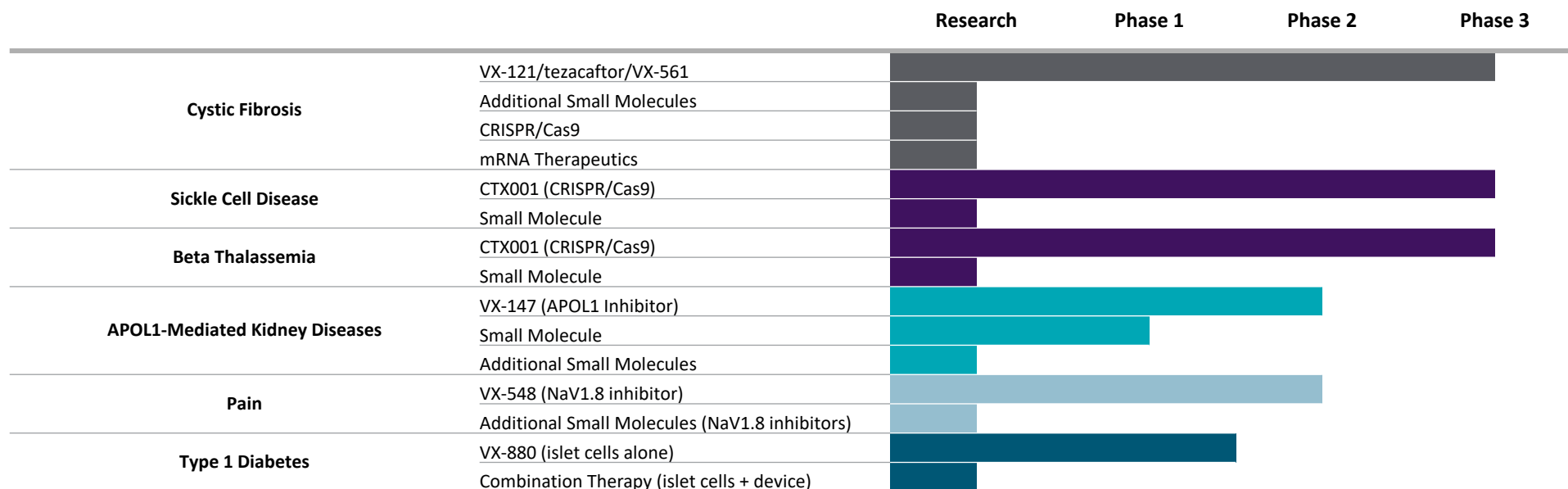
#### Competition






"face strong competition from Vertex's well- established repertoire"<sup>(1)</sup>

"these me-too drugs will mainly serve as alternatives to currently marketed CFTR modulators"<sup>(1)</sup>

(1) Company Filings (2) Barclays Equity Research

## Diversified pipeline to drive future growth



| Cell and Genetic Therapies   | Small Molecules   |
|--|---|
|  <b>Sickle Cell Disease &amp; Beta Thalassemia</b><br>CTX001 in Phase 2  |  <b>APOL1-Mediated Kidney Diseases</b><br>VX-147 in Phase 2   |
| <ul style="list-style-type: none"> <li>More than 45 patients dosed across the two studies</li> <li>Expect to achieve target enrollment in both studies in Q3</li> <li>Anticipate filing for approval in the next 18-24 months</li> </ul> | Potential POC data in APOL1-mediated FSGS on-trial for 2H21   |
|  <b>Type 1 Diabetes</b><br>Phase 1/2 underway with VX-880   |  <b>NaV1.8 inhibitor for Pain</b><br>VX-548 in Phase 2   |
| <ul style="list-style-type: none"> <li>First patient dosed with VX-880 in the "islet cells alone" program</li> <li>Cells + device program progressing in late preclinical studies</li> </ul>   | Two studies in acute pain with opioid reference arm; first data anticipated by early 2022   |
|  |  <b>Alpha-1 Antitrypsin Deficiency</b><br>One or more small molecules expected to enter the clinic in 2022 |

## V. Valuation

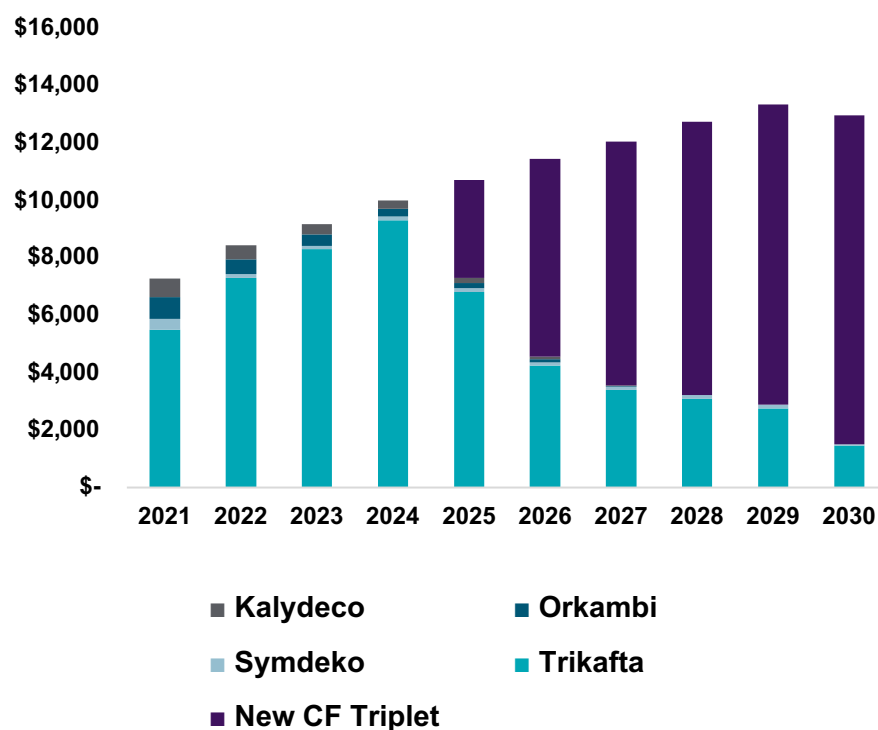
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## Two valuation scenarios

### Cystic Fibrosis Portfolio Only

- Projected **each drug by region (US & EU)**
- Projected using penetration rate of CF population
- CF population **growth rate of 2.2%**
- Used **market rate drug prices**

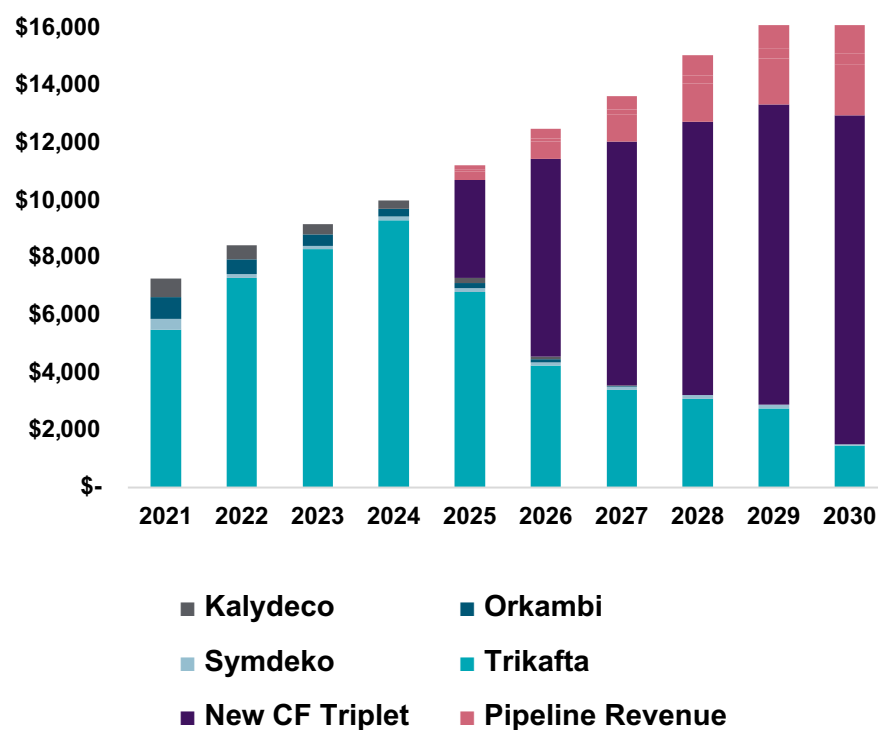
### CF Portfolio Revenue Projections



### Entire Drug Pipeline

- Added CF portfolio and pipeline value
- Completed **risk-adjusted valuation of pipeline**
- Pipeline population **growth rate of 0.7%**
- Used current **treatment cost to estimate prices**

### CF & Pipeline Revenue Projections





## Undervalued cystic fibrosis portfolio coupled with robust pipeline

**Recommendation: Buy**

**Potential Upside: 54%**

### Rates

|               |       |
|---------------|-------|
| Discount Rate | 8.00% |
| LTGR          | 0.00% |

### Cystic Fibrosis Drug Portfolio

| Valuation 10YR             |               |
|----------------------------|---------------|
| Sum FCF                    | \$ 26,898,318 |
| PV of TV                   | \$ 32,273,312 |
| Enterprise Value           | \$ 59,171,629 |
| (+) Cash                   | \$ 6,275,698  |
| (+) Investments            | \$ 685,187    |
| (-) Debt                   | \$ 876,800    |
| Equity Value               | \$ 65,255,714 |
| Diluted Shares Outstanding | 258,988       |
| Value Per Share            | \$ 251.96     |
| Current Share Price        | \$ 188.25     |
| P/V                        | 0.75          |
| Upside                     | 33.85%        |

| LTGR  | Discount Rate |       |       |       |        |
|-------|---------------|-------|-------|-------|--------|
|       | 6.00%         | 7.00% | 8.00% | 9.00% | 10.00% |
| 0.00% | 0.56          | 0.65  | 0.75  | 0.84  | 0.93   |
| 1.00% | 0.56          | 0.65  | 0.74  | 0.84  | 0.93   |
| 2.00% | 0.55          | 0.65  | 0.74  | 0.83  | 0.92   |
| 3.00% | 0.55          | 0.64  | 0.74  | 0.83  | 0.92   |
| 4.00% | 0.55          | 0.64  | 0.73  | 0.82  | 0.91   |

| LTGR  | Discount Rate |        |        |        |        |
|-------|---------------|--------|--------|--------|--------|
|       | 6.00%         | 7.00%  | 8.00%  | 9.00%  | 10.00% |
| 0.00% | \$ 335        | \$ 288 | \$ 252 | \$ 224 | \$ 202 |
| 1.00% | \$ 337        | \$ 289 | \$ 253 | \$ 225 | \$ 203 |
| 2.00% | \$ 339        | \$ 291 | \$ 254 | \$ 226 | \$ 204 |
| 3.00% | \$ 341        | \$ 292 | \$ 256 | \$ 227 | \$ 205 |
| 4.00% | \$ 343        | \$ 294 | \$ 257 | \$ 228 | \$ 206 |

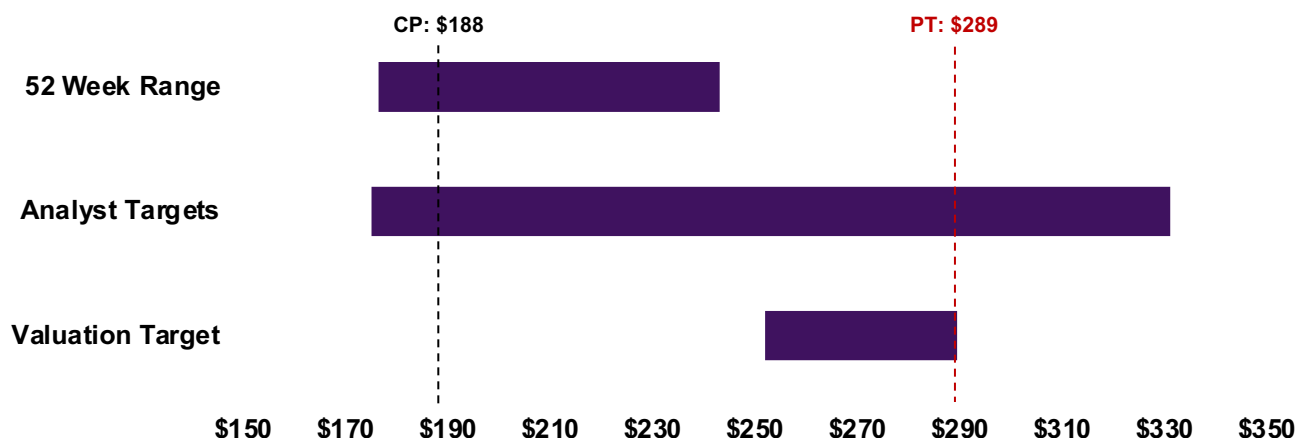
### CF Portfolio and Pipeline Potential

| Valuation 10YR             |               |
|----------------------------|---------------|
| Sum FCF                    | \$ 29,272,293 |
| PV of TV                   | \$ 39,583,246 |
| Enterprise Value           | \$ 68,855,539 |
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| Value Per Share            | \$ 289.36     |
| Current Share Price        | \$ 188.25     |
| P/V                        | 0.65          |
| Upside                     | 53.71%        |

| LTGR  | Discount Rate |       |       |       |        |
|-------|---------------|-------|-------|-------|--------|
|       | 6.00%         | 7.00% | 8.00% | 9.00% | 10.00% |
| 0.00% | 0.48          | 0.57  | 0.65  | 0.74  | 0.82   |
| 1.00% | 0.48          | 0.56  | 0.65  | 0.73  | 0.82   |
| 2.00% | 0.48          | 0.56  | 0.64  | 0.73  | 0.81   |
| 3.00% | 0.47          | 0.56  | 0.64  | 0.72  | 0.81   |
| 4.00% | 0.47          | 0.55  | 0.64  | 0.72  | 0.81   |

| LTGR  | Discount Rate |        |        |        |        |
|-------|---------------|--------|--------|--------|--------|
|       | 6.00%         | 7.00%  | 8.00%  | 9.00%  | 10.00% |
| 0.00% | \$ 391        | \$ 333 | \$ 289 | \$ 256 | \$ 229 |
| 1.00% | \$ 393        | \$ 334 | \$ 291 | \$ 257 | \$ 231 |
| 2.00% | \$ 395        | \$ 336 | \$ 292 | \$ 258 | \$ 232 |
| 3.00% | \$ 398        | \$ 338 | \$ 294 | \$ 260 | \$ 233 |
| 4.00% | \$ 400        | \$ 340 | \$ 295 | \$ 261 | \$ 234 |



## VI. Appendix

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**Pharmaceutical Life Cycle**

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**Monopoly in the Cystic Fibrosis Market**

**Vertex's Pipeline**

**Valuation**

**Valuation Overview**

Model Output: Case 1

Model Output: Case 2

Public Comparables

What is CF? Causes & Symptoms

What is CF? Diagnosis

What is CF? Treatments

Vertex Management 1

Vertex Management 2

Vertex Management 3

Cystic Fibrosis Demographics and Population  
Growth 1

Cystic Fibrosis Demographics and Population  
Growth 2

What will move the model in the next  
two years?

Valuation CF

Cystic Fibrosis Drug Pricing

CF Penetration Rates Over the  
Projection Period (US)

CF Penetration Rates Over the  
Projection Period (EU)

Full Vertex Portfolio Timeline

Pipeline Penetration Rates Over the  
Projection Period (US)

Rare Disease (HIV) Drug Uptake Curves

Valuation SCD & BT

Valuation MKD

Valuation T1D

# Public Comparables



| Company Name  | LTM EV/Rev | LTM EV/EBITDA | LTM EV/EBIT | LTM P/E | LTM B/BV | NTM EV/Rev | NTM EV/EBITDA | NTM P/E |
|---|------------|---------------|-------------|---------|----------|------------|---------------|---------|
| AbbVie Inc. (NYSE:ABBV)                             | 5.0x       | 9.5x          | 13.6x       | 28.0x   | NM       | 4.64x      | 8.96x         | 8.59x   |
| Amgen Inc. (NasdaqGS:AMGN)                          | 5.5x       | 11.4x         | 15.8x       | 21.2x   | NM       | 5.26x      | 8.78x         | 11.99x  |
| BioMarin Pharmaceutical Inc. (NasdaqGS:BMRN)        | 8.0x       | 209.6x        | NM          | NM      | 4.0x     | 7.53x      | 63.13x        | 71.46x  |
| Gilead Sciences, Inc. (NasdaqGS:GILD)               | 3.8x       | 6.9x          | 8.1x        | 11.5x   | NM       | 4.26x      | 7.65x         | 9.79x   |
| Biogen Inc. (NasdaqGS:BIIB)                         | 3.8x       | 13.4x         | 16.3x       | 25.3x   | 15.9x    | 4.03x      | 13.31x        | 14.81x  |
| Regeneron Pharmaceuticals, Inc. (NasdaqGS:REGN)     | 4.4x       | 7.8x          | 8.1x        | 10.3x   | 3.9x     | 4.22x      | 7.90x         | 11.48x  |
| Sarepta Therapeutics, Inc. (NasdaqGS:SRPT)          | 10.1x      | NM            | NM          | NM      | 14.0x    | 7.97x      | NM            | NM      |
| Moderna, Inc. (NasdaqGS:MRNA)                       | 7.6x       | 11.5x         | 11.8x       | 14.5x   | 9.7x     | 3.53x      | 6.67x         | 7.57x   |
| Vertex Pharmaceuticals Incorporated (NasdaqGS:VRTX) | 5.9x       | 15.0x         | 15.8x       | 22.6x   | 5.9x     | 5.14x      | 8.63x         | 14.26x  |
| Summary Statistics                                  | LTM EV/Rev | LTM EV/EBITDA | LTM EV/EBIT | LTM P/E | LTM B/BV | NTM EV/Rev | NTM EV/EBITDA | NTM P/E |
| High  | 10.1x      | 209.6x        | 16.3x       | 28.0x   | 15.9x    | 7.97x      | 63.13x        | 71.46x  |
| Low   | 3.8x       | 6.9x          | 8.1x        | 10.3x   | 3.9x     | 3.53x      | 6.67x         | 7.57x   |
| Mean  | 6.0x       | 38.6x         | 12.3x       | 18.5x   | 9.5x     | 5.18x      | 16.63x        | 19.38x  |
| Median  | 5.2x       | 11.4x         | 12.7x       | 17.9x   | 9.7x     | 4.45x      | 8.78x         | 11.48x  |

# What is Cystic Fibrosis? (1/3)

## *In-depth view at causes & symptoms*

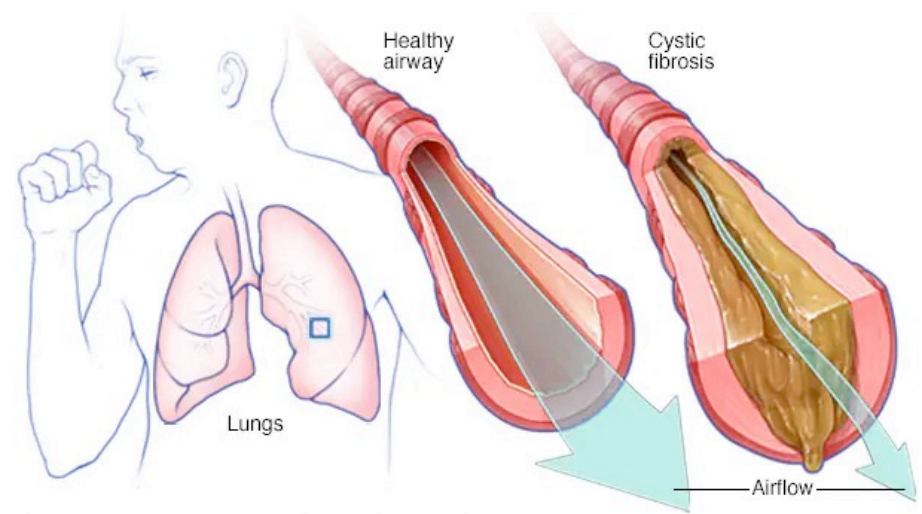
### Causes

- **CF is caused by a faulty gene** a child inherits from both their parents
- Gene means that **some cells struggle to move salt and water across the cell wall** which results in a build-up of thick, sticky mucus in body's tubes and passageways
- For someone to have CF they **must inherit a copy of the faulty gene from both parents**

|   |                                     |                       |  |
|---|-------------------------------------|-----------------------|--|
| Father Carrying Recessive Gene for CF (c) |                                     |                       |  |
| Mother Carrying Recessive Gene for CF (c) | CC                                  | Cc                    |  |
|   | Child not affected or carrier of CF | Child carries CF gene |  |
|   | Cc                                  | CC                    |  |
|   | Child carries CF gene               | Child has CF          |  |

### Symptoms

- **Lung Problems:** recurring chest infections, inflammation of airways, coughing, wheezing and shortness of breath
- **Digestive System Problems:** Bowel obstruction in first few days of life recurring surgery, jaundice, diarrhea, problems with growth/weight, diabetes
- **Other Problems:** Sinusitis, nasal polyps, osteoporosis, swelling and pain in the joints, difficulty conceiving children, liver problems, coughing causing incontinence



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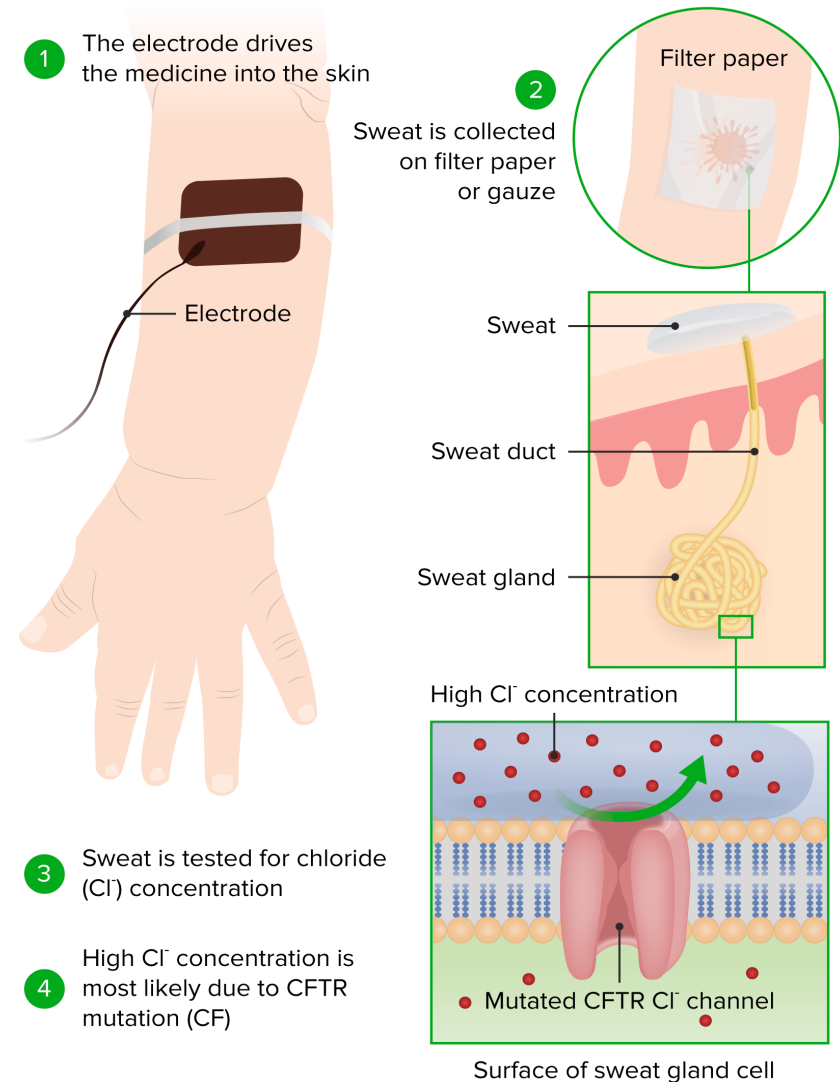
# What is Cystic Fibrosis? (2/3)

## In-depth view at Diagnosis

### Diagnosis

- **Newborn screening:** Blood spot test involving a prick of a newborn's heel
- **Confirming diagnosis:**
  - ▶ **Sweat test** measures the amount of salt in sweat, someone with CF has higher than normal amounts
  - ▶ **Genetic test** sample of blood or saliva is checked for the faulty gene that causes CF
- **Carrier testing** using a blood test or mouth swab to find out if you're a carrier of CF and see if you're at risk of having a child of CF if:
  - ▶ Close relative has CF
  - ▶ Close relative is a known carrier
  - ▶ Your partner is known to carrier the disease

### Cystic Fibrosis Sweat Test



# What is Cystic Fibrosis? (3/3)

## *In-depth view at treatments*

### Treatment

- **No cure for Cystic Fibrosis** treatment can ease symptoms
- **Goals of treatment:**
  - ▶ Preventing & controlling lung infections
  - ▶ Removing & loosening mucus in lungs
  - ▶ Treating and preventing intestinal blockage
  - ▶ Providing adequate nutrition

### Non-Medication Treatments

- **Airway clearance techniques**
  - ▶ Clapping with cupped hands-on chest
  - ▶ Mechanical devices (vests)
- **Pulmonary Rehabilitation**
  - ▶ Long term program focused on increasing lung health
- **Surgical and other procedures**
  - ▶ Nasal/sinus surgery
  - ▶ Oxygen therapy
  - ▶ Noninvasive ventilation
  - ▶ Feeding tube
  - ▶ Bowel surgery
  - ▶ Lung/liver transplant

### Medications

- **Antibiotics** to treat/prevent lung infections
- **Anti-inflammatory medications** to lessen swelling in airways in lungs
- **Mucus-thinning drugs**, such as hypertonic saline
- Inhaled medications called **bronchodilators that can help keep your airways open**
- **Oral pancreatic enzymes** to help your digestive tract absorb nutrients
- **Stool softeners** to prevent constipation/bowel obstruction
- **Acid-reducing medications** to help pancreatic enzymes work better
- **Specific drugs** for diabetes/liver diseases
- **Gene targeting medications:**
  - ▶ Medications that help improve the function of the faulty CFTR protein, improving lung function and weight and reduce the amount of salt in sweat
  - ▶ The FDA has approved four medications for treating CF in people with one or more mutations in the CFTR gene
    - **Trikafta** (Vertex)
    - **Symdeko** (Vertex)
    - **Orkambi** (Vertex)
    - **Kalydeco** (Vertex)

## CEO/President

- **Reshma Kewalramani M.D., FASN**
- **Joined VRTX in 2017 as CMO**
- **12 years at Amgen in Clinical Development and R&D**

## Executive Chairman

- **Jeffrey Leiden, B.A., M.D., Ph.D.**
- **CEO from 2012-2020**
- **Prior to VRTX was a Managing Director at life sciences VC firm and worked for Abbott Labs**

## CSO

- **David Altshuler, M.D., Ph.D.**
- **Joined as CSO in 2015**
- **Worked at Broad Institute of Harvard and MIT, professor of Genetics and Medicine at HMS**



## COO

- **Stuart Arbuckle**
- **Joined VRTX in 2012**
- **30 years of experience in leading global sales and marketing efforts at biopharma companies at Amgen, GlaxoSmithKline**



## Global Med Dev and Med Affairs

- **Carmen Bozic M.D**
- **Joined VRTX in 2019**
- **20 years at Biogen in in Global Development**



## Chief Patient Officer

- **Amit Sachdev, J.D.**
- **Joined as CSO in 2007**
- **Build relationships with CF community and build relationships with new communities across the world**





## Chief of Cell and Gene Therapies

- Bastiano Sanna, Ph.D.
- Joined VRTX in 2019
- Focused on cell and genetic therapy programs
- Previous CEO of Semma Therapeutics, acquired by VRTX in 2019



## CFO

- Charles (Charlie) Wagner joined VRTX in 2019
- Prior to VRTX was CFO at a Carlyle Group Portfolio company and an advisor to Bain & Company



## International Commercial Ops

- Ludovic Fenaux
- Joined VRTX in 2018
- Previously worked for Bristol-Myers Squibb holding multiple international senior leadership positions



## Population growth as patients live longer with lower death rates

### Notes

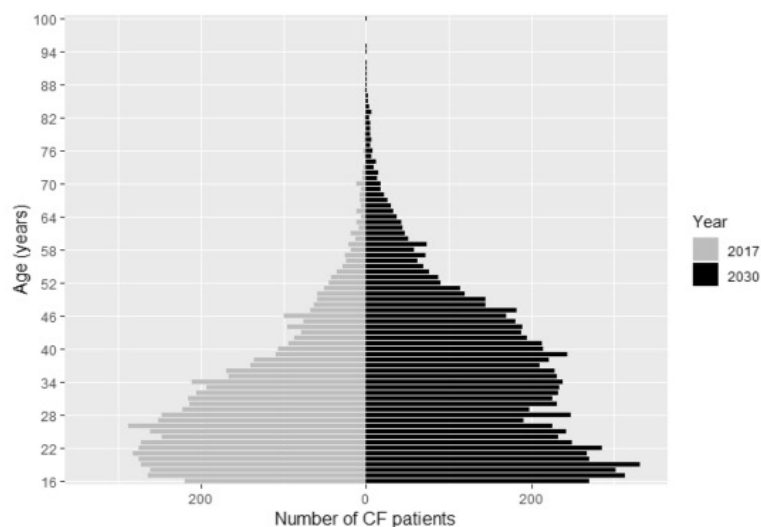
- Study is based on CF patients in the UK
- Done to predict medical needs of the CF population
- Our model takes between the no MR improvement and half MR improvement
- Confident with conservative estimates and CF population entering stage 2 of transition it is good prediction

### Projected Ages of CF Patients 16+ in UK to 2030

Total Aged 18+ Assuming...

| Year | No Mortality Rate Change | MR improve at half the rate of 2008-2017 | MR improve at the same rate of 2008-2017 |
|------|--------------------------|--|--|
| CAGR | 2.23%                    | 2.52%                                    | 2.66%                                    |
| 2013 | 5492                     | 5492                                     | 5492                                     |
| 2014 | 5700                     | 5700                                     | 5700                                     |
| 2015 | 5909                     | 5909                                     | 5909                                     |
| 2016 | 6098                     | 6098                                     | 6098                                     |
| 2017 | 6225                     | 6225                                     | 6225                                     |
| 2018 | 6390                     | 6405                                     | 6407                                     |
| 2019 | 6505                     | 6538                                     | 6544                                     |
| 2020 | 6669                     | 6723                                     | 6735                                     |
| 2021 | 6759                     | 6835                                     | 6856                                     |
| 2022 | 6881                     | 6982                                     | 7013                                     |
| 2023 | 7011                     | 7141                                     | 7184                                     |
| 2024 | 7124                     | 7284                                     | 7342                                     |
| 2025 | 7248                     | 7442                                     | 7517                                     |
| 2026 | 7402                     | 7633                                     | 7726                                     |
| 2027 | 7532                     | 7801                                     | 7915                                     |
| 2028 | 7659                     | 7969                                     | 8106                                     |
| 2029 | 7841                     | 8196                                     | 8358                                     |
| 2030 | 7988                     | 8390                                     | 8579                                     |

### Age distribution of UK patients with CF aged 16 & Older

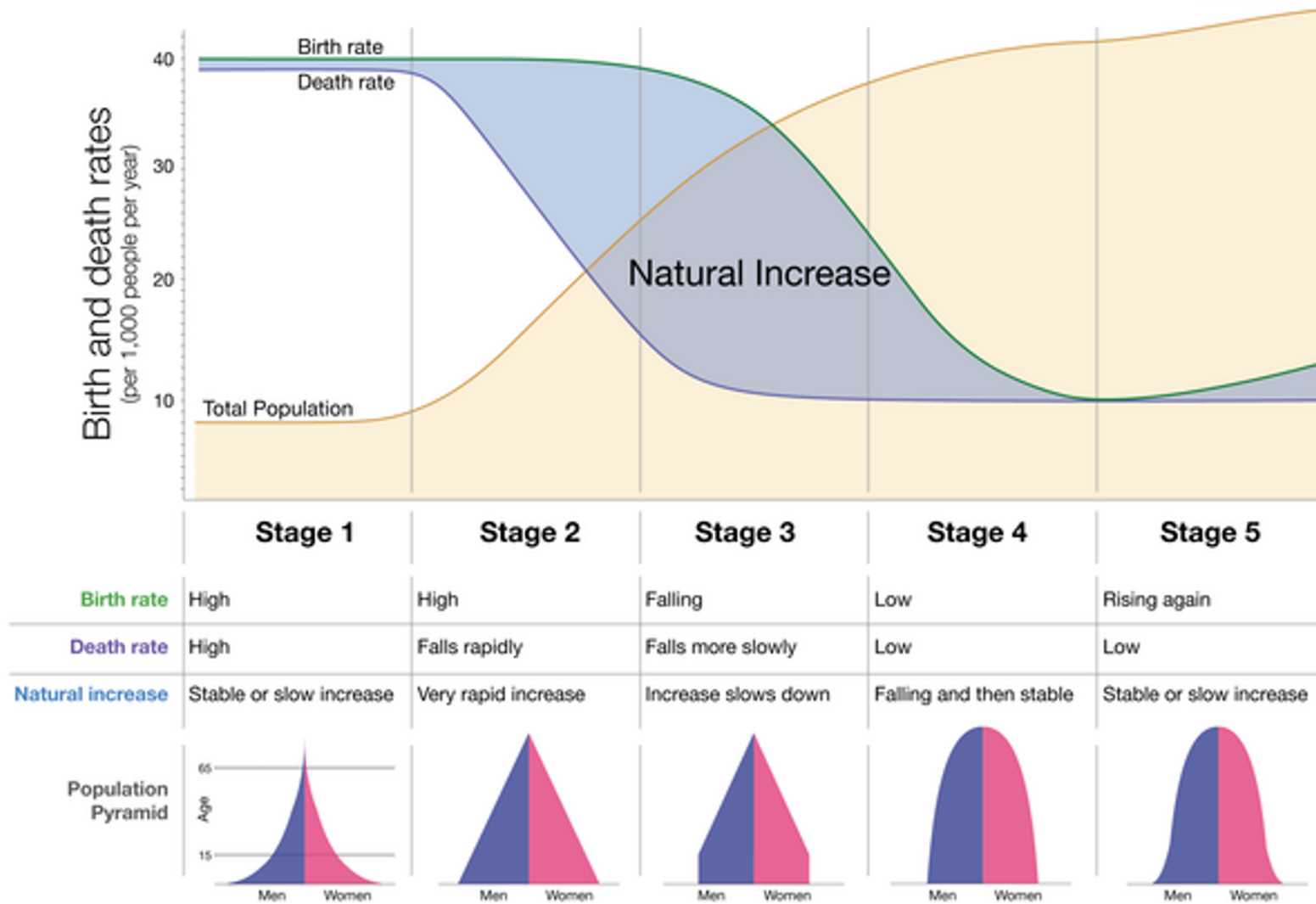


(2) The changing demography of the cystic fibrosis population: forecasting future numbers of adults in the UK



## The demographic transition in 5 stages

Our World  
in Data



The author Max Roser licensed this visualisation under a CC BY-SA license. You find more information at the source: <http://www.OurWorldInData.org/world-population-growth>

From Our World in Data

# What will move the model in the next 2 years?



## Downside

- ✗ **Lower than expected uptake** of Trikafta in the US/EU
- ✗ **Delay in release** of new triplet combination therapy
- ✗ **Lower than current portfolio drug price** (see no reason as the drug is more effective with larger treatment population)
- ✗ Pipeline **failures in all the three disease** segments
- ✗ **Partnership charges fail** to bear fruit
- ✗ Legislation is released **requiring drug prices to be lowered**
- ✗ **Competitor enters the CF modulator space** and creates a similarly effective treatment

## Upside

- ✓ **Faster than expected uptake** of Trikafta in the US/EU
- ✓ **On-time release** of the new triplet combination therapy
- ✓ **Equal or greater than current portfolio drug price** (will at least be equal to current Trikafta price, as the drug is more effective with a larger treatment population)
- ✓ Pipeline **success in two disease** segments
- ✓ Partnership charges **create meaningful research assets** and advance/create drugs in Vertex's pipeline
- ✓ Legislation is not released requiring the drug price to be lowered
- ✓ Competitors continue to **focus on treating the underlying symptoms** of CF and do not enter the modulator space

## *Dominant CF portfolio with room to expand*

### YoY Growth

- Growth higher than US population to account for demographic shift as people are now living longer
- Used the US Cystic Fibrosis Registry to estimate total number of patients in US

### Penetration Rate

- Penetration rate grows overtime as agreements are signed
- Forecast a bump in 2025 due to release of the new three molecule combination (delayed by about 1.5 years)
- Vertex has estimated a total of 90% of patients can be treated with current therapies

### Price

- We used the price per each drug to project forward
- Used the trikafta price to predict triplet price

## *Cystic Fibrosis Breakdown EU and Other Regions*

### YoY Growth

- Growth of Cystic Fibrosis Patients was kept at a 2.2% rate, higher than the population growth rate for two reasons
- The EU Cystic Fibrosis registry is younger than the US Registry, and there is still growth from people registering that were not previously registered
- “Pockets” of Cystic Fibrosis being found as East European countries gain access to medical care/testing

### Price

- EU price per drug at a 25% discount to US price
- We added an additional 15% in for margin of safety for a total discount of 40%
- European Healthcare market is less fragmented due to government health systems giving them increased bargaining power

### Penetration Rate

- Due to the confidentiality of purchase agreements timelines and issues projecting country by country we choose to project a rate for the entire EU
- The quality of Vertex’s therapeutics improving outcomes will increase uptake of the company’s products, even in the strict healthcare market in the EU

### Other Regions

- Vertex does not break out other region revenue or what the full list of countries are
- We chose to take a flat percentage of EU revenue as within the past five years the other region revenue as a percent of EU product revenue had stabilized at near 23%

## Cystics Fibrosis Pricing Concerns

| Pricing Information |            |
|---------------------|------------|
| TRIKAFTA            | \$ 311,000 |
| SYMDEKO/SYMKEVI     | \$ 292,000 |
| ORKAMBI             | \$ 272,000 |
| KALYDECO            | \$ 300,000 |

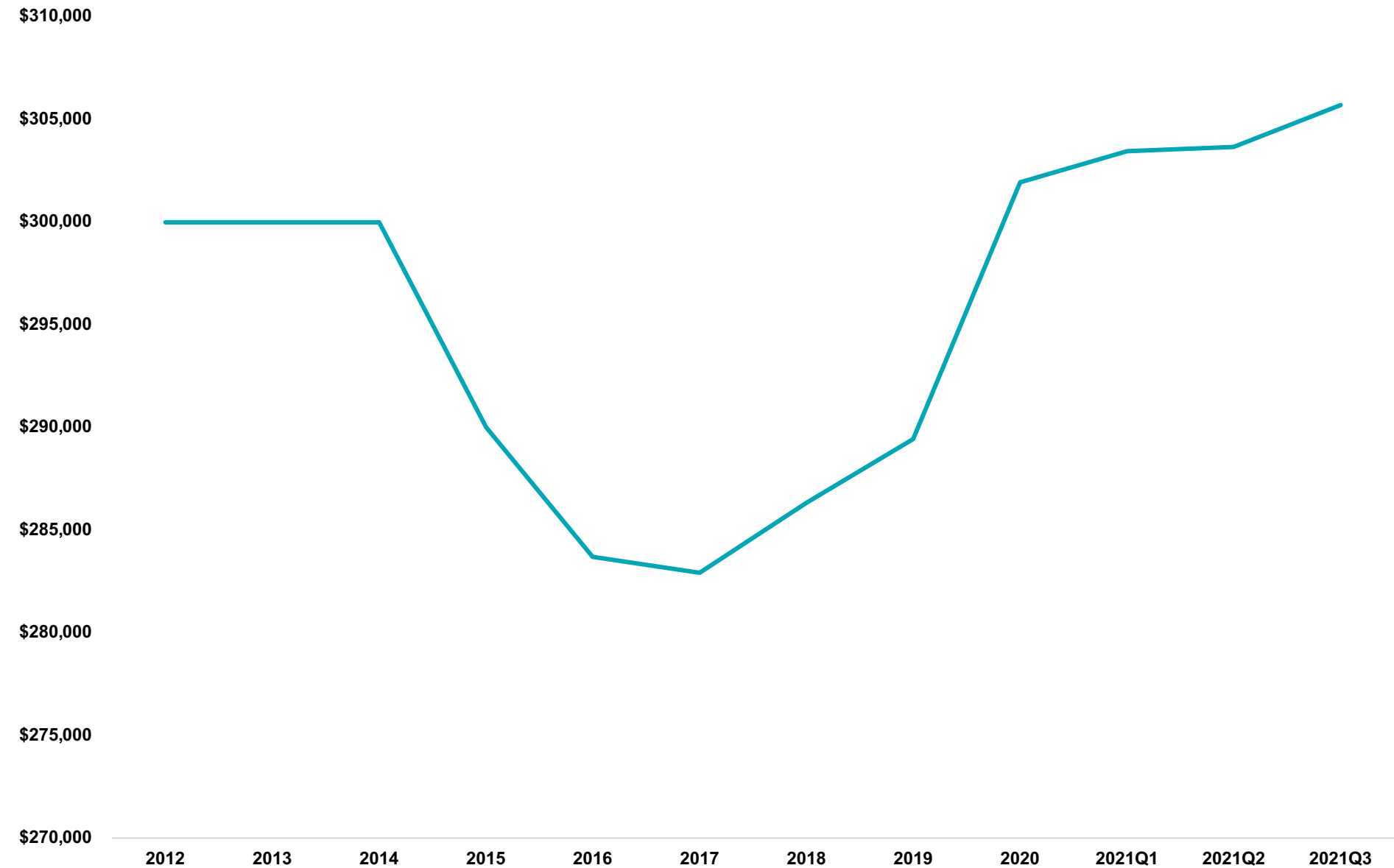
## US v.s. EU

- For EU a 40% discount is assumed vs US prices
- EU prices are pressured to be low because the negotiating block is less fragmented
- Cystic Fibrosis in US not subject to the same pressures because of the high insurance rates of CF patients
- Vertex has increased bargaining power in the US vs EU due to more segmented health providers

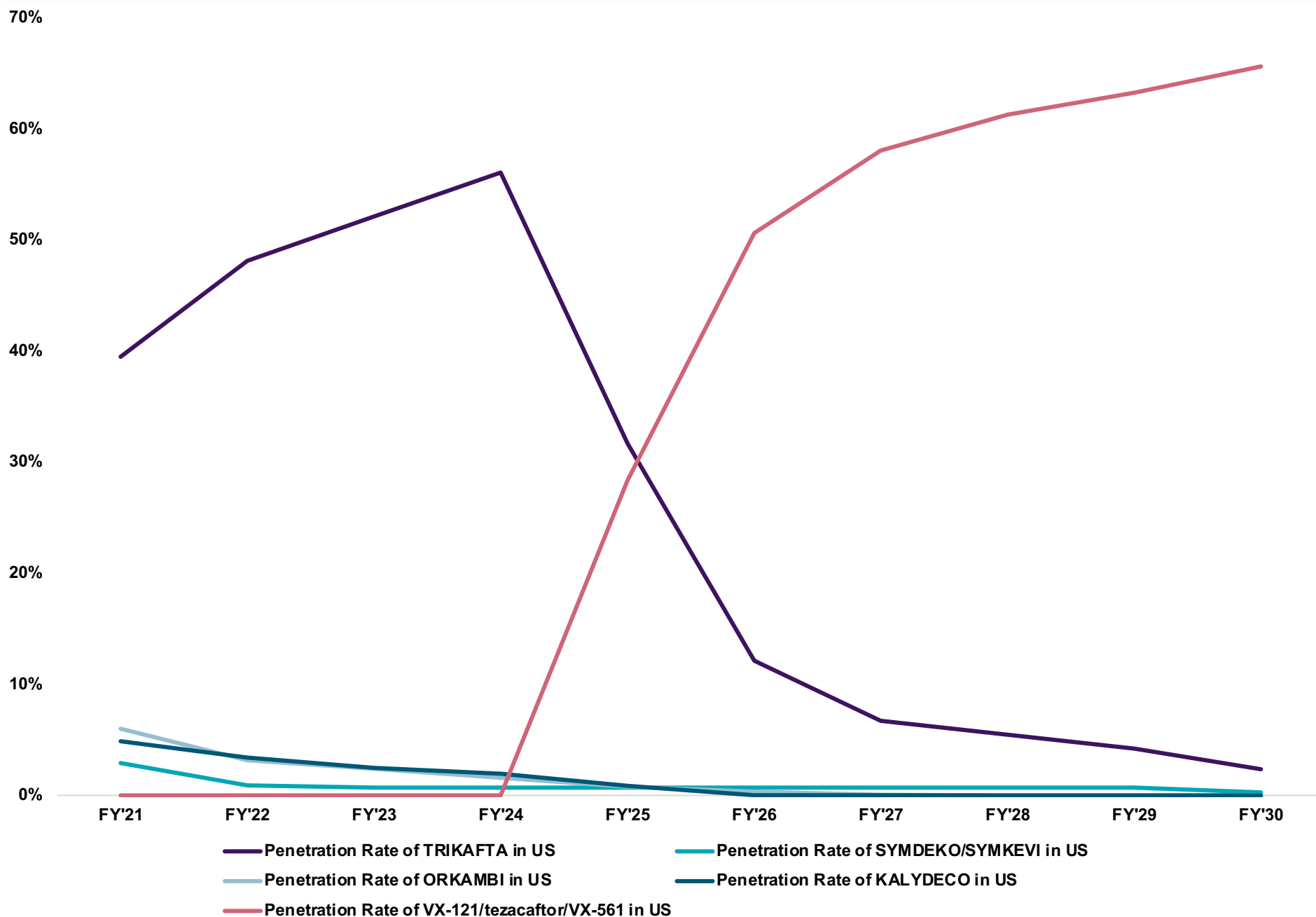
## Insurance Coverage of CF Patients in the US

| Insurance Coverage in 2019                 |              |                 |              |         |
|--|--------------|-----------------|--------------|---------|
|  | Age < 18 (%) | Age 18 - 25 (%) | Age > 26 (%) | All (%) |
| Number of Individuals (n)                  | 13,607       | 5,976           | 11,226       | 30,809  |
| Health insurance (e.g., private insurance) | 50.8         | 63.9            | 65.2         | 58.6    |
| Medicare/Indian Health Services            | 1.1          | 5.8             | 25.2         | 10.8    |
| Medicaid/state programs                    | 54.5         | 41.7            | 25.4         | 41.4    |
| TriCare or other military health plan      | 3.4          | 2.2             | 1.9          | 2.6     |
| Other                                      | 1.7          | 1.5             | 1.8          | 1.7     |
| No health insurance                        | 0.6          | 1.3             | 1.1          | 0.9     |

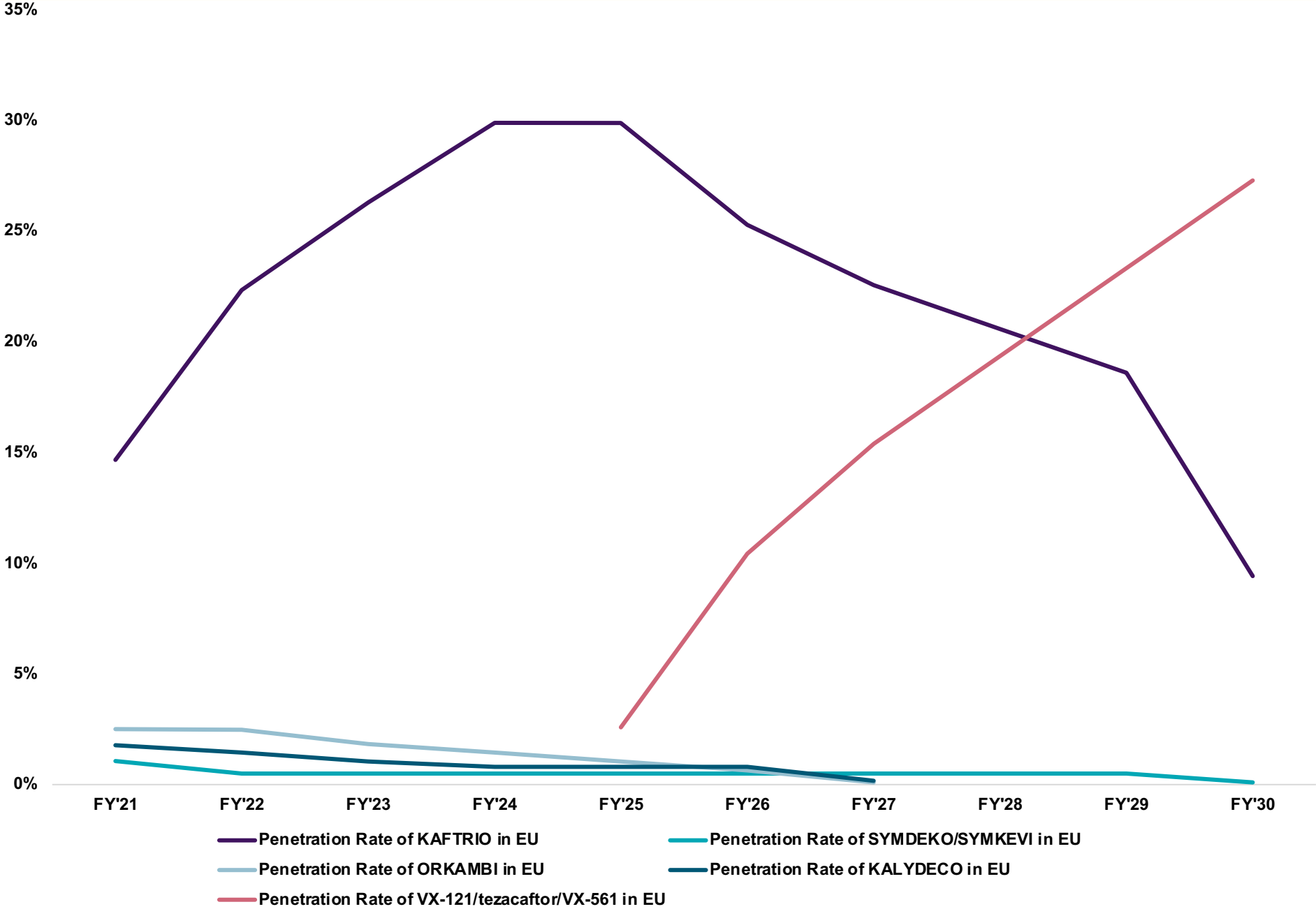
*Breakdown of the average price paid for drugs leading into revenue*



# CF Penetration Rates Over the Projection Period (US)

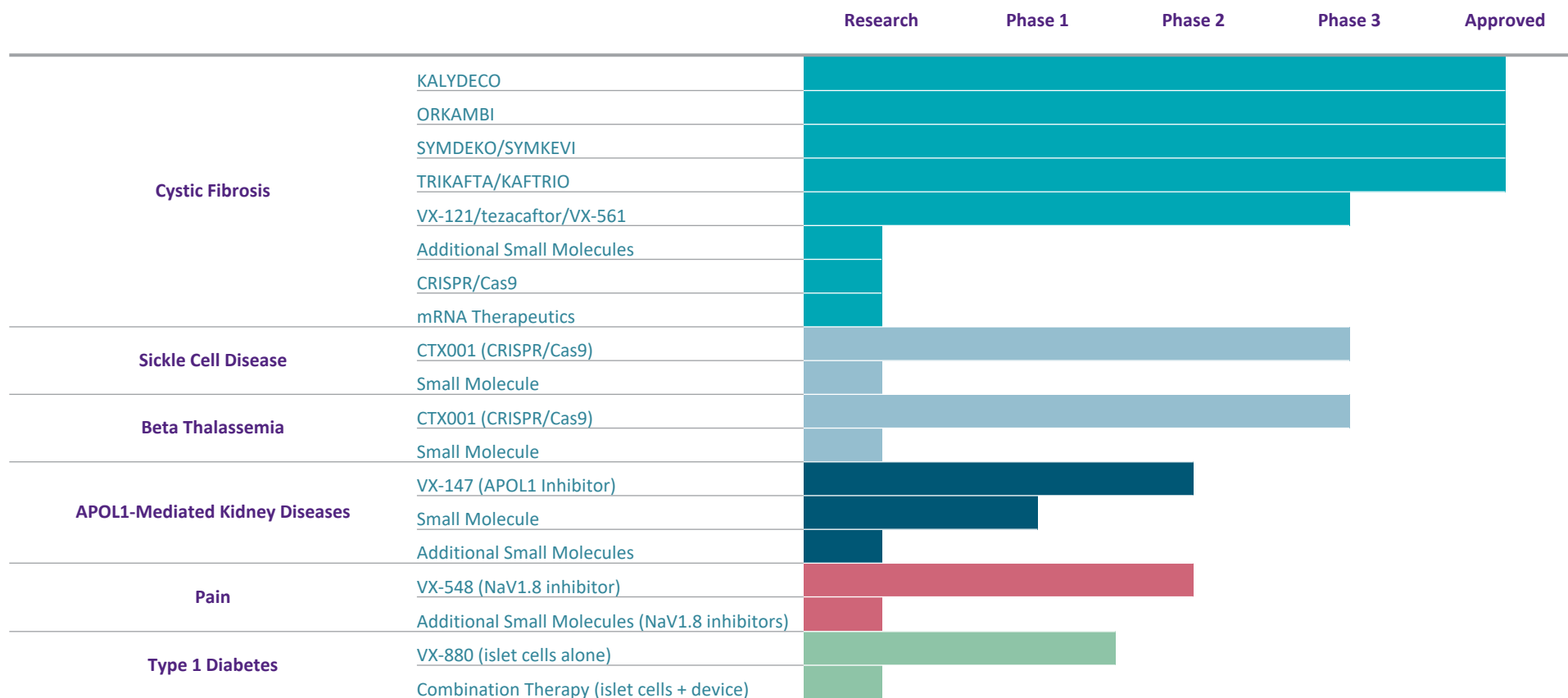


# CF Penetration Rates Over the Projection Period (US)

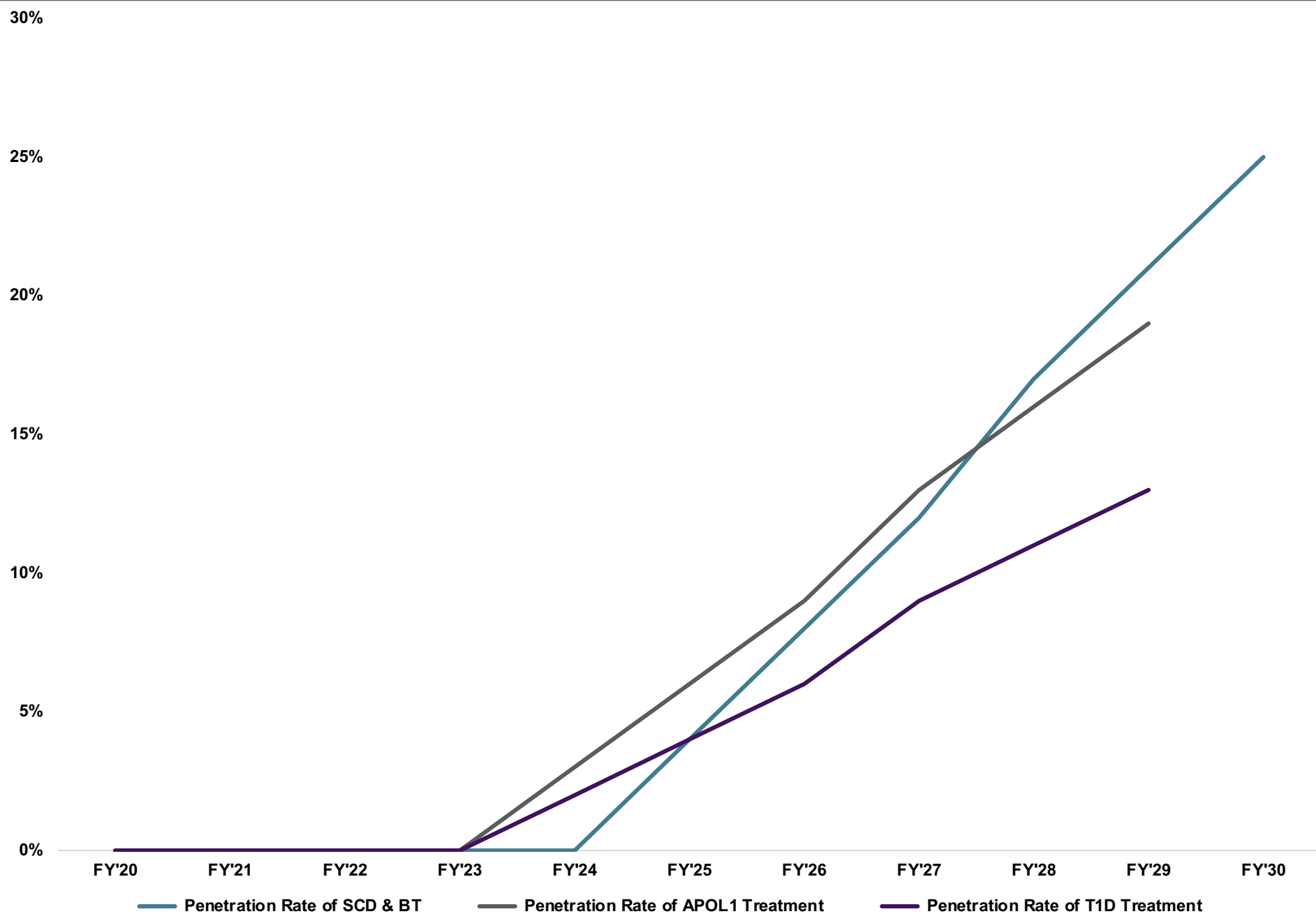




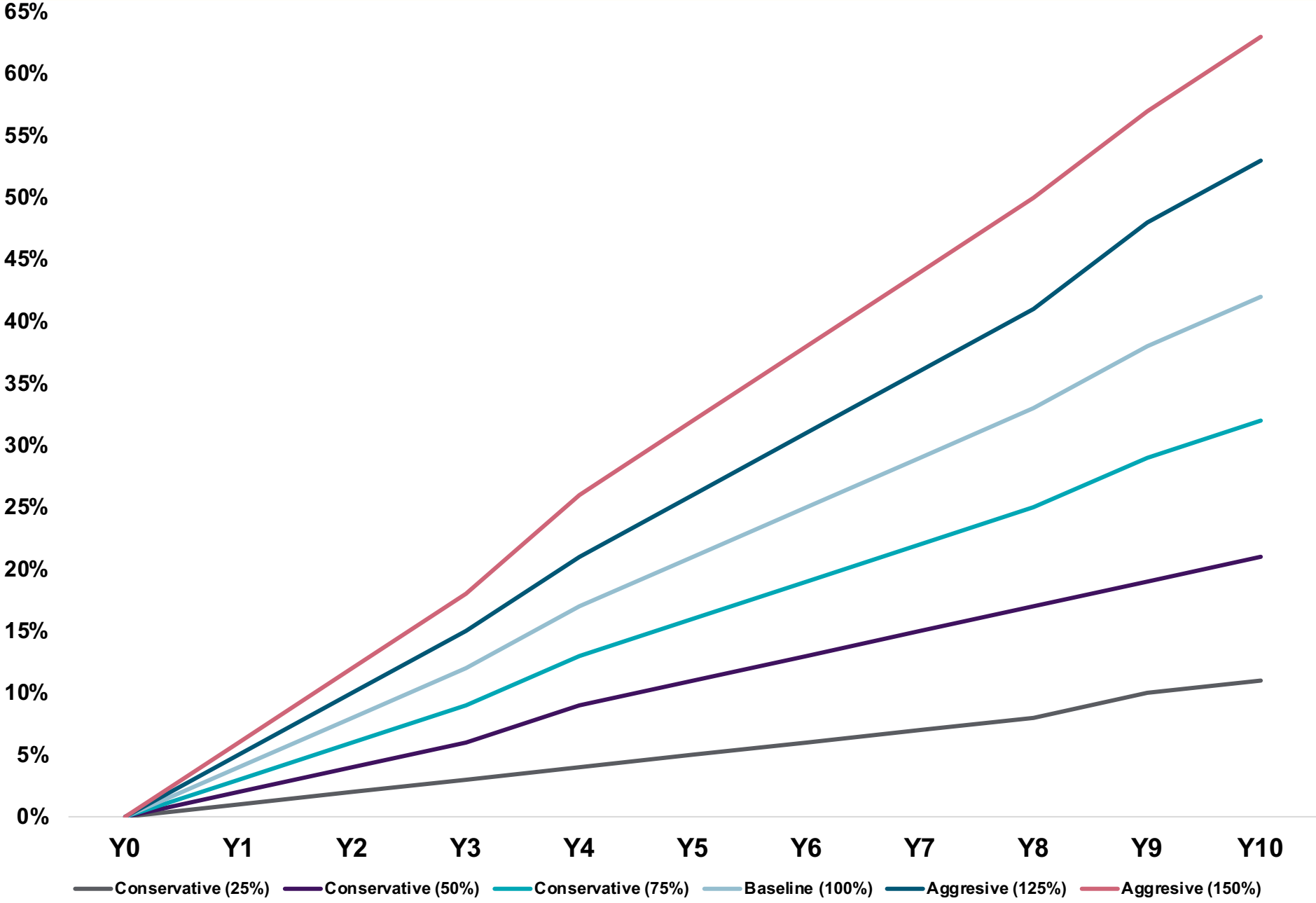
# Full Vertex Portfolio Timeline



# Pipeline Penetration Rates Over the Projection Period (US)



# Rare Disease (HIV) Drug Uptake Curves



## SCD & BT Breakdown

### Patient Population

- Combined SCD and BT patients into one population (BT represents roughly 1,000 patients)
- CDC has the most reliable count, and only for US patients
- Population is grown at the US population rate

### Patients Eligible to be Treated

- Since CTX001 is a “cure” patient population is reduced by already cured patients
- Vertex has estimated between 25-75% of patients can be treated, we start a 40% eligible treatment rate and increase over the life of the drug as treatment protocols improve

### Penetration Rate

- Used a baseline Penetration Rate from drug uptake study

|                    | Projection Year |    |     |     |     |     |     |     |     |     |     |
|--------------------|-----------------|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|                    | Y0              | Y1 | Y2  | Y3  | Y4  | Y5  | Y6  | Y7  | Y8  | Y9  | Y10 |
| Conservative (25%) | 0%              | 1% | 2%  | 3%  | 4%  | 5%  | 6%  | 7%  | 8%  | 10% | 11% |
| Conservative (50%) | 0%              | 2% | 4%  | 6%  | 9%  | 11% | 13% | 15% | 17% | 19% | 21% |
| Conservative (75%) | 0%              | 3% | 6%  | 9%  | 13% | 16% | 19% | 22% | 25% | 29% | 32% |
| Baseline (100%)    | 0%              | 4% | 8%  | 12% | 17% | 21% | 25% | 29% | 33% | 38% | 42% |
| Aggressive (125%)  | 0%              | 5% | 10% | 15% | 21% | 26% | 31% | 36% | 41% | 48% | 53% |
| Aggressive (150%)  | 0%              | 6% | 12% | 18% | 26% | 32% | 38% | 44% | 50% | 57% | 63% |

### Estimated Cost

- Conservatively taking a 40% of lifetime SCD treatment cost
- Product cost will likely be higher due to the quality-of-life improvement, and lowering of risk for insurance companies
- In clinical trials CTX001 has 100% success in reducing the
  - ▶ Need for transfusions
  - ▶ Pain crises

## CTX-001 Chance of Approval Calculation

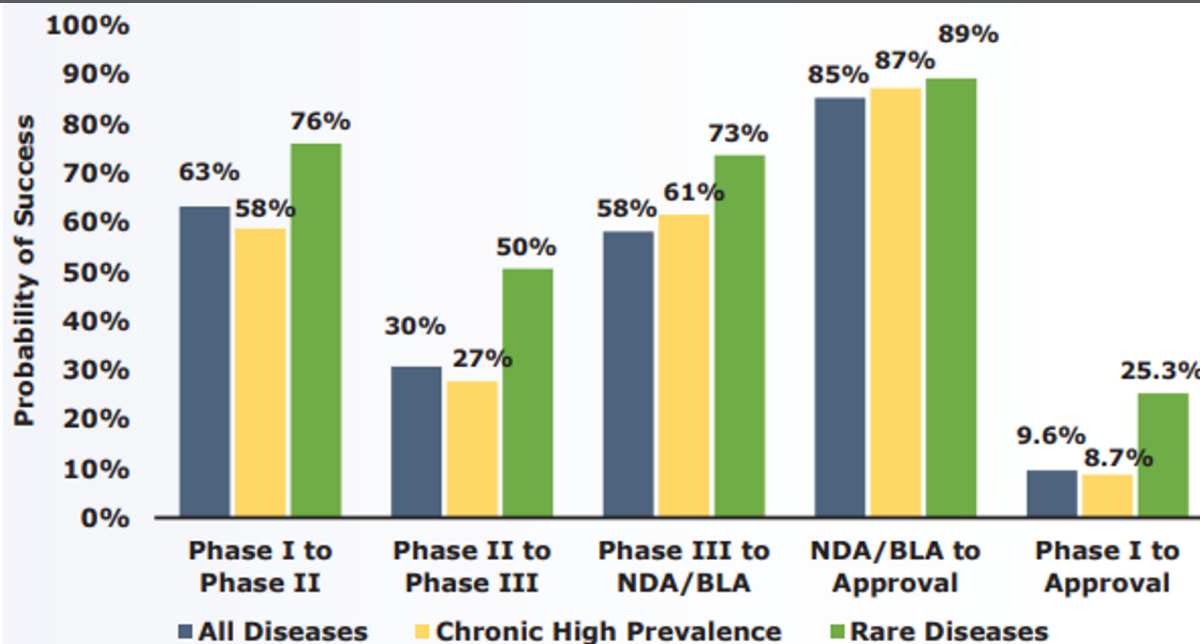
### CTX-001 Stage

- CTX is currently in-between the Phase III to NDA/BLA and NDA/BLA to Approval stage
- Currently working with regulators to finalize the filing package for CTX001 and anticipate filing for approval in the next 18 to 24 months

### Calculating Chance of Approval

- Used Rare Disease rates
- Phase III to NDA/BLA: 73%
- NDA/BLA to Approval: 89%
- Adjusted rate of 64.97% to be approved

### Probability of Success Rare Disease and High Prevalence



## MKD Breakdown

### Patient Population

- 100,000 patients in the US and Eutopre with non-diabetic primary proteinuric kidney disease
- Patient population grown at population growth rate

### Penetration Rate

- Used a conservative 50% Penetration Rate from drug uptake study

|                    | Projection Year |    |     |     |     |     |     |     |     |     |     |
|--------------------|-----------------|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|                    | Y0              | Y1 | Y2  | Y3  | Y4  | Y5  | Y6  | Y7  | Y8  | Y9  | Y10 |
| Conservative (25%) | 0%              | 1% | 2%  | 3%  | 4%  | 5%  | 6%  | 7%  | 8%  | 10% | 11% |
| Conservative (50%) | 0%              | 2% | 4%  | 6%  | 9%  | 11% | 13% | 15% | 17% | 19% | 21% |
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| Baseline (100%)    | 0%              | 4% | 8%  | 12% | 17% | 21% | 25% | 29% | 33% | 38% | 42% |
| Aggressive (125%)  | 0%              | 5% | 10% | 15% | 21% | 26% | 31% | 36% | 41% | 48% | 53% |
| Aggressive (150%)  | 0%              | 6% | 12% | 18% | 26% | 32% | 38% | 44% | 50% | 57% | 63% |

### Estimated Cost

- \$60,000 used for the cost as that is the cost for current treatments
- Note that this number is conservative, and this drug would likely be selling for \$100,000+

### Competitors

| Company                | Drug Name       | Modality       | Mechanism   | Phase | RoA  |
|------------------------|-----------------|----------------|---|-------|--|
| MNK                    | H.P. Acthar Gel | Peptide        | Corticotropin injection   | IV    | Intramuscular (IM), Oral (PO), Subcutaneous (SQ) |
| RTRX                   | Sparsentan      | Small Molecule | Dual antagonist of endothelial receptor type A (ET <sub>A</sub> ) and angiotensin II receptor type 1 (AT <sub>1</sub> ) | III   | Oral (PO)  |
| CCXI                   | CCX140          | Small Molecule | Chemokine Receptor 2 (CCR2) inhibitor   | II    | Oral (PO)  |
| Complexa, Inc.         | CXA-10          | Small Molecule | Upregulation of Nrf2 pathways; inhibition of NF-κB and TLR4; inhibition of xanthine                                     | II    | Oral (PO)  |
| PFE                    | PF-06730512     | Biologic       | SLIT2 antagonist  | II    | Intravenous (IV), Subcutaneous (SQ)              |
| AUPH                   | Voclosporin     | Small Molecule | Calcineurin inhibitor   | II    | Oral (PO)  |
| RETA                   | Bardoxolone     | Small Molecule | Activator of the KEAP1-Nrf2; inhibitor of pro-inflammatory transcription factor NF-κB                                   | II    | Oral (PO)  |
| Angion Biomedica Corp. | ANG-3070        | Small Molecule | Fibronectin inhibitor   | I     | Oral (PO)  |
| Goldfinch Bio          | GFB-887         | Small Molecule | TRPC5 ion channel inhibitor   | I     | -  |
| VRTX                   | VX-147          | Small Molecule | APOL1 inhibitor   | I     | Oral (PO)  |

## VX-147 Chance of Approval Calculation

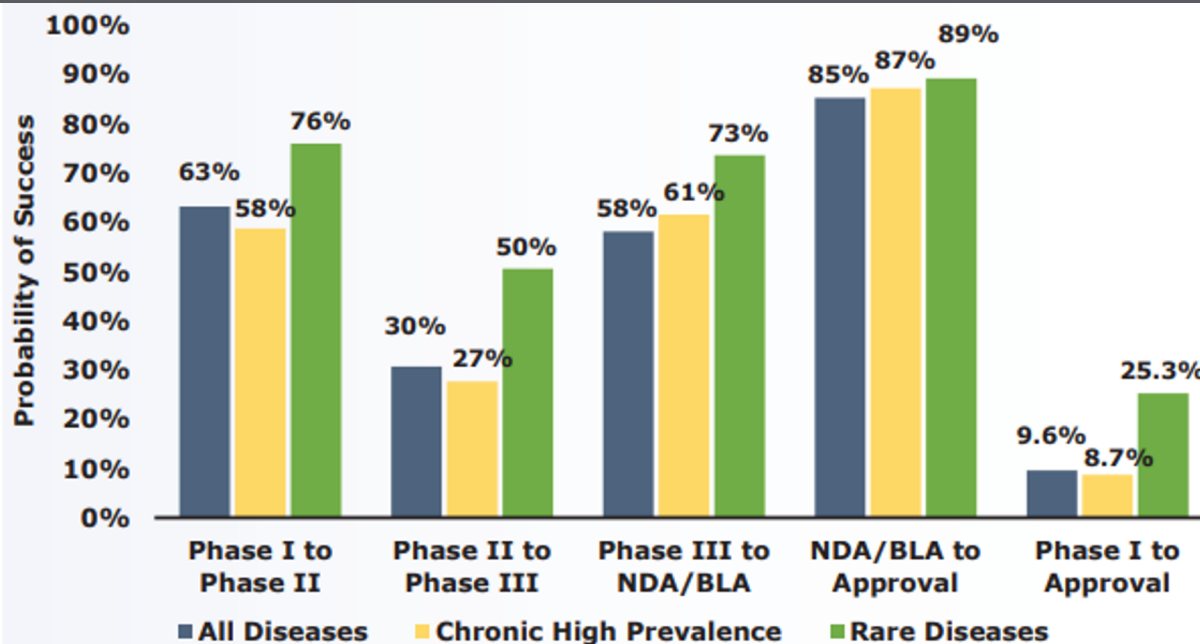
### VX-147 Stage

- Phase II evaluating safety and efficacy
- Proof of concept results expected to be released 2H21

### Calculating Chance of Approval

- Rare disease rates
- Phase II to approval success rate: ~32%

### Probability of Success Rare Disease and High Prevalence



# Valuation Appendix Type 1 Diabetes



## T1 Diabetes Breakdown

### Patient Population

- 60,000 patients with type 1 diabetes who are eligible for treatment (symptomatic hypoglycemia episode patients)
- Patient population growth at US population growth rate

### Penetration Rate

- VX-880 is a cure treatment so patient population is reduced after treatment, used conservative 75% uptake curve

|                    | Projection Year |    |     |     |     |     |     |     |     |     |     |
|--------------------|-----------------|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|                    | Y0              | Y1 | Y2  | Y3  | Y4  | Y5  | Y6  | Y7  | Y8  | Y9  | Y10 |
| Conservative (25%) | 0%              | 1% | 2%  | 3%  | 4%  | 5%  | 6%  | 7%  | 8%  | 10% | 11% |
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| Aggressive (125%)  | 0%              | 5% | 10% | 15% | 21% | 26% | 31% | 36% | 41% | 48% | 53% |
| Aggressive (150%)  | 0%              | 6% | 12% | 18% | 26% | 32% | 38% | 44% | 50% | 57% | 63% |

### Estimated Cost

- Rough estimated cost for cell treatment is \$400,000 per patient

### Competition

- No competitors in the space, Vertex is the company the FDA has allowed to dose patients with naked cells



## VX-880 Chance of Approval Calculation

### VX-880 Stage

- Vertex initiated a Phase I/II study evaluating VX-880

### Calculating Chance of Approval

- Rare disease rates
- Phase II to approval success rate: ~32%

### Probability of Success Rare Disease and High Prevalence

