

INDEX GUIDELINE

Solactive Pharma Breakthrough Value

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Introduction

This document (the “Guideline”) is to be used as a guideline with regard to the composition, calculation and maintenance of the Solactive Pharma Breakthrough Value Index. Any amendments to the rules made to the Guideline are approved by the Oversight Committee. The Index is owned, calculated, administered and published by Solactive AG (“Solactive”) assuming the role as administrator (the “Index Administrator”) under the Regulation (EU) 2016/1011 (the “Benchmark Regulation” or “BMR”). The name “Solactive” is trademarked.

The Guideline and the policies and methodology documents referenced herein contain the underlying principles and rules regarding the structure and operation of the Index. Solactive does not offer any explicit or tacit guarantee or assurance, neither pertaining to the results from the use of the Index nor the level of the Index at any certain point in time nor in any other respect. Solactive strives to the best of its ability to ensure the correctness of the calculation. There is no obligation for Solactive – irrespective of possible obligations to issuers – to advise third parties, including investors and/or financial intermediaries, of any errors in the Index. The publication of the Index by Solactive does not constitute a recommendation for capital investment and does not contain any assurance or opinion of Solactive regarding a possible investment in a financial instrument based on this Index.

1. Index Specifications

The Solactive Pharma Breakthrough Value Index (the “**Index**”) is an equity index owned by Solactive AG (the “**Index Owner**”) and is calculated and distributed by Solactive AG (the “**Calculation Agent**”) and is administered by Solactive AG assuming the role as administrator (the “**Index Administrator**”) under the Regulation (EU) 2016/1011 (the “**Benchmark Regulation**” or “**BMR**”).

The Index aims to track the performance of a basket of stocks of companies that are actively engaged in the research, development and/or manufacturing of orphan drugs. The index selects stocks of such companies that meet certain size and liquidity requirements, across various equity markets, using a two-fold approach that is primarily based on the trend in the valuation of a company’s orphan drug portfolio and its net assets.

The Index is a net total return index, i.e. dividends are reinvested net of tax. The applicable withholding tax rates used to calculate the Net Total Return version can be accessed (under the title “Withholding Tax Rates”) on the Calculation Agent’s website at: <http://www.solactive.com/news/documents/>.

The price of the Index (the “**Index Value**”) is calculated and published in US Dollars.

1.1 Short Name and ISIN

Name	ISIN	Currency	Type	RIC	BBG Ticker
Solactive Pharma Breakthrough Value Index	DE000SLA30N4	USD	NTR	.SOLBIOT	SOLBIOT Index
Solactive Pharma Breakthrough Value Index PR	DE000SL0KCS1	USD	PR	.SOLBIOTP	

1.2 Initial Value

The Index Value at the close of trading on the start date 09 March 2012 was set to be equal to a value of 100. The Index was officially launched on the Index Inception Date.

1.3 Distribution

The Index is published on the website of the Index Administrator (www.solactive.com) and is, in addition, available via the price marketing services of Boerse Stuttgart AG and is distributed to all affiliated vendors. Each vendor decides on an individual basis as to whether they will distribute/display the Index via their information systems.

1.4 Prices and Calculation Frequency

The Index Value is calculated on each Business Day based on the prices of the relevant Index Components on the respective Exchanges on which they are listed. For the purposes of calculating the Index Value on a Business Day, the most recent prices of all relevant Index Components are used. Further, prices of Index Components not listed in the Index Currency are converted into the Index Currency using the current

Intercontinental Exchange (the „ICE“) spot foreign exchange rate. Should there be no current price available for an Index Component, the most recent price or the Trading Price for the preceding Trading Day is used in the calculation.

The Index Value is calculated on each Business Day from 9:00am to 10:30pm, CET. In the event that data cannot be provided to Reuters or to the pricing services of Boerse Stuttgart AG the Index cannot be distributed.

1.5 Weighting

On each Adjustment Day the Index Components are weighted in accordance with the methodology described in *Section 2.2 Ordinary Adjustment*.

1.6 Index Committee

A committee composed of staff from the Index Owner and shall be responsible for decisions regarding the composition of the Index as well as any amendments to the rules (in this document referred to as the “**Index Committee**”). The future composition of the Index shall be determined by the Index Committee on the Selection Days according to the methodology set out in *Section 2.1 Selection of Index Components* of this document. Upon the occurrence of any Extraordinary Event, the Index Committee, in its sole and absolute discretion, shall make decisions that may affect the composition of the Index and implement any necessary adjustments.

Members of the Index Committee may recommend changes to this Index Methodology Document and submit them to the Index Committee for approval.

1.7 Publication

All specifications and information relevant for calculating the Index Value are made available on the webpage:

<http://www.solactive.de> and the relevant sub-page:

<https://www.solactive.com/?s=Solactive%20Biotechnology&index=DE000SLA30N4>.

1.8 Historical Data

Historical data will be maintained from the launch of the Index on the Index Inception Date.

1.9 Licensing

Licences to use the Index as a benchmark for derivative instruments are issued to stock exchanges, banks, financial services providers and investment houses by the Index Owner.

1.10 Index Universe

On each Selection Day that occurs in the month of March, the Index Universe shall be determined based on orphan drug related company data provided by EvaluatePharma as described below. On each Selection Day that occurs in the month of September, the Index Universe shall remain unchanged from the Index Universe determined on the immediately preceding Selection Day.

An “orphan drug” is a pharmaceutical product that has been developed specifically to treat rare diseases or disorders. The assignment of “orphan” status to any drugs developed to treat a rare disease is a matter of public policy in many countries and has resulted in medical breakthroughs that may not have otherwise been achieved due to the economics of drug research and development.

“**EvaluatePharma**” are an independent third-party provider of consensus forecasts of leading industry analysts and analysis of the pharmaceutical and biotechnology healthcare sectors providing exclusive and trusted market intelligence into global performance. They are a part of the Evaluate Group whose official website can be

accessed through the url: www.evaluategroup.com. Evaluate Group is headquartered in London with staff in Europe, United States, Japan and India with over 85 analysts and about 150 employees globally. They serve over 200 clients globally and have thousands of users. Further information on their team of experts and analysts can be accessed through the url: <http://www.evaluategroup.com/public/Expertise.aspx>.

EvaluatePharma maintain a database of global publically listed pharmaceutical and biotechnology companies which, as of 4th September 2017, contained 2,335 companies. They build their database from a drug level upwards; tagging drugs from the earliest possible stage in the development cycle (from research project, pre-clinical, phases I-III and marketed) to their relevant company, pharmaceutical class, diseases, mechanism of action and EphMRA code (among many other classifications).

As part of their data collection process, they identify drugs that have been granted 'Orphan Drug Status' by the three regulatory bodies that can provide this designation:

1. The US Food and Drug Administration (FDA): FDA Orphan Database:
<https://www.accessdata.fda.gov/scripts/opdlisting/ood/>
2. The European Medicines Agency (EMA): EMA Orphan Database:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/orphan_search.jsp
3. NIBIO Orphan Database:
<https://www.nibiohn.go.jp/shinko/orphan/english/index.html>

To enhance this list of drugs with orphan designations, EvaluatePharma apply a further layer of analysis to produce a 'pure' orphan list, which includes the following criteria:

- First indication (disease) approved is for an orphan condition.
- Products expected to generate more than 25% of sales from their orphan indications. This has led to the exclusion of drugs such as Avastin, Enbrel, Herceptin, Humira and Remicade, all of which have orphan designations for indications contributing less than 25% of sales.
- Trial sizes; with smaller Phase III trials suggesting orphan status.
- Drug pricing, higher prices were taken as an indicator of orphan status.

Orphan drugs are then tagged to the relevant company that owns the intellectual property and marketing rights for them within the EvaluatePharma database.

To determine the Index Universe, EvaluatePharma produces a list of companies that are involved in Orphan Drugs by running a search query with the following criteria: publically listed companies with one or more drugs that have been granted an orphan designation and are either in development (R&D) or approved for marketing (orphan drugs that have been suspended or abandoned in R&D are not included).

From the above list of companies that form the Index Universe, EvaluatePharma then apply further analysis to show the following for each company for the purposes of this Index:

- Company name
- Country where it is headquartered
- Total company revenues (current and forecast)
- Orphan drug revenues (current and forecast)
- Aggregate Net Present Values (NPV's) for orphan drugs
- Pipeline / portfolio analysis:
 - Count of orphan drugs in development
 - Count of non-orphan drugs in development
 - Count of approved/marketed orphan drugs
 - Count of approved/marketed non-orphan drugs

In addition to the above, EvaluatePharma publish an annual Orphan Drug report that provides a 5 year, forward-looking view of the key drugs, companies, market dynamics and growth drivers on the orphan drug/rare disease market. The Orphan Drug Report is publicly available and the 2017 edition can be downloaded from the web url: www.evaluategroup.com/orphandrug2017.

The report draws its data from the EvaluatePharma database, the three Orphan disease databases and various publicly available documents (including company reports and regulatory filings). The written analysis is provided by their in-house team of analysts, EP Vantage, who come from a variety of backgrounds including journalism, buy-side and sell-side analyst and strategy roles within large pharmaceutical companies.

Each year the report includes:

- Definitions of orphan drugs and rare diseases
- Financial incentives for companies that develop and market orphan drugs
- Evaluate's methodologies
- Worldwide Orphan Drug Sales (2000-2022)
- Top 100 USA Drug Cost per Patient per Year 2012-2016

- 2016: USA Revenue per Patient per Year for Top 20 Selling Orphan Drugs
- Worldwide Orphan Drug Sales in 2022: Top 20 Companies
- Worldwide Orphan Drug Sales in 2022 Excluding Oncology: Top 20 Companies
- 2022: Top 20 Selling Orphan Drugs in the World
- 2022: Top 10 Selling Orphan Drugs and Pipeline in Europe
- 2022: Top 20 Orphan R&D Products based on NPV
- USA, EU & Japan Orphan Designations per Year & Cumulative (1983-2016)

On each Selection Day, any company included in the ESG Exclusions Enhanced Index as determined by Solactive is then excluded from the Index Universe. Further, any company that is not a part of the Index Universe of the ESG Exclusions Enhanced Index as of the immediately preceding Selection Day of the ESG Exclusions Enhanced Index, shall be excluded from the Index Universe.

The ESG Exclusions Enhanced Index is reconstituted by Solactive on a semi-annual basis and the methodology by reference to which the ESG Exclusions Enhanced Index is constructed, together with the most recent applicable categories and inclusion criteria, is available on the following website: [link](#).

The applicable categories and inclusion criteria of the ESG Exclusions Enhanced Index as of February 2022 are set out in Annex C of this document.

1.11 Orphan Drugs NPV Calculation

On each Selection Day, in respect of each company comprised within the Index Universe, EvaluatePharma determines and provides the Calculation Agent with the net present value of the company that is attributable to orphan drugs (the “**Orphan Drugs NPV**”) for the purposes of calculating the index. This is determined as the sum of the discounted annual future cash flows attributable to orphan drugs.

For instance, as of the Index Inception Date, the Orphan Drugs NPV calculation estimates future sales and costs in three parts - (i) using analyst consensus forecasts up to 2022, (ii) using a projection of sales, costs and resulting cash flows beyond 2022 over the life of the product up to 2037, and (iii) applying a terminal growth methodology to calculate cash flows beyond 2037, known as the product’s terminal value. A discount rate is then applied to all cash flows to express them as present values, which are summed up to calculate the Orphan Drugs NPV.

Mathematically it can be expressed as:

$$NPV = \sum_t \frac{CF_t}{(1+i)^t}$$

where:

t = time of the cash flow

i = applicable discount rate that is based on the company size as described below

CF_t = the estimated cash flow at time t

The discount rate applied to cash flows is based on the company size in order to reflect the different expected returns/risk assumptions associated with smaller companies and allow the use of weighted average cost of capital. The rates chosen are those typically used within industry and allowing us to factor in the company size and risk into valuation. As of the Index Inception Date, the discount rates used were:

- 6.5% for a large-cap company (i.e., market capitalization of over \$30bn)
- 9% for a mid-cap company (i.e., market capitalization between \$2.5bn - \$30bn)
- 11.5% for a small-cap company (i.e., market capitalization between \$250m - \$2.5bn)
- 14% for a micro-cap company (i.e., market capitalization between \$100m - \$250m)
- 14% of a nano-cap company (i.e., market capitalization below \$100m)

Further information on the calculation of Orphan Drugs NPV is available upon request from the Calculation Agent.

2. Composition of the Index

2.1 Selection of the Index Components

This section sets out the methodology used to determine the initial composition of the Index and to make periodic adjustments to the composition of the Index.

In respect of each Selection Day, the Calculation Agent shall determine the Index Components in accordance with the methodology described below:

1. If such Selection Day occurs in the month of March, the Calculation Agent shall determine the securities that constitute the Index Universe in accordance with the methodology described in *Section 1.10 Index Universe*. And, if such Selection Day occurs in the month of September, the Index Universe shall be the same as the Index Universe determined on the immediately preceding Selection Day.
2. The Calculation Agent shall select the securities that are eligible for inclusion in the Index (the “**Eligible Securities**”) from the Index Universe in the following manner:

A Security shall be deemed to be an Eligible Security if:

- a. it is listed on an Eligible Exchange;
 - b. it has, as of the Selection Day, a Free Float Market Capitalization of at least USD 200 million, unless such Security is an existing Index Component, in which case, the Free Float Market Capitalization must be at least USD 150 million;
 - c. its Three Month Average Daily Value Traded, as of the Selection Day, is at least USD 1,000,000; and
 - d. the relevant company has at least one Marketed Orphan Drug and has an Orphan Drug Revenue Share that is greater than zero;
3. On each Selection Day, an Eligible Security shall be deemed to be an Index Component if, in respect of such Eligible Security:
 - a. the Orphan Drug Revenue Share is within the top two quartiles (i.e. the median) of the Orphan Drug Revenue Shares of all Securities that satisfy criteria 2.a – 2.d above;
 - b. the relevant company has at least two (2) Marketed Orphan Drugs; and
 - c. the YoY NPV Change is greater than zero or the Estimated Book-Value Per Share is greater than the Book-Value Per Share.

Notwithstanding steps 1, 2 and 3 above, if the total number of Index Components is less than fifteen (15), then the above methodology shall be repeated without provision 3.a.

2.2 Ordinary Adjustment

The composition of the Index shall be adjusted on each Adjustment Day that is deemed to be a Rebalancing Day by the Calculation Agent.

Each Adjustment Day that occurs in the month of March and September shall be deemed to be a Rebalancing Day. In addition, if the Calculation Agent determines that the Index Component Weight of any Index Components is greater than 15% on any other Review Day, then the Adjustment Day that occurs immediately after such Review Day shall be deemed to be a Rebalancing Day.

On each SELECTION DAY each INDEX COMPONENT is weighted in accordance with the following steps

- i) Each Index Component is initially weighted equally w_i^* ;
- ii) Then, for each Index Component the maximum weight $w_{i,max}$ is calculated as:

$$w_{i,max} = \text{Min}\{w_{i,max}^{liquidity}, w_{i,max}^{ownership}\}$$

where,

$$w_{i,max}^{liquidity} = \frac{(1 - \text{Haircut}) \times \text{Liquidity Measure} \times \text{Participation} (\%)}{\text{AuM} \times \text{Turnover}}$$

$$w_{i,max}^{ownership} = \frac{\text{Market Cap} \times \text{Max Ownership}}{\text{AuM}}$$

and,

AuM refers to the maximum of total assets under management in US Dollars of ETFs tracking the index as listed in Annex D and US Dollars 50 million;

Haircut assumed to be 10%;

Liquidity Measure refers to the 3-month **AVERAGE DAILY VALUE TRADED** in US Dollars;

Market Cap refers to the **FREE FLOAT MARKET CAPITALIZATION** of a company in US Dollars;

Max Ownership assumed to be 7.5%;

Participation (%) assumed to be 100%;

Turnover refers to the hypothetical fund turnover in respect of each rebalancing date and is assumed to be 40%.

- iii) In respect of Index Components whose initial weight w_i^* is greater than $w_{i,max}$, the Target Index Weight w_i shall be set to be equal to $w_{i,max}$, and the excess weight is then calculated as follows:

$$w_{i,excess} = w_i^* - w_{i,max}$$

The cumulative excess weight is calculated as the sum of $w_{i,excess}$ in respect of all Index Components whose initial weight w_i^* is greater than $w_{i,max}$.

The cumulative excess weight is then proportionally distributed across all Index Components whose initial weight w_i^* is less than $w_{i,max}$ such that the above maximum weight cap condition is fulfilled. This can be an iterative process until 100% weight is fully allocated and all conditions above are fulfilled.

The composition of the Index shall be determined on each Selection Day in accordance with the methodology described in *Section 2.1 Selection of Index Components*. The Calculation Agent shall publish any changes made to the Index composition on the Selection Day and consequently with sufficient notice before the Adjustment Day.

2.3 Extraordinary adjustment

An extraordinary adjustment, if applicable, shall be triggered and applied in compliance with the rules set forth in the Solactive Guideline for Extraordinary Corporate Actions that is available for download at the web url: <https://www.solactive.com/wp-content/uploads/2017/02/ECA-Solactive-Guideline.pdf>.

3. Calculation of the Index

3.1 Index Formula

The Index Value on a Business Day at the relevant time is calculated in accordance with the following formula:

$$\text{Index}_t = \sum_{i=1}^n \frac{(x_{i,t} \times p_{i,t} \times f_{i,t})}{D_t}$$

where:

$x_{i,t}$ = Number of Total Shares of the Index Component i on Trading Day t

$p_{i,t}$	= Price of Index Component i on Trading Day t
$f_{i,t}$	= Foreign exchange rate to convert the Price of Index Component i on Trading Day t into the Index Currency
D_t	= Divisor on Trading Day t

In respect of the Start Date, the Divisor shall be calculated according to the following formula:

$$D_t = \frac{\sum_{i=1}^n (p_{i,t} \times f_{i,t} \times x_{i,t})}{100}$$

After the close of trading on each Adjustment Day t , the Divisor in respect of the immediately following Trading Day shall be calculated according to the following formula:

$$D_{t+1} = \frac{\sum_{i=1}^n (p_{i,t} \times f_{i,t} \times x_{i,t+1})}{\text{Index}_t}$$

where:

$x_{i,t+1}$ = Number of Total Shares of the Index Component i in respect of the immediately preceding Selection Day

In respect of a Trading Day t that is (i) not an Adjustment Day and (ii) a day on which there are no Corporate Actions, then the Divisor shall be calculated according to the following formula:

$$D_t = D_{t-1}$$

where:

$t - 1$ means the immediately preceding Business Day.

3.2 Accuracy

In respect of each Business Day, the Index Value, rounded to two decimal places, shall be published on Reuters and Bloomberg.

Trading Prices and spot foreign exchange rates used to calculate the Index Value shall be rounded to six decimal places.

Divisors shall be rounded to six decimal places.

3.3 Adjustments

Indices need to be adjusted for systematic changes in prices once these become effective. This requires the new Number of Total Shares of the affected Index Component and the Divisor to be calculated on an ex-ante basis.

Following the Index Committee's decision, the Index is adjusted for distributions, capital increases and stock splits.

This procedure ensures that the first ex quote can be properly reflected in the calculation of the Index. This ex-ante procedure assumes the general acceptance of the Index calculation formula as well as open access to the parameter values used. The calculation parameters are provided by the Calculation Agent.

3.4 Dividends and other Distributions

Dividend payments and other distributions are included in the Index. They cause an adjustment of the Divisor. The new Divisor is calculated as follows:

$$D_{t+1} = D_t \times \frac{\sum_{i=1}^n (p_{i,t} \times f_{i,t} \times x_{i,t}) - (x_{i,t} \times y_{i,t} \times g_{i,t})}{\sum_{i=1}^n (p_{i,t} \times f_{i,t} \times x_{i,t})}$$

where:

$p_{i,t}$	= Price of Index Component i on Trading Day t
$f_{i,t}$	= Foreign exchange rate to convert the Price of Index Component i on Trading Day t into the Index Currency
$x_{i,t}$	= Number of Total Shares of the Index Component i on Trading Day t
$y_{i,t}$	= Distribution of Index Component i with ex date $t + 1$ multiplied by the Dividend Correction Factor
$g_{i,t}$	= Foreign exchange rate to convert the amount of the distribution of Index Component i on Trading Day t into the Index Currency
D_t	= Divisor on Trading Day t
D_{t+1}	= Divisor on Trading Day $t + 1$

3.5 Corporate Actions

3.5.1 Principles

Following the announcement by an issuer of Index Components of the terms and conditions of a corporate action (“**Corporate Action**”), the Calculation Agent shall determine whether such corporate action has a dilutive, concentrative or similar impact on the price of the relevant Index Component. If this should be the case, the Calculation Agent shall make the necessary adjustments that are deemed appropriate in order to take into account the dilutive, concentrative or similar impact on the price of the relevant Index Components and shall determine the date on which such adjustments shall come into effect.

Amongst other things, the Calculation Agent can take into account the adjustment made by an Affiliated Exchange as a result of the corporate action with regard to option and futures contracts on the respective share traded on this Affiliated Exchange.

Adjustments to the index to account for corporate actions will be made in compliance with the Equity Index Methodology with the exception of section 2.1.4 (Rights Issue) and section 2.1.5 (Capital Decrease), which is available on the Solactive website: <https://www.solactive.com/documents/equity-index-methodology/>. This document contains for each corporate action a brief definition and specifies the relevant adjustment to the index variables. For rights issues and capital decreases the treatment described in sections 3.5.2 and 3.5.2.1 applies.

3.5.2 Rights Issues (Capital Increases)

A “**Rights Issue**” raises the Market Capitalization of a company, shareholders receive the right to pre-purchase newly issued shares for a pre-defined subscription price (“SP”) on a pro rata basis, i.e., in accordance with their existing number of the company’s shares.

The price adjustment factor (“PAF”) for a Rights Issue is calculated as follows:

$$PAF_{i,t+1} = \frac{p_{i,t}}{\left(\frac{1 * p_{i,t} + T * SP}{1 + T} \right)}$$

with:

PAF	price adjustment factor
$P_{i,t}$	Price of Index Component i on Trading Day t
T	issue terms
SP	subscription price

The theoretical close price after a Rights Issue is calculated as follows:

$$ap_{i,t+1} = \frac{p_{i,t}}{PAF_{i,t+1}}$$

with:

ap adjusted price

The number of shares prior to the ex-date is increased with the PAF. Following that, a Rights Issue does not affect the Index market capitalization and no divisor change is implemented.

$$ax_{i,t+1} = x_{i,t} * PAF_{i,t+1}$$

With:

ax adjusted fraction of shares

3.5.2.1 Capital Decreases

The opposite procedure to a Rights Issue which increases capital is a “**Capital Decrease**”. A company may offer its shareholders the option to sell their shares at an agreed price.

The price adjustment factor (“PAF”) for a Capital Decrease is calculated as follows:

$$PAF_{i,t+1} = \frac{p_{i,t}}{\left(\frac{1 * p_{i,t} - T * SP}{1 - T} \right)}$$

with:

PAF	price adjustment factor
$P_{i,t}$	price of Index Component i on Trading Day t
T	issue terms
SP	subscription price

The theoretical close price after a Capital Decrease is calculated as follows:

$$ap_{i,t+1} = \frac{p_{i,t}}{PAF_{i,t+1}}$$

with:

ap adjusted price

The number of shares prior to the ex-date is decreased with the PAF. Following that, a Capital Decrease does not affect the Index market capitalization and no divisor change is implemented.

$$ax_{i,t+1} = x_{i,t} * PAF_{i,t+1}$$

ax adjusted fraction of shares

3.5.3 Share Splits

In the case of share splits with ex-date on Trading Day $t + 1$, it is assumed that the prices change in ratio of the terms of the split. The new Number of Total Shares is calculated as follows:

$$x_{i,t+1} = x_{i,t} \times B$$

where:

$x_{i,t+1}$	= Number of Total Shares of the affected Index Component on Trading Day $t + 1$
$x_{i,t}$	= Number of Total Shares of the affected Index Component on Trading Day t
B	= Shares after the share split for every share held before the split

3.5.4 Stock Distributions

In the case of stock distributions with ex-date on Trading Day $t + 1$, it is assumed that the prices change according to the terms of the distribution. The new Number of Total Shares is calculated as follows:

$$x_{i,t+1} = x_{i,t} \times (1 + B)$$

where:

$x_{i,t+1}$	= Number of Total Shares of the affected Index Component on Trading Day $t + 1$
$x_{i,t}$	= Number of Total Shares of the affected Index Component on Trading Day t
B	= Shares received for every share held

3.6 Correction Policy

The Calculation Agent shall make the greatest possible effort to accurately calculate and maintain its indices. However, the occurrence of errors in the index determination process cannot be ruled out. In such cases, the Calculation Agent adheres to its publicly available Correction Policy which can be downloaded from the following url: <https://www.solactive.com/news/documents/>.

3.7 Market Disruption

In periods of market stress, the Calculation Agent shall calculate the Index following predefined and exhaustive arrangements set out in its publicly available Disruption Policy which can be downloaded from the following url: <https://www.solactive.com/news/documents/>.

3.8 Consequences of an Extraordinary Event

In respect of a Business Day on which an Extraordinary Event comes into effect, the Trading Price for an Index Component on such day shall be the last available market price for such Index Component quoted on the Exchange on the day the event came into effect (or, if a market price is not available for the day the event came into effect, the last available market price quoted on the Exchange on a day specified as appropriate by the Calculation Agent), as determined by the Calculation Agent, and this price is used as the Trading Price of the particular Index Component until the end of the day on which the composition of the Index is next set.

In the event of an Insolvency of an issuer of an Index Component the Index Component shall remain in the Index until the next Adjustment Day. As long as a market price for the affected Index Component is available on a Business Day, this shall be applied as the Trading Price for this Index Component on the relevant Business Day, as determined in each case by the Calculation Agent. If a market price is not available on a Business Day the Trading Price for this Index Component is set to zero. The Index Committee may also decide to eliminate the respective Index Component at an earlier point in time prior to the next Adjustment Day. The procedure in this case is identical to an elimination due to and Extraordinary Event.

4. Definitions

“Adjustment Day” means each day that occurs on the 3rd Friday of each calendar month, and if such day is not a Trading Day, the immediately following Trading Day.

“Affiliated Exchange” means, in respect of an Index Component, an exchange, a trading or quotation system on which options and futures contracts on the Index Component in question are traded, as specified by the Calculation Agent.

“Book-Value Per Share” means, in respect of a Security and a Selection Day, the book value (i.e., net asset value) of the relevant company divided by the total number of shares outstanding in the relevant share class, as published on the most recent annual company report and sourced using the FactSet Formula FF_BPS.

“Business Day” means each calendar day other than Saturdays and Sundays.

“Calculation Agent” means Solactive AG or any other appropriately appointed successor in this function.

“Capital Decrease” shall have the meaning as defined in Section 3 of the Equity Index Methodology, which is available on the Solactive website: <https://www.solactive.com/documents/equity-index-methodology/>

“Corporate Action” shall have the meaning as defined in *Section 3.5.1. Principles*.

“Daily Traded Value” means, in respect of a Security and of an Trading Day, the product of (i) the closing price of such Share (denominated in the Index Currency) as provided by the Exchange and (ii) the volume traded (measured as a number of Shares) of such Share on the Exchange during such Exchange Trading Day.

“DATA PROVIDER II” is Sustainalytics. For more information, please visit: www.sustainalytics.com.

“Delisting” means, in respect of an Index Component, an event where the Exchange announces pursuant to the Exchange regulations that the listing of, the trading in or the issuing of public quotes on the Index Component at the Exchange has ceased immediately or will cease at a later date, for whatever reason (provided delisting is not because of a Merger or a Takeover bid), and the Index Component is not immediately listed, traded or quoted again on an exchange, trading or listing system, acceptable to the Calculation Agent.

“Dividend Correction Factor” is calculated as 1 minus the applicable withholding tax rate and/or other applicable tax rate currently prevalent in the respective country. The withholding tax rates are published at the webpage <https://www.solactive.com/news/documents/> under ‘Withholding Tax Rates’ and are determined using publicly available information.

“Eligible Exchange” means an exchange listed under column ‘Exchanges’ in *Table 1: Eligible Exchanges* in Annex A.

“Estimated Book-Value Per Share” means, in respect of a Security and a Selection Day, the estimated book value (i.e., net asset value) of the relevant company divided by the total number of shares outstanding in the relevant share class, as estimated and provided by FactSet (or any reference source taking the place of FactSet and providing comparable data items, acceptable to and as determined by the Index Calculator) who are an independent third-party financial data provider.

“EvaluatePharma” shall have the meaning as defined in *Section 1.10 Index Universe*.

“Exchange” (collectively “Exchanges”) means, in respect of Index and an Eligible Security, the primary exchange where such Eligible Security has its primary listing. The Index Committee may decide to designate a different stock exchange as the “Exchange” in respect of an Eligible Security for tradability reasons, even if the relevant company is only listed there via a Stock Substitute.

“Extraordinary Event” means any of the following events:

- a Merger
- a Takeover bid
- a Delisting
- the Nationalisation of a company
- Insolvency.

“FactSet” is an independent third-party financial data provider.

“FactSet Formula” means the formula used to access specific financial data on the relevant software provided by FactSet.

“Free Float Market Capitalization” means, in respect of a Security and a Selection Day, the free float adjusted market capitalization of the relevant company. As at the date of this document Free Float Market Capitalization is calculated as the multiplication of the Free Float Percentage (as sourced from Thomson Reuters and calculated as Free Float Shares divided by Total Shares Outstanding) multiplied with the Market Capitalization in Index Currency of the share class as of the respective Selection Day.

“Index Committee” shall have the meaning as defined in *Section 1.6 Index Committee*.

“Index Component” means, in respect of a Selection Day, each Security that shall be included in the Index.

“Index Component Weight” means, in respect of a Selection Day and an Index Component, the weight determined in accordance with the methodology described in *Section 2.2 Ordinary Adjustment*.

“Index Currency” means the US Dollar (USD).

“Index Inception Date” means the date on which the Index was launched and is equal to December 07, 2017.

“Index Owner” means Solactive AG or any other appropriately appointed successor in this function.

“Index Universe” means, in respect of a Selection Day, all Securities in respect of companies that are actively engaged in the research, development and/or the manufacturing of orphan drugs and deemed to be as such by EvaluatePharma as described in *Section 1.10 Index Universe*. As of the Index Inception Date, the Index Universe consisted of stocks listed in *Table 2 Index Universe in Annex B*.

“Index Value” shall have a meaning as defined in *Section 1. Index Specifications*.

“Insolvency” occurs with regard to an Index Component if (A) all shares of the respective issuer must be transferred to a trustee, liquidator, insolvency administrator or a similar public officer as result of a voluntary or compulsory liquidation, insolvency or winding-up proceedings or comparable proceedings affecting the issuer of the Index Components or (B) the holders of the shares of this issuer are legally enjoined from transferring the shares.

“Marketed Orphan Drugs” means, in respect of a Security and a Selection Day, the Orphan Drugs that are currently manufactured and marketed by the relevant company as provided by EvaluatePharma based on the data published in the relevant company’s most recent annual company report and cross referenced with three regulatory bodies (US Food and Drug Administration, European Medicines Agency and NIBIO Orphan databases).

“Merger” means, in respect of an Index Component, any of the following events:

- (i) a change in the security class or a conversion of this share class that results in a transfer or an ultimate definite obligation to transfer all the shares in circulation to another legal person,
- (ii) a merger (either by acquisition or through forming a new structure) or a binding obligation on the part of the issuer to exchange shares with another legal person (except in a merger or share

exchange under which the issuer of this Index Component is the acquiring or remaining company and which does not involve a change in security class or a conversion of all the shares in circulation),

- (iii) a takeover offer, exchange offer, other offer or another act of a legal person for the purposes of acquiring or otherwise obtaining from the issuer 100% of the shares issued that entails a transfer or the irrevocable obligation to transfer all shares (with the exception of shares which are held and controlled by the legal person), or
- (iv) a merger (either by acquisition or through forming a new structure) or a binding obligation on the part of the issuer of the share or its subsidiaries to exchange shares with another legal person, whereby the issuer of the share is the acquiring or remaining company and it does not involve a change in the class or a conversion of the all shares issued, but the shares in circulation directly prior to such an event (except for shares held and controlled by the legal person) represent in total less than 50% of the shares in circulation directly subsequent to such an event.

“Merger Date” means the date on which a Merger is concluded or the date specified by the Calculation Agent if such a date cannot be determined under the law applicable to the Merger.

“Nationalisation” means a process whereby all shares or the majority of the assets of the issuer of the shares are nationalised or are expropriated or otherwise must be transferred to public bodies, authorities or institutions.

“Orphan Drugs NPV” means, in respect of a Security and a Selection Day, the net present value of the relevant company that is attributable to Orphan Drugs, as calculated and provided by EvaluatePharma as described in *Section 1.11 Orphan Drugs NPV Calculation*.

“Orphan Drugs Revenue Share” means, in respect of a Security and a Selection Day, the total revenue of the relevant company that is attributable to Orphan Drugs expressed as a percentage of the total revenue of such company, as provided by EvaluatePharma based on the data published in the relevant company’s most recent annual company report.

“Rebalancing Day” means a day on which the composition of the Index shall be adjusted.

“Review Day” means each day that occurs on the 1st Friday of each calendar month and if such day is not a Business Day, the immediately following Business Day.

“Rights Issue” shall have the meaning as defined in Section 3 of the Equity Index Methodology, which is available on the Solactive website: <https://www.solactive.com/documents/equity-index-methodology/>

“Security” means, in respect of a company, any common share that is actively traded on a stock exchange.

“Selection Day” means each day that occurs on the 1st Friday of March and 1st Friday of September, and if such day is not a Business Day, the immediately following Business Day.

“Stock Substitute” includes in particular American Depositary Receipts (ADR) and Global Depositary Receipts (GDR).

“Takeover bid” means a bid to acquire, an exchange offer or any other offer or act of a legal person that results in the related legal person acquiring as part of an exchange or otherwise more than 10% and less than 100% of the voting shares in circulation from the issuer of the Index Component or the right to acquire these shares, as determined by the Calculation Agent based on notices submitted to public or self-regulatory authorities or other information considered by the Calculation Agent to be relevant.

“Three Month Average Daily Traded Value” means, in respect of a Security and a Selection Day, the sum of daily traded value over a three month period immediately preceding such Business Day divided by the number of Trading Days that occur during such three month period. It is sourced using the FactSet Formula `AVG(XP_TURNOVER)`.

“Total Shares” is in respect of an Index Component and any given Business Day the number or fraction of shares included in the Index. It is calculated for any Index Component as the ratio of (A) the Index Component Weight of an Index Component multiplied by the Index value and the Divisor and (B) its Trading Price (converted into the index currency according to the principles laid out in *Section 1.4 Prices and Calculation Frequency* of this document).

“Trading Day” means, in respect of an Index, a day on which London Stock Exchange, New York Stock Exchange, Tokyo Stock Exchange and Deutsche Borse Xetra are all open for trading (subject to market disruption events), excluding days on which trading may be ceased prior to the normal Exchange closing time. The Calculation Agent is ultimately responsible as to whether a certain day is a Trading Day with regard to the Index or an Index Component or in any other connection relating to this document.

“Trading Price” means, in respect of a Trading Day and an Index component (subject to the provisions given above under “Extraordinary Events”), the closing price on such day determined in accordance with the Exchange regulations. If the Exchange has no closing price for an Index Component, the Calculation Agent shall determine the Trading Price and the time of the quote for the share in question in a reasonable manner.

“YoY NPV Change” means, in respect of a Security and a Selection Day, the relative change in the Orphan Drugs NPV since the Selection Day that occurred a year ago and calculated as (i) the Orphan Drugs NPV in respect of such Selection Day divided by the Orphan Drugs NPV in respect of the Selection Day that occurred a calendar year ago, minus (ii) one.

Annex A

Table 1: Eligible Exchanges

No.	Exchange Code	Exchange
1	NA	Equity Euronext Amsterdam Netherlands
2	FP	Equity Euronext Paris France
3	FH	Equity Helsinki Stock Exchange Finland
4	HK	Equity Hong Kong Stock Exchange China
5	KQ	Equity Korea Exchange Korea
6	LN	Equity London Stock Exchange United Kingdom
7	UQ	Equity Nasdaq Global Market United States
8	UW	Equity Nasdaq Global Select Market United States
9	UN	Equity New York Stock Exchange United States
10	NO	Equity Oslo Norway
11	VX	Equity SIX Swiss (formerly Virt-X Switzerland)
12	SW	Equity SIX Swiss Exchange Switzerland
13	SS	Equity Stockholm Stock Exchange Sweden
14	TT	Equity Taiwan Stock Exchange Taiwan
15	JT	Equity Tokyo Stock Exchange Japan
16	TO	Equity Toronto Stock Exchange Canada
17	GY	Equity Xetra Germany
18	LI	Equity London International Exchange
19	AH	Equity Australian Securities Exchange Australia
20	AV	Equity Vienna Stock Exchange Austria
21	NZ	Equity New Zealand Exchange
22	ID	Equity Irish Stock Exchange Ireland
23	DC	Equity NASDAQ OMX Copenhagen Denmark
24	SB	Equity Barcelona Stock Exchange Spain
25	SN	Equity Madrid Stock Exchange Spain
26	SQ	Equity Sociedad de Bolsas Spain
27	IM	Equity Borsa Italiana Italy
28	PL	Equity Euronext Lisbon Portugal
29	SP	Equity Singapore Exchange Singapore
30	BB	Equity Euronext Brussels Belgium

Annex B

Table 2: Index Universe

Table below shows the Index Universe as of the Index Inception Date.

Company Name	ISIN	Exch Code	BIODELIVERY SCIENCES INTL	US09060J1060	US
3M CO	US88579Y1010	US	BIOGEN INC	US09062X1037	US
4SC AG	DE000A14KL72	DE	Company Name	ISIN	Exch Code
AB SCIENCE SA	FR0010557264	FR	BIOMARIN PHARMACEUTICAL INC	US09061G1013	US
ABBOTT LABORATORIES	US0028241000	US	BIOSPECIFICS TECHNOLOGIES	US0909311062	US
ABBVIE INC	US00287Y1091	US	BIOTEST AG	DE0005227201	DE
ABEONA THERAPEUTICS INC	US00289Y1073	US	BIOVERATIV INC	US09075E1001	US
ABLYNX NV	BE0003877942	BE	BLUEBIRD BIO INC	US09609G1004	US
ACCELERON PHARMA INC	US00434H1086	US	BLUEPRINT MEDICINES CORP	US09627Y1091	US
ACORDA THERAPEUTICS INC	US00484M1062	US	BORYUNG PHARMACEUTICAL CO	KR7003850005	KR
ACTELION LTD-REG	CH0010532478	CH	BRISTOL-MYERS SQUIBB CO	US1101221083	US
ACTINIUM PHARMACEUTICALS INC	US00507W1071	US	BTG PLC	GB0001001592	GB
ACTIVE BIOTECH AB	SE0001137985	SE	BUKWANG PHARMACEUTICAL CO	KR7003000007	KR
ADURO BIOTECH INC	US00739L1017	US	CASI PHARMACEUTICALS INC	US14757U1097	US
ADVAXIS INC	US0076242082	US	CATALYST PHARMACEUTICALS INC	US14888U1016	US
AEGERION PHARMACEUTICALS INC	US00767E1029	US	CELGENE CORP	US1510201049	US
AEOLUS PHARMACEUTICALS INC	US00765G1094	US	CELLDEX THERAPEUTICS INC	US15117B1035	US
AETERNA ZENTARIS INC	CA0079754028	US	CELSION CORP	US15117N5032	US
AGENUS INC	US00847G7051	US	CEMPRA INC	US15130J1097	US
AGIOS PHARMACEUTICALS INC	US00847X1046	US	CERULEAN PHARMA INC	US15708Q1058	US
AKARI THERAPEUTICS PLC-ADR	US00972G1085	GB	CFR PHARMACEUTICALS SA	CL0001762831	CL
AKORN INC	US0097281069	US	CHELSEA THERAPEUTICS INTERNA	US1634281059	US
ALCOBRA LTD		US	CHEMOCENTRYX INC	US16383L1061	US
ALEXION PHARMACEUTICALS INC	US0153511094	US	CHINA MEDICAL SYSTEM HOLDING	KYG211081248	CN
ALFRESA HOLDINGS CORP	JP3126340003	JP	CHINA MEDICINE CORP	US1694911074	CN
ALKERMES PLC	IE00B56GVS15	IE	CHUGAI PHARMACEUTICAL CO LTD	JP3519400000	JP
ALLERGAN PLC	IE00BY9D5467	US	CLEVELAND BIOLABS INC	US1858602022	US
ACTAVIS GROUP HF	IS0000000420	IS	CLINUVEL PHARMACEUTICALS LTD	AU000000CUV3	AU
ALLIANCE PHARMA PLC	GB0031030819	GB	CLOVIS ONCOLOGY INC	US1894641000	US
ALMIRALL SA	ES0157097017	ES	CONATUS PHARMACEUTICALS INC	US20600T1088	US
ALNYLAM PHARMACEUTICALS INC	US02043Q1076	US	CONCORDIA INTERNATIONAL CORP	CA20653P1027	CA
AMAG PHARMACEUTICALS INC	US00163U1060	US	CONCEPT THERAPEUTICS INC	US2183521028	US
AMBIT BIOSCIENCES CORP	US02318X1000	US	CSL LTD	AU000000CSL8	AU
AMGEN INC	US0311621009	US	CTI BIOPHARMA CORP	US12648L6011	US
AMICUS THERAPEUTICS INC	US03152W1099	US	CUBIST PHARMACEUTICALS LLC	US2296781071	US
ANGES INC	JP3127700007	JP	CUMBERLAND PHARMACEUTICALS	US2307701092	US
ANGIODYNAMICS INC	US03475V1017	US	CURIS INC	US2312691015	US
ANTHERA PHARMACEUTICALS INC	US03674U3005	US	CYCLACEL PHARMACEUTICALS INC	US23254L4059	US
APPLIED GENETIC TECHNOLOGIES	US03820J1007	US	CYTOKINETICS INC	US23282W6057	US
APRICUS BIOSCIENCES INC	US03832V3078	US	CYTORI THERAPEUTICS INC	US23283K2042	US
APTOSE BIOSCIENCES INC	CA03835T2002	CA	CYTRX CORP	US2328286081	US
ARADIGM CORP	US0385054004	US	DAIICHI SANKYO CO LTD	JP3475350009	JP
ARBUTUS BIOPHARMA CORP	CA03879J1003	CA	DELCATH SYSTEMS INC	US24661P5008	US
ARIAD PHARMACEUTICALS INC	US04033A1007	US	DEPOMED INC	US2499081048	US
ARQULE INC	US04269E1073	US	DONG-A SOCIO HOLDINGS CO LTD	KR7000640003	KR
ARRAY BIOPHARMA INC	US04269X1054	US	DONG-A ST CO LTD	KR7170900005	KR
ASKA PHARMACEUTICAL CO LTD	JP3541200006	JP	DR. REDDY'S LABORATORIES-ADR	US2561352038	IN
ASTELLAS PHARMA INC	JP3942400007	JP	DYAX CORP	US26746E1038	US
ASTEX PHARMACEUTICALS	US04624B1035	US	EAGLE PHARMACEUTICALS INC	US2697961082	US
ASTRAZENECA PLC	GB0009895292	GB	EISAI CO LTD	JP3160400002	JP
ATARA BIOTHERAPEUTICS INC	US0465131078	US	ELI LILLY & CO	US5324571083	US
ATHERSYS INC	US04744L1061	US	EMERGENT BIOSOLUTIONS INC	US29089Q1058	US
AURIS MEDICAL HOLDING AG	CH0249375764	CH	ENDO INTERNATIONAL PLC	IE00BJ3V9050	IE
AUSPEX PHARMACEUTICALS INC	US05211J1025	US	ENDOCYTE INC	US29269A1025	US
AUXILIUM PHARMACEUTICALS INC	US05334D1072	US	IMMUNE PHARMACEUTICALS INC	#N/A N/A	US
AVEO PHARMACEUTICALS INC	US0535881090	US	EPIZYME INC	US29428V1044	US
AVEXIS INC	US05366U1007	US	ERYTECH PHARMA	FR0011471135	FR
BASILEA PHARMACEUTICA-REG	CH0011432447	CH	EXELIXIS INC	US30161Q1040	US
BAXALTA INC	US07177M1036	US	EYEGATE PHARMACEUTICALS	US30233M1071	US
BAXTER INTERNATIONAL INC	US0718131099	US	FIBROGEN INC	US31572Q8087	US
BAYER AG-REG	DE000BAY0017	DE	FIVE PRIME THERAPEUTICS INC	US33830X1046	US
BELLEROPHON THERAPEUTICS INC	US0787711029	US	FOREST LABORATORIES INC	US3458381064	US
BIOCRIST PHARMACEUTICALS INC	US09058V1035	US	FORTRESS BIOTECH INC	US34960Q1094	US

FRESENIUS SE & CO KGAA	DE0005785604	DE	NIPPON KAYAKU CO LTD	JP3694400007	JP
GENMAB A/S	DK0010272202	DK	NIPPON SHINYAKU CO LTD	JP3717600005	JP
GENTIUM-SRL	US37250B1044	IT	ALPINE IMMUNE SCIENCES INC	US02083G1004	US
GENVEC INC	US37246C4069	US	NORTHWEST BIOTHERAPEUTICS	US66737P6007	US
GERON CORP	US3741631036	US	NOVARTIS AG-REG	CH0012005267	CH
GILEAD SCIENCES INC	US3755581036	US	NOVELION THERAPEUTICS INC	CA67001K2020	CA
GLAXOSMITHKLINE PLC	GB0009252882	GB	NOVO NORDISK A/S-B	DK0060534915	DK
GLYCOMIMETICS INC	US38000Q1022	US	SHIRE-NPS PHARMACEUTICALS IN	US62936P1030	US
GREEN CROSS MEDICAL SCIENCE	KR7142280007	KR	OCERA THERAPEUTICS INC	US67552A1088	US
GRIFOLS SA	ES0171996087	ES	OMEROS CORP	US6821431029	US
GTX INC	US40052B2079	US	ONCOLYTICS BIOTECH INC	CA6823101077	CA
GW PHARMACEUTICALS PLC	GB0030544687	GB	ONCOMED PHARMACEUTICALS INC	US68234X1028	US
HALOZYME THERAPEUTICS INC	US40637H1095	US	ONCONOVA THERAPEUTICS INC	US68232V3069	US
HORIZON PHARMA PLC	IE00BQPVQZ61	US	ONO PHARMACEUTICAL CO LTD	JP3197600004	JP
HOSPIRA INC	US4410601003	US	ONYX PHARMACEUTICALS INC	US6833991093	US
HORIZON THERAPEUTICS LLC	US44915N1019	US	OPKO HEALTH INC	US68375N1037	US
IMMUNE DESIGN CORP	US45252L1035	US	OPTIMER PHARMACEUTICALS LLC	US68401H1041	US
IMMUNE PHARMACEUTICALS INC	US45254C2008	US	ORION OYJ-CLASS B	FI0009014377	FI
IMMUNOCELLULAR THERAPEUTICS	US4525362046	US	OSIRIS THERAPEUTICS INC	US68827R1086	US
IMMUNOGEN INC	US45253H1014	US	OTSUKA HOLDINGS CO LTD	JP3188220002	JP
IMMUNOMEDICS INC	US4529071080	US	PACIRA PHARMACEUTICALS INC	US6951271005	US
IMPAX LABORATORIES INC	US45256B1017	US	PDL BIOPHARMA INC	US69329Y1047	US
INCYTE CORP	US45337C1027	US	PERRIGO CO PLC	IE00BGH1M568	IE
INDIVIOR PLC	GB00BRS65X63	GB	PFIZER INC	US7170811035	US
INFINITY PHARMACEUTICALS INC	US45665G3039	US	PHARMACYCLICS INC	US7169331060	US
INSMED INC	US4576693075	US	PHARMA MAR SA	ES0169501030	ES
INSPYR THERAPEUTICS INC	US45782A2050	US	PHARMAXIS LTD	AU000000PXS5	AU
INTERCELL AG	AT0000612601	AT	PHARMING GROUP NV	NL0010391025	NL
INTERCEPT PHARMACEUTICALS IN	US45845P1084	US	PHARMSTANDARD PJSC	RU000A0JP7F5	RU
INTERMUNE INC	US45884X1037	US	PLURISTEM THERAPEUTICS INC	US72940R1023	IL
IONIS PHARMACEUTICALS INC	US4622221004	US	PORTOLA PHARMACEUTICALS INC	US7370101088	US
IPSEN	FR0010259150	FR	PROGENICS PHARMACEUTICALS	US7431871067	US
JAZZ PHARMACEUTICALS PLC	IE00B4Q5ZN47	IE	PROQR THERAPEUTICS NV	NL0010872495	NL
JOHNSON & JOHNSON	US4781601046	US	PROSENSA HOLDING NV	NL0010524443	NL
JUNO THERAPEUTICS INC	US48205A1097	US	PROTALIX BIOTHERAPEUTICS INC	US74365A1016	IL
HUMANIGEN INC	US4448631048	US	PROTEON THERAPEUTICS INC	US74371L1098	US
KAMADA LTD	IL0010941198	IL	PROTHENA CORP PLC	IE00B91XRN20	IE
KARYOPHARM THERAPEUTICS INC	US48576U1060	US	PROVECTUS BIOPHARMACEUTICA-A	US74373P1084	US
KISSEI PHARMACEUTICAL CO LTD	JP3240600001	JP	PSIVIDA CORP	US74440J1016	US
KITE PHARMA INC	US49803L1098	US	PTC THERAPEUTICS INC	US69366J2006	US
KURA ONCOLOGY INC	US50127T1097	US	HORIZON PHARMACEUTICAL LLC	US75382F1066	US
KYORIN HOLDINGS INC	JP3247090008	JP	RECKITT BENCKISER GROUP PLC	GB00B24CGK77	GB
KYOWA HAKKO KIRIN CO LTD	JP3256000005	JP	RECORDATI SPA	IT0003828271	IT
LABORATORIOS FARMACEUTICOS R	ES0157261019	ES	REGENERON PHARMACEUTICALS	US75886F1075	US
LEXICON PHARMACEUTICALS INC	US5288723027	US	REGULUS THERAPEUTICS INC	US75915K1016	US
LIGAND PHARMACEUTICALS	US53220K5048	US	RETROPHIN INC	US7612991064	US
IOVANCE BIOTHERAPEUTICS INC	US4622601007	US	RIGEL PHARMACEUTICALS INC	US7665596034	US
LOXO ONCOLOGY INC	US5488621013	US	ROCHE HOLDING AG-GENUSSCHEIN	CH0012032048	CH
H LUNDBECK A/S	DK0010287234	DK	SAGENT PHARMACEUTICALS INC	US7866921031	US
MACROGENICS INC	US5560991094	US	SALIX PHARMACEUTICALS LTD	US7954351067	US
MALLINCKRODT PLC	IE00BBGT3753	US	SANGAMO THERAPEUTICS INC	US8006771062	US
SAVARA INC	US8051111016	US	SANOFI	FR0000120578	FR
MATEON THERAPEUTICS INC	US57667K1097	US	SANTARUS INC	US8028173040	US
MEDA AB-A SHS	SE0000221723	SE	SANTEN PHARMACEUTICAL CO LTD	JP3336000009	JP
MEDICIS PHARMACEUTICAL CORP	US5846903095	US	SANTHERA PHARMACEUTICALS-REG	CH0027148649	CH
MEDIGENE AG	DE000A1X3W00	DE	SAREPTA THERAPEUTICS INC	US8036071004	US
MEI PHARMA INC	US55279B2025	US	SAVIENT PHARMACEUTICALS INC	US80517Q1004	US
MERCK & CO. INC.	US58933Y1055	US	SCICLONE PHARMACEUTICALS INC	US80862K1043	US
MERCK KGAA	DE0006599905	DE	SEATTLE GENETICS INC	US8125781026	US
MERRIMACK PHARMACEUTICALS IN	US5903282094	US	SHIONOGI & CO LTD	JP3347200002	JP
MESOBLAST LTD	AU000000MSB8	AU	SHIRE PLC	JE00B2QKY057	US
MIRATI THERAPEUTICS INC	US60468T1051	US	SIGA TECHNOLOGIES INC	US8269171067	US
MITSUBISHI TANABE PHARMA	JP3469000008	JP	SMITH & NEPHEW PLC	GB0009223206	GB
MOCHIDA PHARMACEUTICAL CO	JP3922800002	JP	SPARK THERAPEUTICS INC	US84652J1034	US
MOMENTA PHARMACEUTICALS INC	US60877T1007	US	SPECTRUM PHARMACEUTICALS INC	US84763A1088	US
MORPHOSYS AG	DE0006632003	DE	STADA ARZNEIMITTEL AG	DE0007251803	DE
MYLAN NV	NL0011031208	US	STEADYMED LTD	IL0011348997	IL
NEKTAR THERAPEUTICS	US6402681083	US	STEMLINE THERAPEUTICS INC	US85858C1071	US
NESTLE SA-REG	CH0038863350	CH	SUCAMPO PHARMACEUTICALS-CL A	US8649091068	US
NEURALSTEM INC	US64127R4011	US	SUMITOMO DAINIPPON PHARMA CO	JP3495000006	JP
NEUROGESX INC	US6412521014	US	SUNESIS PHARMACEUTICALS INC	US8673287004	US
NEWLINK GENETICS CORP	US6515111077	US	SWEDISH ORPHAN BIOVITRUM AB	SE0000872095	SE
NICHI-IKO PHARMACEUTICAL CO	JP3687200000	JP	SYMBIO PHARMACEUTICALS LTD	JP3383050006	JP

SYNAGEVA BIOPHARMA CORP	US87159A1034	US	ZIOPHARM ONCOLOGY INC	US98973P1012	US
TAKEDA PHARMACEUTICAL CO LTD	JP3463000004	JP	ADAPTIMMUNE THERAPEUTICS-ADR	US00653A1079	GB
TEIJIN LTD	JP3544000007	JP	ADMA BIOLOGICS INC	US0008991046	US
TESARO INC	US8815691071	US	ANTARES PHARMA INC	US0366421065	US
TEVA PHARMACEUTICAL-SP ADR	US8816242098	IL	AUDENTES THERAPEUTICS INC	US05070R1041	US
TG THERAPEUTICS INC	US88322Q1085	US	BEIGENE LTD-ADR	US07725L1026	CN
MOLECULAR TEMPLATES INC	US6085501095	US	BRAINSTORM CELL THERAPEUTICS	US10501E2019	US
THROMBOGENICS NV	BE0003846632	BE	CASCADIAN THERAPEUTICS INC	US14740B6065	US
TORAY INDUSTRIES INC	JP3621000003	JP	CORBUS PHARMACEUTICALS HOLDI	US21833P1030	US
TRANSGENE SA	FR0005175080	FR	DIMENSION THERAPEUTICS INC	US25433V1052	US
UCB SA	BE0003739530	BE	DIURNAL GROUP PLC	GB00BDB6Q760	GB
ULTRAGENYX PHARMACEUTICAL IN	US90400D1081	US	GALAPAGOS NV	BE0003818359	BE
UNIQUE NV	NL0010696654	NL	IDERA PHARMACEUTICALS INC	US45168K3068	US
UNITED THERAPEUTICS CORP	US91307C1027	US	IMMUNOVACCINE INC	CA45254B1031	CA
VALEANT PHARMACEUTICALS INTE	CA91911K1021	US	JCR PHARMACEUTICALS CO LTD	JP3701000006	JP
VALNEVA SE	FR0004056851	FR	MYOKARDIA INC	US62857M1053	US
VECTURA GROUP PLC	GB00B01D1K48	GB	NANTKWEST INC	US63016Q1022	US
VERASTEM INC	US92337C1045	US	NORDIC NANOVECTOR ASA	NO0010597883	NO
VERICEL CORP	US92346J1088	US	ONXEO	FR0010095596	FR
VERSARTIS INC	US92529L1026	US	RA PHARMACEUTICALS INC	US74933V1089	US
VERTEX PHARMACEUTICALS INC	US92532F1003	US	REATA PHARMACEUTICALS INC-A	US75615P1030	US
VICAL INC	US9256022032	US	TIZIANA LIFE SCIENCES PLC	GB00BKWNZY55	GB
VIFOR PHARMA AG	CH0364749348	CH	TORII PHARMACEUTICAL CO LTD	JP3635800000	JP
SHIRE VIROPHARMA INC	US9282411084	US	TRACON PHARMACEUTICALS INC	US89237H1005	US
WINDTREE THERAPEUTICS INC	US97382D1054	US	WAVE LIFE SCIENCES LTD	SG9999014716	US
XENON PHARMACEUTICALS INC	CA98420N1050	CA	WILSON THERAPEUTICS AB	SE0008293674	SE
XOMA CORP	US98419J2069	US	XENCOR INC	US98401F1057	US
3745350 CANADA INC	CA9842381050	CA	ZERIA PHARMACEUTICAL CO LTD	JP3428850006	JP
YUHAN CORP	KR7000100008	KR	LION BIOTECHNOLOGIES INC	US53619R1023	US
ZAFGEN INC	US98885E1038	US			

Annex C

As of February 2022 the following inclusion criteria for the categories below were applicable.

Please refer to the most recent document available under the URL as specified in section '2.1. Index Universe Requirements' above for the most recent applicable categories and inclusion criteria.

Categories	Inclusion criterion
Established norms around Environment, Human Rights, Corruption and Labour Rights	Non-Compliance with the UNGC
Controversy	Controversies with the Level 5
Tobacco	(5% Production <OR> 5% Retail <OR> 5% Related Products/Services)*
Defense – Weapons	(5% Military Contracting Weapons <OR> 5% Military Contracting Weapons – Related Products)*
Defense – Controversial Weapons	Any direct Involvement or any indirect Involvement through corporate ownership
Small Arms	(5% Civilian customers (Assault and non-assault weapons) <OR> 5% Key Components <OR> 5% Military/law enforcement customers <OR> 5% Retail/Distribution)*
Coal	(5% Thermal Coal Extraction <OR> 5% Power Generation <OR> 5% Supporting Products/Services <OR> Power Generation Capacity Increase)*
Conventional Oil & Gas	(5% Generation <OR> 5% Production <OR> 5% Supporting Products/Services <OR> Capacity Increase) *
Unconventional Oil & Gas	(5% Oil Sands Extraction <OR> 5% Artic Oil & Gas Exploration/Extraction <OR> 5% Shale Energy Extraction <OR> Capacity Increase)*
Nuclear Power	(5% Production <OR> 5% Distribution <OR> 5% Supporting Products <OR> Capacity Increase)*
Alcohol	(5% Production <OR> 5% Retail <OR> 5% Related Products/Services)*
Gambling	(5% Operations <OR> 5% Specialized Equipment <OR> 5% Supporting Products/Services)*
Adult Entertainment	(5% Production <OR> 5% Distribution)*

Note:

- % figures refer to revenue threshold (for degree of involvement). The criterion is fulfilled if involvement is equal to or above such threshold.
- Capacity increase refers to any increase in capacity from the immediately preceding Selection Day of the ESG Exclusions Enhanced Index
- The terminology used in the table above is specific to the DATA PROVIDER II and may change from time to time.

*this includes significant corporate ownership (were a company holds a stake greater than 50% in an involved company, the revenues of the involved company are attributed to the company).

Any company which fulfills any of the criteria set out above shall be a component of the ESG Exclusions Enhanced Index. The primary listing for each company is selected as Index Component of the ESG Exclusions Enhanced Index. For the avoidance of doubt, any company for which an evaluation of the criteria is not possible due to the non-availability of relevant data from the DATA PROVIDER II, shall be a component of the ESG Exclusions Enhanced Index.

ANNEX D

Name of the ETF used to determine the AuM:

L&G Pharma Breakthrough UCITS ETF, ISIN: IE00BF0H7608

1. HISTORY OF INDEX CHANGES

Version	Date	Description
1.0		Index Guideline creation (<i>initial version</i>)
3.0	13 February 2023	Inclusion of ESG filter and amendment of weighting concept
3.1	18 May 2023	Addition of 3.5.2 Rights Issue (Capital Increase) and 3.5.2.1 Capital decrease definitions

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