VALUATIONLAB
FINANCIAL ANALYSIS

COSMO PHARMACEUTICALS

FOCUS AREA: ENDOSCOPY (FOR COLON CANCER PREVENTION), GASTROINTESTINAL (DIGESTIVE SYSTEM) AND SKIN DISORDERS

KEY DATA			SIX: COPN
MARKET CAPITALIZATION (CHF MN)	960	**PRICE ON 03 MAY 2023**	55
ENTERPRISE VALUE (CHF MN)	719	**RISK-ADJUSTED NPV PER SHARE** (CHF)	92
CASH (31 DECEMBER 2022) (CHF MN)	240	**UPSIDE/DOWNSIDE** (%)	68%
MONTHLY OPERATING EXPENSE (CHF MN)	3.4	**RISK PROFILE**	MEDIUM
CASH LIFE	SUSTAINABLE	**SUCCESS PROBABILITY LEAD R&D PROJECT**	82.5%
BREAK-EVEN (YEAR)	2021	**EMPLOYEES**	295
FOUNDED (YEAR)	1997	**LISTED** (YEAR)	2007

KEY PRODUCTS:	STATUS
- LIALDA & UCERIS/CORTIMENT (ULCERATIVE COLITIS)	LAUNCHED 2007 I 2013
- ELEVIEW (LESION RESECTION CUSHION)	LAUNCHED 2017
- GI GENIUS (LESION DETECTION)	LAUNCHED 2019 (EU) I 2021 (US)
- BYFAVO (PROCEDURAL SEDATION)	LAUNCHED 2020 (US)
- LUMEBLUE (LESION DETECTION)	LAUNCH 2022 (EU) I PHASE III (US)
- AEMCOLO/RELAFALK (TRAVELERS' DIARRHEA/IBS-D*)	LAUNCHED I PHASE II (IBS-D)
- WINLEVI (ACNE)	LAUNCHED 2021 (US)
- BREEZULA (HAIR LOSS MEN)	PHASE III (2022)

MAJOR SHAREHOLDERS:	(%)
- COSMO HOLDING S.A.R.L.	34.8
- HEINRICH HERZ AG / LOGISTABLE GROUP	8.4
- DIEVINI HOPP BIOTECH HOLDING GMBH & CO. KG	3.8
- FREE FLOAT (EXCL. COSMO HOLDING S.A.R.L.)	**65.2**
- AVERAGE DAILY VOLUME (3 MONTHS)	13,234

UPCOMING CATALYSTS:	DATE
- BREEZULA - START PHASE III MALE ALOPECIA TRIAL	Q2 2023
- WINLEVI - LICENSING AGREEMENTS	DURING 2023
- WINLEVI - EU FILING	H2 2023

ANALYST(S): BOB POOLER
BP@VALUATIONLAB.COM
+41 79 652 67 68

* IBS-D = IRRITABLE BOWEL SYNDROME - DIARRHEA PREDOMINANT

ESTIMATES AS OF 3 MAY 2023

SOURCE: VALUATIONLAB ESTIMATES, COSMO PHARMACEUTICALS

Back to the roots

Record results – Medtronic AI collaboration expanded

Cosmo Pharmaceuticals (Cosmo) is focused on developing therapies for 1) Endoscopy (solutions to reduce the risk of colon cancer), including GI Genius, an artificial intelligence (AI) enhanced system for colonoscopy; Lumeblue, a colonic lesion detection dye; Eleview, a lesion resection cushion; and Byfavo for procedural sedation; 2) Dermatology (skin disorders), including Winlevi for acne and Breezula for hair loss, and 3) Gastrointestinal (GI) Disorders (e.g., colon infections) including Lialda/Mezavant and Uceris/Cortiment both for ulcerative colitis; and Aemcolo/Relafalk for travelers' diarrhea and IBS-D (phase II completed). Cosmo revenues are a mix of sales royalties, manufacturing revenue, and milestone payments from its commercialization partners. Additionally, the company participates in the long-term value creation of its equity stakes in RedHill (14.8% stake), PAION (7.3% stake), and Eagle Pharma (0.7% stake). We derive a sum-of-parts risk-adjusted NPV (rNPV) value of CHF 92 per share with an 82.5% success rate for its lead pipeline project Winlevi (only available in the US yet). We consider Cosmo Medium Risk with a strong balance sheet and eight marketed products (GI Genius, Winlevi, Lumeblue, Eleview, Aemcolo/Relafalk, Byfavo, Lialda/Mezavant, and Uceris/Cortiment) contributing to revenues and sustained profitability.

Key catalysts:

1) **Start phase III trial Breezula in male alopecia (Q2 2023):** EUR 400 mn peak sales potential; our rNPV rises by CHF 3/share with a 65% (phase III) success rate
2) **Winlevi licensing agreements (during 2023):** to advance Winlevi global sales with new licensing and supply agreements in the ROW
3) **Winlevi filing for EU approval (H2 2023):** EUR 90 mn peak sales in the EU due to lower pricing than in the US; our rNPV increases by CHF 2/share with a 90% success rate, the average of EU filing (80%) and US launched (100%)

Recent developments

Below is an overview of the latest developments since our last Cosmo Valuation Report was issued in March 2023.

March 30 – Territory expansion agreement for Lumeblue with China Medical System
The existing license agreement for Lumeblue with China Medical System (CMS), including Greater China (China, Hong Kong, Macao, Taiwan), was expanded to include several countries belonging to the Pan-Asia region. These include countries in Central Asia (Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, Uzbekistan), Eastern Asia (Republic of Korea, Mongolia), Southeastern Asia (Brunei Darussalam, Cambodia, Indonesia, Lao People's Democratic Republic, Malaysia, Myanmar, Philippines, Singapore, Thailand, Timor-Leste, Vietnam) and Southern Asia (Afghanistan, Bangladesh, Bhutan, Iran, Maldives, Nepal, Pakistan, Sri Lanka). Cosmo will continue to be the exclusive supplier of Lumeblue for all these regions. CMS filed for a new drug application (NDA) in China in December 2022 and has received confirmation of the acceptance of filing in Q1 2023. The filing was based on the positive phase III trial of Lumeblue conducted by CMS in China and announced in December 2022.

March 23 – FY 2022 results beat guidance on solid Winlevi and GI Genius uptake
Cosmo reported record FY 2022 results, which exceeded guidance, and proposed to increase its dividend considering these results and the outlook for 2023. Cosmo will expand its artificial intelligence (AI) collaboration with Medtronic on GI Genius.

COSMO	FY 2022 RESULTS IN A NUTSHELL			
(IN EUR MN)	FY 2022	FY 2021	CHANGE (%)	COMMENT
SELECTED PRODUCTS:				
WINLEVI	26.7	0.1	23303%	SUCCESSFUL US LAUNCH TRIGGERS TERRITORY EXPANSION SUN PHARMA & OTHER AGREEMENTS (EUR 15.3 MN UPFRONTS)
GI GENIUS	10.0	7.1	41%	US ROLLOUT EXPECTED TO ACCELERATE WHILE SUBSCRIPTION REVENUES SHOULD KICK IN THE NEXT FEW YEARS
LIALDA	29.6	27.8	6%	REBOUND IN GROWTH IN THE US CONTINUES ON STRONG COMPETITIVE PROFILE COMPARED TO CHEAP GENERICS
UCERIS / CORTIMENT	16.4	7.3	124%	BOOSTED BY EUR 9 MN MILESTONES FROM FERRING ON CORTIMENT CROSSING CERTAIN SALES LEVELS
ELEVIEW	1.7	2.0	-17%	MEDTRONIC NOW RESPONSIBLE FOR GLOBAL SALES (EXCEPT CANADA BY PENDOPHARM) - RELAUNCH AFTER PANDEMIC
AEMCOLO / RELAFALK	0.1	1.4	-93%	NO RECOVERY AFTER SALES IMPACTED BY THE DROP IN TRAVEL IMPACTED BY THE COVID-19 PANDEMIC
LUMEBLUE	0.1	4.1	-99%	1ST LAUNCH IN ITALY IN APRIL 2022; IN H1 2021 COSMO RECEIVED A EUR 4 MN UPFRONT MILESTONE FROM ALFASIGMA
CONTRACT MANUFACTURING	12.0	10.7	13%	REVENUE FROM DRUG DEVELOPMENT AND MANUFACTURING ON BEHALF OF THIRD PARTIES
OTHERS	5.7	4.5	25%	
TOTAL REVENUE	**102.1**	**65.1**	57%	BOOSTED BY MILESTONES AND STRONG UNDERLYING PRODUCT REVENUE GROWTH, IN PARTICULAR FROM WINLEVI
COGS	-40.5	-33.0	23%	INCREASE IN RAW MATERIALS AND CONSUMABLES ASSOCIATED WITH HIGHER PRODUCT SALES
GROSS PROFIT	**61.6**	**32.1**	92%	
OTHER INCOME	1.9	0.8	131%	INCLUDES SETTLEMENT OF LEGAL PROVISIONS, REVERSAL ACCOUNTS PAYABLE NO LONGER DUE, R&D TAX CREDITS
R&D COSTS	-15.5	-11.4	37%	BOOSTED BY DEVELOPMENT COSTS FOR BREEZULA (PREVIOUSLY CASSIOPEA)
S,G&A COSTS	-19.9	-10.5	90%	IMPACTED BY HIGHER ADVISORY COSTS ASSOCIATED WITH THE CASSIOPEA TRANSACTION
OPERATING PROFIT	**28.1**	**11.1**	153%	BOOSTED BY MILESTONES AND STRONG UNDERLYING PRODUCT REVENUE GROWTH, IN PARTICULAR FROM WINLEVI
SHARE OF RESULT ASSOCIATE	0.0	17.8		SHARE OF RESULT OF CASSIOPEA (NOW COSMO DERMATOLOGY) NO LONGER IN COSMO ACCOUNTS
LOSS INVESTMENT IN ASSOCIATE	0.0	-0.6		LOSS FROM REMEASUREMENT OF PREVIOUSLY HELD INVESTMENT IN CASSIOPEA (NOW COSMO DERMATOLOGY)
NET FINANCIAL INCOME/(EXPENSE)	-3.6	-4.3	-16%	LOWER TOTAL FINANCIAL EXPENSES IN 2022 OFFSETTING SLIGHTLY HIGHER TOTAL FINANCIAL INCOME
PROFIT/(LOSS) BEFORE TAXES	**24.5**	**24.0**	2%	
TAXES	-7.0	-2.3	199%	HIGHER TAXES AS WINLEVI (CASSIOPEA) PROFITS TAXED IN ITALY, OTHER PROFITS FROM COSMO TAXED IN IRELAND
NET PROFIT/(LOSS)	**17.5**	**21.7**	-19%	

SOURCE: COSMO, VALUATIONLAB ESTIMATES

FY 2022 RESULTS:

- **Total revenue** increased by 57% to EUR 102.1 mn, exceeding guidance, and was boosted by the solid performance of its new growth products, Winlevi (acne) and GI Genius (artificial intelligence enhanced colonoscopy), as well as a rebound in its legacy products Lialda and Uceris/Cortiment, both for treating ulcerative colitis.
- **Milestones** amounted to EUR 24.3 including 15.3 mn upfront milestone payments for new Winlevi agreements and EUR 9 mn sales milestones from Ferring for Cortiment crossing several sales thresholds.
- **Operating profit** increased by 153% to EUR 28 mn, exceeding guidance, and was boosted by solid total revenue growth and lower costs.
- **Net cash flow from operating activities** increased by 164% to EUR 33.2 mn.

- **Cash and short-term investments (31 December 2022):** increased by EUR 19.5 mn to EUR 241 mn, sufficient to fully repay the EUR 175 mn convertible bonds in 2023, if needed.

KEY PRODUCTS:

- **Winlevi (acne):** revenue jumped to EUR 26.7 mn with 565,355 accumulated total prescriptions (TRx) since its launch, with over 14,270 unique prescribers, representing 82% of total healthcare practitioners in dermatology. In the US, Winlevi continues to be the #1 branded acne prescription product. In 2022, four licensing transactions were announced, including Sun Pharma (territory expansion including Japan, Australia, New Zealand, Brazil, Mexico, Russia), 3SBIO (Greater China), InfectoPharm (Germany, Italy, Austria), and Hyphens (Southeast Asia). Planned expansion in other dermatology indications.
- **GI Genius (AI-enhanced colonoscopy):** revenue increased by 41% to EUR 10 mn. Medtronic's mid-teens growth in chronic and colorectal was driven by strong US GI Genius performance in their last earnings call. Medtronic has an extensive marketing campaign ongoing backed by impressive clinical results from a US trial with GI Genius showing a 50% reduction in missed colorectal polyps, and GI Genius named in the prestigious Fortune 2022 "Change the World" list recognizing companies and products that address society's most pressing needs. A contract for 115 GI Genius modules was awarded by the US Department of Veteran Affairs.
- **Lialda (ulcerative colitis):** revenue increased by 6.5% to EUR 29.6 mn due to an increase in volumes in the US and Japan.
- **Uceris/Cortiment (ulcerative colitis):** revenue increased by 124% to EUR 16.4 mn, boosted by 14% underlying volume growth and two sales milestones amounting to EUR 9 mn from Ferring. A EUR 8 mn milestone on Cortiment achieving cumulative net sales of EUR 100 mn and a EUR 1 mn milestone on annual net sales crossing EUR 20 mn. Future growth of Cortiment is expected to continue strongly, with Ferring submitting an NDA filing for Japan, the second largest IBD market. Launch in Japan is expected by August 2023.

PIPELINE:

- **Breezula (male hair loss):** pivotal phase III trial in males for the treatment of androgenic alopecia is expected to start in Q2 2023.
- **CB-03-10 (cancer):** a phase I safety trial started in patients with advanced refractory solid tumors, with US clinical sites activated with six patients treated with an excellent safety profile, to date.
- **CB-01-33 (bile acid diarrhea):** formulation and intellectual property (IP) protections of colesevelam completed and planning of clinical development underway.

Cosmo Intelligent Medical Devices (expanded AI cooperation with Medtronic): starting with GI Genius, Medtronic will create its AI Access Platform, a set of solutions designed to enable and scale up the application of AI in its healthcare products. Cosmo Intelligent Medical Devices (IMD – www.cosmoimd.com) – a fully owned subsidiary of Cosmo Pharmaceuticals – will simultaneously develop Cosmo's Innovation Center (www.cosmoimd.com/innovation-center), a cloud-native development platform, to provide external Software as a Medical Device (SaMD) developers a way to accelerate innovation and bring AI-powered applications to market faster. The SaMD apps will be hosted on the GI Genius modular infrastructure and marketed by Medtronic with Cosmo

having a 20% of Medtronic sales impact on their profit. Cosmo will use NVIDIA's Holoscan (a real-time AI computing software platform for building medical devices) and NVIDIA IGX (an industrial-grade edge AI hardware platform) with Cosmo IMD's full-stack framework for SaMD development to offer more leaner and powerful development standards and attract a larger community of developers.

COSMO FY 2022 RESULTS AND 2023 GUIDANCE IN A NUTSHELL

IN EUR MN	FY 2023 GUIDANCE	FY 2022	FY 2021	% CHANGE
TOTAL REVENUES	**110** (+7,7%) **- 120** (+17.5%)	**102.1**	65.1	57%
TOTAL REVENUES (EXCL. MILESTONES)	**110** (+41.4%) **- 120** (+54.2%)	**77.8**	59.6	31%
OPERATING PROFIT	**25** (-11.0%) **- 35** (+24.6%)	**28.1**	11.1	153%
DIVIDEND (EUR/SHARE)	**1.05** (+10.5%)	**0.95**	-	

SOURCE: VALUATIONLAB, COSMO PHARMACEUTICALS

FY 2023 Guidance

Cosmo confirmed its FY 2023 guidance that it provided at the 2022 preliminary results release in February. For FY 2023, Total revenue is expected to increase by roughly 8% to 18%, which amounts to around 41% to 54% if the EUR 24.3 mn upfront and sales milestones from Winlevi agreements and Cortiment sales in 2022 are excluded. Operating profit is growth guided to range between roughly -11% and +25%.

Dividend In light of the record 2022 results and the 2023 outlook, Cosmo also proposed a 10.5% increase in the dividend payment to EUR 1.05 per share in 2023 from previously EUR 0.95 per share.

Corporate - Board change

Alexis de Rosnay resigned from Cosmo's board of directors due to compliance reasons following his recent appointment as Chairman of Barclays Global Healthcare Investment Banking division. A replacement will be proposed at the upcoming AGM on 26 May 2023.

March 22 – AI cooperation with Medtronic extended to host an ecosystem of new apps for GI Genius and accelerate the development cycle

Cosmo's fully owned subsidiary Cosmo Intelligent Medical Devices (IMD) expanded its cooperation with Medtronic to accelerate the development of artificial intelligence (AI) applications in the healthcare system and bring new AI-based solutions into patient care. Cosmo's GI Genius technology platform was designed with a modular architecture with the aim of building an ecosystem of different software applications (apps) for real-time endoscopy procedures or any clinical procedure performed by a physician using a screen. GI Genius, with its first software application, the detection of difficult-to-spot lesions, obtained FDA approval through the "de novo" application process in April 2021. Other apps could include optical biopsy, detecting and monitoring inflammation in chronic gastrointestinal diseases, or augmented reality.

GI Genius is the base technology platform for Medtronic to create an AI Access Platform, a set of solutions to enable and scale up the implementation of AI in the endoscopy suite. Simultaneously, Cosmo IMD will develop Cosmo's Innovation Center to provide Software as a Medical Device (SaMD) application developers with a sandbox, an isolated testing environment that allows software developers to design and test medical AI software applications using a virtual version of the GI Genius hardware. Software as a Medical Device

(SaMD) is specific software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device.

The SaMD applications (apps) are intended to be uploaded and implemented on GI Genius, the hardware medical device, with the potential to accelerate AI innovation for better patient care. The SaMD apps from external as well as internal developers leverage the GI Genius technology platform and will be marketed by Medtronic, with Cosmo having a 20% of Medtronic sales impact on their profit.

Cosmo IMD will use NVIDIA Holoscan and NVIDIA IGX within Cosmo IMD's full-stack framework for SaMD development to offer leaner and more powerful development standards to speed up the medical device cycle and expand access to real-time AI in procedures, thereby attracting a larger community of developers. NVIDIA Holoscan, a domain-specific AI computing platform, delivers the full-stack infrastructure needed for scalable, software-defined, real-time processing of streaming data at the edge, so developers can build devices and deploy AI applications directly into clinical settings. NVIDIA IGX is an industrial-grade platform that combines enterprise-level hardware, software, and support. As a single, holistic platform, IGX allows companies to focus on application development and realize the benefits of AI faster. The opening of the architecture to external developers will accelerate the introduction of AI in every healthcare context.

The expanded collaboration will enable developers to work on Medtronic's GI Genius AI Access Platform and Cosmo's Innovation Center to efficiently train and validate SaMD apps by assisting with the hardware (GI Genius), AI software (NVIDIA Holoscan, IGX), science, data, regulatory authorities, and certification.

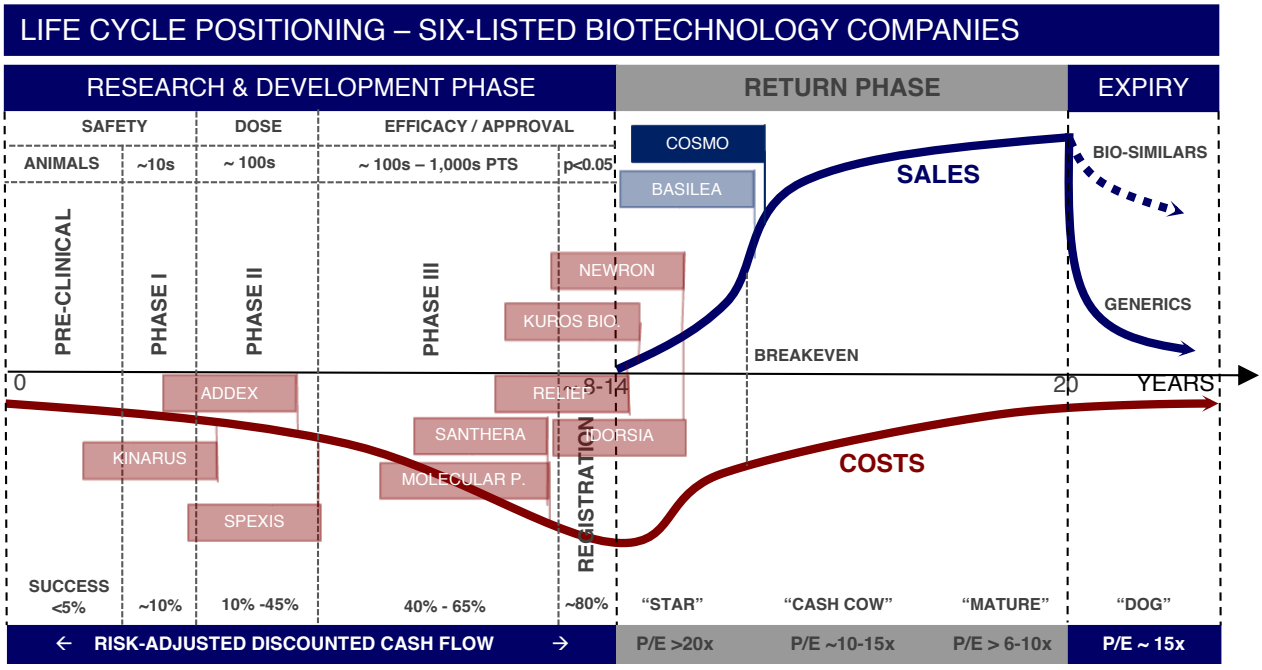
Investment Case, Strategy & Cash

Investment case in a nutshell

Cosmo is one of the few SIX-listed biopharma companies with sufficient cash resources to fund its clinical development plans and even pay dividends thanks to a strong balance sheet and sustainable revenues and profits from 8 marketed products. Its legacy business, including Lialda/Mezavant and Uceris/Cortiment, both for treating ulcerative colitis, and revenues from drug development and manufacturing for third parties, provides a stable and high-margin revenue stream. Recently launched products such as GI Genius, a breakthrough artificial intelligence (AI) enhanced device compatible with all major brands of endoscopes, and Winlevi, the first-ever topical anti-androgen on the US market for treating acne, should provide substantial growth and margin expansion in the near and long-term, with the potential of annual dividends. We qualify Cosmo as a Medium Risk investment due to its stable revenues from a broad range of marketed products.

Life Cycle Positioning - Medium Risk

We qualify Cosmo as Medium Risk due to its solid balance sheet, revenues from eight marketed products (Lialda/Mezavant, Uceris/Cortiment, Aemcolo/Relafalk, Eleview, GI Genius, Byfavo, Winlevi, and Lumeblue), manufacturing revenues for third parties, and financial equity stakes in RedHill (14.8%), PAION (7.3%), and Eagle (0.7%), which can be easily monetized. Cosmo has always been prudent by staying within its financial reach when making investment decisions. With the elimination of the US cost base, a global commercialization structure in place for nearly all key products (except for Lumeblue in the US), and the recent acquisition of Cassiopea, Cosmo has returned to sustainable profitability, boosted by the global rollout of its products thanks to commercialization partnerships with strong players such as Medtronic in major markets. (See “Important Research Disclosures” for our Risk Qualification).



SOURCE: VALUATIONLAB

The successful transformation from a manufacturing company to a hybrid pharmaceutical, medtech, and health-tech company

Cosmo Pharmaceuticals is a hybrid pharmaceutical, medtech, and health-tech company focused on developing and manufacturing best-in-class treatments in endoscopy, gastrointestinal (GI), and skin disorders, with a staff of 295 employees. The company was founded in 1997 by purchasing the Italian contract manufacturing facility from Parke Davis (when Pfizer acquired Parke Davis) in Lainate (Milan), Italy. Cosmo was gradually transformed into a hybrid GI and dermatology prescription drug, medtech, and health-tech development company, generating significant revenues through its commercialization partners. Cosmo was listed on the Swiss Stock Exchange (ticker: COPN) in March 2007. Only a year later, the company became profitable, thanks to the successful launch of its first product Lialda/Mezavant, for treating ulcerative colitis by Shire Pharmaceuticals (acquired by Takeda), reaching peak sales of USD 792 mn before generics entered the market. In December 2021, Cosmo reacquired its dermatology franchise Cassiopea, an earlier spin-off of its dermatology pipeline, which was listed on the SIX Swiss Stock Exchange in 2015. Dermatology products such as Winlevi for acne should also contribute strongly to Cosmo's revenues. Cosmo is a Dutch entity incorporated in the Netherlands, with headquarters in Dublin, Ireland, and manufacturing facilities in Lainate, Italy. Since April 2021, Cosmo has traded on XETRA (ticker: C43) in Frankfurt to provide easier access and visibility to European investors and increase overall liquidity in the trading of Cosmo shares.

Cosmo is engaged in two distinct business fields:

I. Development and commercialization of proprietary pharmaceutical, medical and health-tech products with a particular focus on three therapeutic areas:

1) **ENDOSCOPY:** solutions to improve procedures to examine the digestive tract and prevent colorectal cancer include:
    - **GI Genius** (artificial intelligence-enhanced colonoscopy device): EU launch October 2019, US launch May 2021 by global partner Medtronic)
    - **Lumeblue** (lesion detection dye for entire colon): approved in the EU in August 2020, EU rights licensed to Alfasigma SpA in February 2021; Chinese rights licensed to China Medical System (CMS) Holdings in December 2020; discuss with the FDA if a second confirmatory phase III trial for US approval is needed after CMS reported a positive phase III trial in China; US partnering agreement required for US launch
    - **Eleview** (dyed lesion resection cushion): Medtronic is the global commercialization partner, excluding Canada (Pendopharm)
    - **Byfavo** (fast-acting sedation for colonoscopy): approved in the US in 2020; Eagle Pharmaceuticals is now responsible for commercialization; Cosmo only benefits from its equity stake in PAION and Eagle, and is eligible for up to EUR 105 mn in potential milestone payments
    - **Qolotag** (lesion detection dye for sigmoid colon): approved in the EU

2) **DERMATOLOGY:** treatments for skin disorders include:
    - **Winlevi** (acne vulgaris): launched in the US in November 2021 by Sun Pharma, which has exclusive rights for the US, Japan, Australia, New Zealand, Brazil, Mexico, and Russia; 3SBio has exclusive rights for Greater China (China, Taiwan, Hong Kong, and Macau); InfectoPharm has

exclusive rights for Germany, Italy, and Austria; Hyphens Pharma has exclusive rights for Southeast Asia
- **Breezula** (androgenic alopecia): phase II completed in male hair loss; phase III trials to start in Q2 2023; mixed POC results in female hair loss (further clinical development to be determined)

3) **GASTROINTESTINAL:** treatments for digestive system disorders include:
   - **Aemcolo/Relafalk** (travelers' diarrhea (TD) / irritable bowel syndrome – diarrhea-predominant (IBS-D)): approved for travelers' diarrhea in US and EU in November 2018; Dr. Falk is the development & commercialization partner in EU/ROW; RedHill in the US; positive phase II IBS-D results in January 2021, phase III IBS-D development in planning
   - **CB-01-33 / colesevelam** (bile acid diarrhea): preclinical development; the formulation and IP protection have been completed, and clinical development is in planning

   LEGACY PRODUCTS:
   - **Lialda/Mezavant** (ulcerative colitis): marketed by Takeda/Giuliani/Nogra
   - **Uceris/Cortiment** (ulcerative colitis): marketed by Bausch Health/Ferring

II. **Manufacturing pharmaceutical products for third parties** (at Cosmo's GMP-approved plant) and related services (e.g., product formulations & stability evaluations, document preparation for pharmaceutical product registration).

A business model based on three pillars to increase opportunities and reduce risk
Cosmo aims to achieve superior long-term returns on investment by applying an entrepreneurial approach to assessing opportunities and risks. Existing financial resources need to be available for all projects before the company decides to start clinical development. Its business model is based on three pillars to increase opportunities and decrease risk, including

1) **Development and manufacturing of its own products**
2) **Selective strong partnerships to commercialize these products**
3) **Drug development and manufacturing on behalf of third parties**

This enables Cosmo to focus on multiple R&D opportunities, and have a lean and straightforward cost base, not bearing the cost for commercial infrastructure, thereby increasing profitability as new products generate revenues.

Global sales infrastructure established, leading to increasing profitability
Through strategic partnerships, Cosmo has established a global sales infrastructure for almost all its major products except for Lumeblue in the US (see Appendix, page 59) Cosmo plans to sign on with a US partner before starting the second phase III confirmatory trial required by the FDA for approval of Lumeblue in the US.

Cosmo commercializes its products through selective players in exchange for:

- **Equity, milestones, and royalties:** Aemcolo US (14.8% stake in RedHill)

- **Equity stakes and milestones:** Byfavo US (0.7% stake in Eagle Pharmaceuticals, which acquired Acacia in June 2022) and a 7.3% stake in PAION), with Cosmo eligible for up to EUR 105 mn sales milestones
- **Milestones and royalties:** Lialda (Shire/Takeda/Giuliani); Uceris US (Bausch Health); Cortiment ROW (Ferring); Relafalk ROW (Dr. Falk); Lumeblue EU (Alfasigma), Lumeblue China (China Medical System Holdings); Winlevi US, Japan,
- **Revenue split:** GI Genius, Eleview, and all upcoming medical devices (Medtronic)

The value of Cosmo's equity-for-product stakes in its commercialization partners amounts to EUR 22 mn. Cosmo benefits from milestones and royalties of its partnered products and the long-term value creation of its partner's entire product and pipeline portfolio, which should further boost the value of its equity stakes (see Appendix, page 60).

Success in the USD 75 bn colonoscopy market should be transformational

Colorectal cancer is the third most common cancer diagnosed in the US, which can largely be prevented by timely and regular screening through, e.g., colonoscopy. Cosmo's endoscopy product pipeline, with a special focus on cancer prevention through improved colonoscopies, targets a large market opportunity. With an estimated 19 mn colonoscopies per year in the US with an average cost of USD 3,081 per procedure (according to Blue Cross Blue Shield) and an additional 25 mn in EU/ROW (conservative number) with an assumed cost of USD 655 per procedure (2012 Comparative Price Report), we estimate the global market amounts to almost USD 75 bn per year. Additional costs of polyp removal and biopsy testing (USD ~200-300 per polyp) are excluded from these numbers. This number is set to grow with the aging of the population and structured cancer screening programs. Even low penetration rates for Cosmo's endoscopy products could be transformational, boosted further by capturing more value in the lucrative US market through the GI Genius and Eleview partnership with Medtronic, the world's leading medical device company with considerable marketing muscle.

Targeting a USD 20+ bn IBD market driven by biologics and new treatments

According to Evaluate Pharma, Cosmo's gastrointestinal drugs target a global IBD (inflammatory bowel disease) drug market estimated at USD 19.8 bn in 2020 and expected to increase to USD 20.3 bn in 2026. Biologic therapies such as Abbvie's JAK1 inhibitor Rinvoq (upadacitinib tartrate) or JNJ's IL-12/23 monoclonal antibody Stelara (ustekinumab) are expected to be the main drivers of growth over the forecast period due to increased use and substantially higher treatment costs than other IBD treatments such as 5-ASA's, corticosteroids, antibiotics, and immunosuppressants. IBD affects approximately 0.5% of the Western global population. The primary forms of IBD are Crohn's disease and ulcerative colitis. The ulcerative colitis market is valued at USD 6.8 bn. The 5-ASA market dropped to around USD ~430 mn in 2020 from a USD 2 bn peak in 2016 due to the lack of new branded treatments and the emergence of generics impacting the lucrative US market, in particular. Nevertheless, Cosmo's treatments for ulcerative colitis, Lialda/Mezavant and Uceris/Cortiment, have established substantial market penetration due to their improved efficacy and safety profile.

New antibiotics needed for colon infections due to increasing bacterial resistance

Cosmo's therapeutic focus also includes colon infections caused by bacteria. These infections are among the most encountered infections in primary care and span a wide range of diseases, which typically cause (bloody) diarrhea, dehydration, and fever. While they may not always be severe and often resolve rapidly, they can be serious in specific healthcare

settings or patient populations. Cosmo's novel antibiotic rifamycin SV MMX (branded "Aemcolo" in the US and marketed by RedHill and branded "Relafalk" in Dr. Falk territories outside the US) targets travelers' diarrhea and IBS-D (irritable bowel syndrome – diarrhea-predominant) among others, which affect tens of millions of people annually, with increasing bacterial resistance to current antibiotic treatments.

Proprietary "MMX" technology provides the base for new best-in-class GI drugs

At the core of Cosmo's product pipeline is the proprietary "MMX" (**M**ulti-**M**atri**X**) technology, a patented oral controlled-release formulation technology for off-patent drugs that target the gastrointestinal tract. The MMX technology provides an excellent base for developing new, patentable products with a lower risk than NCEs (new chemical entities) with a unique once-a-day dosing regimen. Cosmo may also target riskier NCEs with a longer composition of matter patent protection to extend its business model now that the MMX formulation patent expired in 2020.

Artificial intelligence is a new and revolutionary pillar of growth for Cosmo

Artificial intelligence (AI) is an emerging technology that will become a new and revolutionary pillar of growth that should generate substantial revenues for Cosmo starting in endoscopy with potential additional applications. GI Genius, combined with the global marketing muscle of Medtronic, is set to become a game-changer in colonoscopy, in our view. This real-time automatic polyp detection system based on AI can be seen as a "second set of eyes" that will alert the endoscopist more consistently and reliably than a human assistant (and at significantly lower costs). Additional upgrades such as optical biopsy, other gastrointestinal applications, or procedural documentation and administration could make this an invaluable system in colonoscopy. Other endoscopy products such as Eleview (lesion resection) and Lumeblue (lesion enhancing detection dye) can piggyback on the success of GI Genius and the Medtronic partnership.

Near-term key priorities and strategy in the next 12-18 months:

- **GI Genius:** successfully launched AI-enhanced colonoscopy in the US, across all EU member states, and ROW by global partner Medtronic; host and accelerate an ecosystem of new apps on GI Genius through the expanded cooperation with Medtronic.
- **Lumeblue:** licensed in the EU, Switzerland, EEA countries, Russia, and Mexico by partner Alfasigma; discuss with US FDA the need of a second phase III trial after the positive outcome of the phase III trial in China run by CMS; contract a US commercialization partner, conclude commercialization partnerships for major markets outside the EU (Alfasigma) and China (CSM Holdings).
- **Winlevi:** successfully launched in the US by partner Sun Pharma; seek regulatory approval in key markets outside the US and sign on commercialization partners for these regions, e.g., Sun Pharma territory expansion agreement (Japan, Australia, New Zealand, Brazil, Mexico, Russia), 3SBIO (Greater China), InfectoPharm (Germany, Italy, Austria), Hyphens Pharma (Southeast Asia).
- **Aemcolo/Relafalk:** successfully relaunch in travelers' diarrhea by RedHill in the US and by Dr. Falk in the EU; finalize discussions with the US and EU regulators to start phase III trials in IBS-D; out license ROW rights (ex-US & EU).
- **Eleview:** progress launch in the US/ROW with global partner Medtronic and Canada (Pendopharm).
- **CB-03-10:** progress phase I clinical trial in patients with solid tumors.

- **Expand pipeline:** assess new chemical entities as possible MMX projects or in-license new GI, endoscopy, and dermatology treatments; potentially host an R&D Day to discuss new pipeline projects.

Sustainable cash generation to fund all development plans and pay dividends

Cosmo's gross cash position (including bonds) of EUR 241 mn (CHF 240 mn) on 31 December 2022, together with additional milestone payments and increasing royalty and manufacturing income, is sufficient to finance all development and commercialization plans while also paying a dividend. The substantial cash position is targeted to expand Cosmo's product offering through internal development projects and external transactions. Consequently, the company needs no external funding to execute its clinical development plans, including the second pivotal phase III trial necessary for US approval of Lumeblue or to fully develop the recently reacquired dermatology pipeline, including Breezula in male alopecia (hair loss).

Valuation Overview

Risk-adjusted sum-of-parts NPV points to CHF 92 per share

We derive a risk-adjusted (r)NPV for Cosmo of CHF 92 per share with gross cash and bonds of CHF 15 per share (31 December 2022) and overhead expenses (conservatively including the repayment of the EUR 175 mn convertible bonds in 2023) of CHF 16 per share with a WACC of 7% (reflecting the low Swiss interest environment).

SUM OF PARTS

PRODUCT NAME	INDICATION	PEAK SALES (EUR MN)	LAUNCH YEAR (EST)	UNADJUSTED NPV/SHARE	SUCCESS PROBABILITY	RISK-ADJUSTED NPV/SHARE	PERCENTAGE OF TOTAL
GI GENIUS	AI ENHANCED COLONOSCOPY	313	2019 (EU)/2021 (US)	17	100%	**17**	16%
LUMEBLUE	LESION DETECTION DYE	106	2020 (EU)/2026 (US)	6	82.5%	**5**	5%
ELEVIEW	LESION RESECTION CUSHION	83	2017	5	100%	**5**	4%
BYFAVO	FAST-ACTING SEDATION	164	2020	1	80%	**1**	1%
WINLEVI (TOPICAL ANTI-ANDROGEN)	ACNE	396	2021 (US)/2025 (EU)	23	82.5%	**19**	17%
BREEZULA (TOPICAL ANTI-ANDROGEN)	ALOPECIA (HAIR LOSS, MEN)	382	2026	18	50%	**9**	8%
AEMCOLO / RELAFALK	TRAVELERS' DIARRHEA	47	2019	3	100%	**3**	2%
AEMCOLO / RELAFALK	IBS-D	375	2026	22	50%	**11**	10%
LIALDA / MEZAVANT	ULCERATIVE COLITIS	709	2007	13	100%	**13**	12%
UCERIS / CORTIMENT	ULCERATIVE COLITIS	75	2013	3	100%	**3**	3%
CB-03-10	ONCOLOGY (NON-CORE)	TBD	TBD	TBD	<15%	**TBD**	
CONTRACT MANUFACTURING				6		**6**	6%
"EQUITY FOR PRODUCT" STAKES E.G. REDHILL (14.8%); PAION (6.8%); EAGLE (0.7%)				1		**1**	1%
CASH & SHORT-TERM INVESTMENTS (31 DECEMBER 2022)		241		15		**15**	14%
TOTAL ASSETS				134		**108**	**85%**
OVERHEAD EXPENSES (INCL. REPAYMENT OF EUR 175 MN CONVERTIBLE BOND IN 2023)				-16		**-16**	
NPV/SHARE (CHF)				119		**92**	
SHARE PRICE ON 03 MAY 2023						55	
PERCENTAGE UPSIDE / (DOWNSIDE)						68%	

* NOTE: 16.3 MN SHARES USED FOR NPV/SHARE CALCULATION AS WE ASSUME PAY BACK EUR 175 MN CONVERTIBLE BOND IN 2023 (INCLUDED IN OVERHEAD EXPENSES)
NOTE: 17.5 MN SHARES OUTSTANDING INCLUDES 1.2 MN TREASURY SHARES RESERVED FOR POTENTIAL CONVERSION OF THE CONVERTIBLE BOND
ESTIMATES AS OF 3 MAY 2023

SOURCE: VALUATIONLAB ESTIMATES

Key drivers of growth for Cosmo include:

1) ENDOSCOPY:

GI Genius (AI-enhanced colonoscopy) – rNPV of CHF 17 per share

GI Genius is the first-ever AI (artificial intelligence)-enhanced device approved for colonoscopy with an estimated 2-3 years lead over competitor devices. Combined with the global marketing muscle of Medtronic, we believe this system will be a game-changer in colonoscopy with substantial upside from future upgrades and additional indications (not in our forecasts). We conservatively forecast peak sales of EUR 300+ mn (booked by Medtronic), with Cosmo retaining a net margin above 20%. We calculate an NPV of CHF 17 per share with the device approved and launched in the major global regions. Unfortunately, the launches were severely hampered by the COVID-19 pandemic. We expect the colonoscopy market to rebound with the pandemic becoming endemic.

Lumeblue (colonic lesion detection dye) - rNPV of CHF 5/share

Lumeblue is a novel MMX formulation of the existing liquid colon staining dye methylene blue in a more convenient oral tablet with proven clinical efficacy in detecting lesions. Lumeblue was approved in the EU in August 2020 and is complementary to Cosmo's GI Genius as the dye enhances difficult-to-spot lesions even further with higher contrast. The EU rights were out-licensed to Alfasigma, with the first EU launch in Italy in 2022. China Medical System (CMS) Holding acquired the rights for China. Cosmo will discuss with the FDA about needing another confirmatory phase III trial for US approval. The positive phase III trial conducted by CMS in China with 1,800 patients could now be considered the second confirmatory phase III trial. We conservatively assume the FDA will require an additional phase III trial with US approval expected in 2025 and the launch by a commercialization

partner in 2026. Based on lowered pricing assumptions, we conservatively forecast global peak sales of approximately EUR 100+ mn, as total pricing for a colonoscopy may be affected by the additional fees for GI Genius. We calculate an rNPV of CHF 5 per share with a 75% success rate, the average of EU (100%) approved and US (50%) phase III.

Eleview (dyed lesion resection cushion) – NPV of CHF 5 per share
Eleview is an injectable lesion resection cushion that allows physicians a faster and less risky excision (removal) of adenoma or polyps discovered during endoscopy. Eleview is injected between the mucosal layers, where it separates and flags them with methylene blue dye for easy removal. Medtronic is responsible for global commercialization except in Canada (Pendopharm), replacing previous agreements with EA Pharma, Olympus, and Fujifilm. We forecast a significant increase in sales after the recall of the competing product Orise (Boston Scientific) with EUR 80 mn peak sales with an NPV of CHF 5/share.

Byfavo (fast-acting sedation) – rNPV of CHF 1 per share
Byfavo (remimazolam) is a fast-acting sedative for procedural sedation in endoscopy and complements Cosmo's endoscopy offering. In 2016, Cosmo acquired US rights from originator PAION and currently holds a 7.3% stake. As of June 2022, Eagle Pharmaceuticals is responsible for commercialization in the US, with Cosmo retaining a 0.7% stake in Eagle. Consequently, Cosmo will largely benefit from the long-term value creation through its equity stakes in PAION and Eagle and is eligible to receive a total of up to USD 105 mn payable on Byfavo reaching certain sales milestones. We calculate an NPV of CHF 1 per share for the remaining milestone payments.

2) DERMATOLOGY:

Winlevi (acne) - rNPV of CHF 19 per share
Winlevi became the first-ever topical anti-androgen on the US market for treating acne, with good efficacy and an excellent safety and tolerability profile. Winlevi is off to a flying start in the US, triggering an expansion of the Sun Pharma agreement to include Canada, Japan, Australia, New Zealand, Brazil, Mexico, and Russia. Moreover, 3SBIO acquired the exclusive licensing rights of Winlevi for Greater China, followed by InfectoPharm (Germany, Italy, Austria) and Hyphens Pharma (Southeast Asia). We calculate an rNPV of CHF 19/share for Winlevi in acne with an 82.5% success probability, an average of 100% (launched) in the US, and 65% (phase III) in the EU, with global peak sales, conservatively amounting to EUR 400 mn.

Breezula (hair loss) - rNPV of CHF 9 per share
Breezula is a different formulation and 7.5x higher dosage strength of clascoterone as in Winlevi for the treatment of androgenic alopecia (AGA) the most common type of hair loss. Positive phase IIb dose-ranging results were reported for Breezula in male alopecia. Upon finalizing the phase III program for men with the FDA, phase III trials in men could potentially start in Q2 2023. We assume the first launches for Breezula to occur in 2026 with peak sales of EUR 400 mn. We calculate an rNPV of CHF 9/share with a 50% (phase II completed) success probability for Breezula in male alopecia alone. Currently, we do not include forecasts for female alopecia, although Breezula may be developed for a subgroup of women (under 30 years) based on POC results reported in September 2021.

3) GASTROINTESTINAL:

Aemcolo/Relafalk (TD & IBS-D) – rNPV of CHF 14/share
Aemcolo/Relafalk (rifamycin SV MMX) has potential in TD (travelers' diarrhea) and IBS-D (irritable bowel syndrome – diarrhea predominant), among others. The antibiotic was approved in the US and EU for travelers' diarrhea in November 2018, with its first launch in 2019. Dr. Falk has global rights, excluding the US, where RedHill recently acquired the rights and will now sell the drug through a novel online DTC business model directly to US travelers as well as through its specialist sales force. Dr. Falk brands the drug Relafalk. Outside Dr. Falk's territories, the antibiotic is branded Aemcolo. Revenues were severely impacted by the global COVID-19 pandemic and restricted travel. We conservatively forecast global peak sales of EUR 50 mn in travelers' diarrhea due to the short treatment duration (3 days) with an NPV of CHF 3 per share. Aemcolo/Relafalk should also be developed in IBS-D, a far larger indication with longer treatment times (~14 days), with global peak sales of EUR 350+ mn and an rNPV of CHF 11 per share with a 50% (phase II completed) success probability and first launches in 2026.

LEGACY PRODUCTS:

Lialda/Mezavant (ulcerative colitis) - NPV of CHF 13 per share
Lialda/Mezavant (mesalamine MMX) is Cosmo's first prescription drug using its proprietary MMX technology for treating ulcerative colitis and was launched by Shire (acquired by Takeda in 2019) in 2007. Sales peaked at EUR 709 mn in 2016 before sales were impacted by cheap generics. Cosmo receives manufacturing revenue to produce Lialda tablets for Takeda and its partners. In 2022, Lialda revenues increased by 6% to CHF 29.6 mn, mainly due to the increase in net sales in the US and Japan. We base our Lialda revenues on the number of tablets shipped, expecting single-digit increases in the next few years. We calculate an NPV of CHF 13 per share.

Uceris/Cortiment (ulcerative colitis) - NPV of CHF 3 per share
Uceris/Cortiment (budesonide MMX) is Cosmo's second treatment for ulcerative colitis with far better economics than Lialda. Ferring commercializes the drug in the EU and ROW (excluding Japan) branded Cortiment, while Bausch Health sells the drug, branded Uceris, in the US. Although the peak sales potential was similar to Lialda, sales likely peaked at EUR 139 mn in 2016 due to the "at-risk" launch of a generic version of Uceris by Actavis (Teva) in the US in 2018. We lowered our US sales to reflect the impact of cheap generics in the US while maintaining a solid uptake outside the US by Ferring. We calculate an NPV of CHF 3 per share.

Contract Manufacturing 3rd parties – NPV of CHF 6 per share
Cosmo continues to manufacture API's (active pharmaceutical ingredients) for third parties including generics and specialty drugs in the range of approximately EUR 15 mn, which adds up to an NPV of CHF 6 per share.

"Equity-for-product" investments – NPV of CHF 1 per share
These investments consist of a 14.8% stake in RedHill, a 7.3% stake in PAION, and a 0.7% stake in Eagle, and stakes in VolitionRx (3.5%) and AIMM Therapeutics (6.5%), which adds up to EUR 22 mn or CHF 1 per share. Note that Cosmo will benefit not only from the successful launch of its own products by its commercialization partners but also through the value creation of its partners' product pipeline through its "equity-for-product" stakes.

No value contributed to several pipeline projects, yet

We do not include any forecasts for **CB-03-10** in cancer as the compound currently lacks clinical proof-of-concept (POC), providing a real potential option. CB-03-10 is a synthetic steroidal antiandrogen and is derived from cortexolone, just like the company's dermatology compounds Winlevi (acne) and Breezula (hair loss). In May 2022, Cosmo started a phase I trial of CB-03-10 in up to 90 patients with solid tumors, including pancreas, colon, and prostate cancer, with topline results due in ~18 months from the trial start. On positive phase I results, Cosmo plans to seek a strong oncology partner to fully develop and commercialize CB-03-10 in return for upfront, development, regulatory and sales milestones, and royalties on sales.

CB-01-33 (colesevelam) is a novel bile acid sequestrant formulation for bile acid diarrhea (BAD) that affects approximately 1% of the population, with the potential to overcome the current concerns for bile acid sequestrant treatments for BAD. CB-01-33 is in preclinical development and is therefore excluded from our forecasts.

Sensitivities that can influence our valuation

Development and regulatory risk: We believe the risk is not considerable considering almost all of Cosmo's major products (Lialda/Mezavant, Uceris/Cortiment, Eleview, GI Genius, Aemcolo/Relafalk, Byfavo, Lumeblue, Winlevi) are on the market. Lumeblue has been approved in the EU, and CMS has just concluded a second positive phase III trial in China with 1,800 patients. We assume an 82.5% success rate for Lumeblue, the average of EU (100%) approved and US (65%) phase III development. We assume a 50% success rate for Aemcolo/Relafalk (IBS-D) and Breezula (male hair loss), which will increase to 65% upon the start of phase III development.

Pricing and reimbursement: Pricing for products such as Aemcolo and Byfavo is straightforward as there have been comparable branded products on the market treating the same indications to make a good pricing reference. Cosmo has put considerable effort into determining the right market price for its novel colonoscopy products, such as Eleview, GI Genius (determined by Medtronic globally), and Lumeblue (determined by Alfasigma in the EU), which provide cost-effective solutions compared to current standards. In the EU, pricing and reimbursement occur on a country-by-country base, which can lead to differences in the timing of market launch and sales uptake for each member state.

Partnering and commercialization: Product sales will now be entirely dependent on external commercialization partners such as Medtronic (GI Genius/Eleview), RedHill (Aemcolo), Dr. Falk (Relafalk), Acacia (Byfavo), Alfasigma (Lumeblue) and Sun Pharma (Winlevi) to position successfully and market Cosmo's drugs. Cosmo intends to sign a US commercialization partner for Lumeblue before starting the US phase III trial. Global partner Medtronic will be instrumental in the commercial success of GI Genius and Eleview and future medical devices. Actual sales uptake, upfront, regulatory and sales milestones, and sales royalties may differ from our forecasts as the pace of launching and signing on partners, and terms may differ.

Patent and market exclusivity: Cosmo built a comprehensive patent estate protecting its MMX technology and products from generic competition. Several market exclusivities, such as 10 years of data exclusivity in the EU and 5 years of NCE (new chemical entity) exclusivity or QIDP (qualified infectious disease product) designation with 5 years of additional exclusivity, can further extend market protection. Although Lialda enjoyed composition of matter protection until June 2020 in the US (US6773720) and EU (EU1198226, EU1287822), the FDA has approved a generic version of Lialda from the Indian generic manufacturer Zydus. Uceris has US patent protection until September 2031 through various patents. In July 2018, Actavis' generic received FDA approval and has been launched "at-risk". We assume patent protection and/or market exclusivity for Lumeblue (until 2033), Eleview (until 2034), Byfavo (until 2033), Aemcolo/Relafalk (until 2028), Qolotag (until 2035) and GI Genius (until 2039 largely based on trade secrets). Medical use patents protect Winlevi and Breezula until 2022 (EU/ROW) and 2023 (US), while patents covering all crystalline forms provide protection until 2028 (EU/ROW) and 2030 (US). The use patent for CB-06-01 expires in 2023 (EU/ROW) and 2026 (US), while a US provisional application covering the topical composition in acne filed in 2015 extends protection potentially up to 2035. The use patent for CB-06-02 expires in 2025 (EU/ROW) and 2031 (US), while a US provisional application covering the topical composition filed in 2015 extends protection potentially up to 2035.

Catalysts

CATALYST TIMELINES

TIME LINE	PRODUCT	INDICATION	MILESTONE	COMMENT	IMPACT ON RNPV (CHF/SHARE)
2023					
DURING 2023	WINLEVI	ACNE	LICENSING AGREEMENTS	EXPAND WINLEVI FRANCHISE IN THE REST OF THE WORLD THROUGH LICENSING AND SUPPLY AGREEMENTS WITH DERMATOLOGY COMPANIES	
16 FEB			PRELIMINARY 2022 RESULTS	RECORD TOTAL REVENUE AND OPERATING PROFIT EXCEEDS GUIDANCE; FY 2022 TOTAL REVENUE OF CHF 102.1 MN (2022 GUIDANCE: CHF 90 - 100 MN) AND OPERATING PROFIT OF CHF 28 MN (2022 GUIDANCE: CHF 20 -25 MN) BOOSTED BY GROWTH PRODUCTS WINLEVI AND GI GENIUS AND LEGACY PRODUCTS LIALDA AND UCERIS/CORTIMENT; FY 2023 GUIDANCE: TOTAL REVENUE OF CHF 110 -120 MN AND OPERATING PROFIT OF CHF 25 - 35 MN; PHASE III BREEZULA TRIAL IN MALE HAIR LOSS TO START IN Q1 2023	
23 MAR			FY 2022 RESULTS	RECORD FY 2022 RESULTS EXCEED GUIDANCE; SUSTAINABLE CASH AND CASH EQUIVALATENTS EUR 187 MN (31 DECEMBER 2022); 2023 GUIDANCE: TOTAL REVENUE: EUR 110 MN (+8%) TO EUR 120 MN (+18%), TOTAL REVENUE (EXCL. MILESTONES): EUR 110 MN (+41%) TO EUR 120 MN (+54%), OPERATING RESULT: EUR 25 MN (-11%) TO EUR 35 MN (+25%); DIVIDEND: EUR 1.05 PER SHARE (+11%)	
Q2	BREEZULA	MALE ALOPECIA	START PHASE III	START PHASE III DEVELOPMENT OF BREEZULA IN MALE ALOPECIA AFTER FINALIZING US SPA (SPECIAL PROTOCOL ASSESSMENT) AND TRIAL DESIGN INCLUDING PRO (PATIENT REPORTED OUTCOME) WITH FDA	+ CHF 3
7-9 MAY	GI	AI-ENHANCED LESION DETECTION PLATFORM	DIGESTIVE DISEASE WEEK	NEW DATA SHOWING THE PERFORMANCE OF GI GENIUS ON THOUSANDS OF PATIENTS IN A REAL CLINICAL SETTING TO BE PRESENTED AT THE DIGESTIVE DISEASE WEEK (DDW) IN CHICAGO; THE DATA WILL SHOW THAT GI GENIUS SIGNIFICANTLY REDUCES POLYP MISS RATES AND THEREFORE EFFECTIVE IN REDUCING COLORECTAL CANCER	
26 MAY			AGM	ANNUAL GENERAL MEETING	
27 JUL			H1 2023 RESULTS	H1 RESULTS RELEASE AND INVESTOR CALL	
TBD	AEMCOLO / RELAFALK	IBS-D	START PHASE III	START PHASE III DEVELOPMENT (TRIAL DURATION OF ~18 MONTHS) OF SECOND INDICATION IN IRRITABLE BOWEL SYNDROME WITH DIARRHEA (IBS-D)	+ CHF 3
TBD	LUMEBLUE	LESION DETECTION (ENTIRE COLON)	US PARTNERING FIRST / US PHASE III NEEDED?	DISCUSS WITH FDA IF POSITIVE PHASE III TRIAL IN CHINA COULD BE SUFFICIENT FOR US APPROVAL; OTHERWIZE FINALIZE PROTOCOL AND STATISTICAL ANALYSIS PLAN FOR 2ND CONFIRMATORY PHASE III TRIAL REQUIRED FOR US APPROVAL; START OF TRIAL ONLY AFTER CONCLUDING A US (CO-DEVELOPMENT) LICENSING AGREEMENT	+ CHF 0.3
H2	WINLEVI	ACNE	EU FILING		+ CHF 2
AROUND YEAR-E	GI GENIUS	AI-ENHANCED LESION DETECTION PLATFORM	NEW APPS	EXPAND GI GENIUS BUSINESS WITH MEDTRONIC THROUGH NEW APPS INCLUDING THIRD-PARTY DEVELOPERS WITH THE PLATFORM NOW OPEN TO NEW DEVELOPERS	
AUG	CORTIMENT		JAPAN APPROVAL	APPROVAL AND LAUNCH IN JAPAN, THE SECOND LARGEST INFLAMMATORY BOWEL DISEASE (IBD) MARKET	

ESTIMATES AS OF 3 MAY 2023

SOURCE: VALUATIONLAB, COSMO PHARMACEUTICALS

Technology & Pipeline

Proprietary technology platform consisting of three core technologies
With the inclusion of Cassiopea's dermatology product pipeline, Cosmo's technology platform now consists of three core technologies with a continued focus on gastrointestinal (digestive system) disorders, endoscopy to prevent colon cancer, and dermatology (skin disorders), which includes:

1. **MMX technology:** a formulation technology that leads to a controlled release of drugs over the length of the colon with the potential to extend patent life, such as with Lialda/Mezavant and Uceris/Cortiment in ulcerative colitis, Aemcolo/Relafalk in travelers' diarrhea, and IBS-D, and Lumeblue in chromoendoscopy
2. **Artificial Intelligence:** a new and rapidly emerging technology based on machine and deep learning to improve physician treatment outcomes, such as better detection of lesions during colonoscopy with GI Genius
3. **Anti-androgens:** expertise in anti-androgen compounds derived from cortexolone, involved in skin disorders and cancer (non-core), which includes Winlevi for acne and Breezula for hair loss and new compound CB-03-10 discovered for treating cancer (non-core) to be partnered on successful phase I development

1) MMX Technology - changing systemic drugs to convenient locally active agents
At the core of Cosmo's technology platform is the so-called **M**ulti **M**atri**x** "MMX" technology, a proprietary formulation technology that leads to a controlled release of existing drugs over the length of the colon. The company has developed a range of pharmaceutical products that are based on its MMX technology, including Lialda/Mezavant (mesalamine MMX), Uceris/Cortiment (budesonide MMX), Aemcolo/Relafalk (rifamycin SV MMX), and Lumeblue (methylene blue MMX).

The MMX technology delivers APIs (active pharmaceutical ingredients) inside the colon's interior through oral tablets in a delayed and controlled manner so that the API can be applied to the entire colon length. The tablets manufactured according to the MMX technology are coated with pH-resistant acrylic copolymers, which delay the release until the tablet reaches the indicated intestinal location where the programmed dissolution begins. That protects the active substances from adverse pH (acidic) conditions and enzymatic presence in the upper digestive tracts (e.g., stomach, small intestines). The controlled release over the length of the colon not only simplifies the application for the patients but also allows for the topical application of the APIs to the whole bowel surface that is affected by inflammation or infection.

Cosmo developed its MMX technology based on a clear market need
Cosmo discovered that many drugs that were being developed and prescribed for colon diseases had compliance and safety issues, which could be addressed by their proprietary MMX technology platform. By developing new MMX compounds with existing drugs, the company established a broad knowledge of the colon's physiology and the absorption of pharmaceutical products in the gastrointestinal tract. The unique characteristics of the MMX technology, combined with the broad knowledge of the colon, provide Cosmo a strong competitive edge in developing new drugs for the colon without the need to invest in expensive and high-risk NCEs. Cosmo's MMX compounds have improvements over existing

drugs in terms of efficacy, safety, and tolerability. A lower pill burden leads to higher patient compliance with lower development and regulatory risk than NCEs.

2) Artificial Intelligence – Emerging technology radically changing business models

Artificial intelligence (AI) has become the company's second technology platform that will transform Cosmo. AI systems for healthcare have the potential to transform the diagnosis and treatment of disease, which could help ensure that patients get the right diagnosis, and the right treatment at the right time, enhancing physician treatment outcomes. AI is an area of computer science that emphasizes the creation of intelligent machines that work and react like humans based on machine and deep learning. Machine learning uses algorithms to analyze and learn from data and make informed decisions based on what it has learned. A subfield of machine learning is deep learning, which structures algorithms in layers to an artificial neural network that can learn and make intelligent decisions on its own. This technology can be used to help physicians and patients to make better healthcare decisions.

Prime examples of artificial intelligence outside healthcare include smartphones with speech recognition assistants such as Alexa or Siri, smart cars with autonomous driving, digital cameras with face, eye, or even smile detection, and social media feeds, to name a few. These AI platforms have revolutionized existing business models or have created totally new business models, often with rapid adoption.

GI Genius was developed thanks to Lumeblue images and Linkverse cooperation

Thanks to the clinical development of Lumeblue generating thousands of videos of colonoscopies stored in the first high-definition lossless video database and the cooperation and investment in Linkverse that produced the ad-hoc recording devices and the cloud platform dedicated to this service, Cosmo is now at the frontline of artificial intelligence enhanced colonoscopy with GI Genius. Linkverse, based in Rome and now a fully-owned subsidiary of Cosmo, is an innovative company at the forefront of healthcare information technology, specializing in cloud-based management systems and AI analysis tools for biomedical images, video, and data either for medical practice or for clinical research. Applying modern computer science, Linkverse provides a new, intelligent way of presenting data to make complex problems easily understandable.

GI Genius and Medtronic agreement to capitalize on emerging AI in colonoscopy

Cosmo plans to capitalize on the arrival of AI in colonoscopy through GI Genius, a game-changer, which provides physicians a "second set of expert eyes" that never get tired, combined with Medtronic's global distribution platform. Medtronic is the world's leading medical device company with the knowledge, capital, drive, and marketing muscle to launch Cosmo's GI Genius in colonoscopy successfully. A key success factor is rapidly establishing and locking in a customer base and leveraging this base with future upgrades such as optical biopsy, procedural documentation, or other GI applications. Medtronic provides GI Genius for free, which can easily be fitted in the existing colonoscopy towers/stacks, in return for a relatively small fee per colonoscopy with an estimated yearly fee per GI Genius of USD 30,000 in the US and USD 20,000 in the EU/ROW. The estimated net margin for Cosmo is guided to be above 20%. Furthermore, Cosmo plans to leverage GI Genius to create a platform capable of extending the use of the GI Genius technology to all settings in healthcare where the overlay of AI content is required on a real-time video flow. In March 2023, expanded the cooperation on GI Genius with Medtronic to accelerate the development of new AI software applications (apps) for GI Genius and open the architecture to external developers to host their apps on the GI Genius ecosystem.

3) Anti-androgens – targeting skin disorders and various cancers (non-core)
Cosmo owns a compound library that focuses on diseases dependent on the androgen receptor or so-called anti-androgens. This class of drugs prevents androgens like testosterone or dihydrotestosterone (DHT) from mediating their biological effects in the body. They are involved in skin disorders such as acne or hair loss and various cancers such as prostate cancer, among others. Research in dermatology has become core again with the recent acquisition of Cassiopea and its dermatology product pipeline.

Several Cosmo compounds were derived from cortexolone and were screened for use in a specific treatment. Most notable is the novel anti-androgen clascoterone, a new chemical entity (NCE) and core compound that is being developed in different topical formulations and strengths for indications such as acne (branded Winlevi) and androgenic alopecia also known as pattern hair loss (branded Breezula). In early November 2021, Winlevi was launched in the US by partner Sun Pharma becoming the first truly new mechanism of activity (MOA) to treat acne in nearly 40 years. Clascoterone is quickly metabolized to cortexolone, a naturally occurring metabolite found throughout all human tissues, cells, blood, and urine, with a well-characterized safety and metabolic profile. Due to its rapid metabolism and local activity, clascoterone does not produce systemic side effects. CB-03-10 (non-core) is a potent oral anti-androgen derived from cortexolone, with potent anti-tumor activity across many cancers, such as pancreatic, colon, and prostate cancer.

PRODUCT PIPELINE

PRODUCT	DRUG CLASS	INDICATION	STATUS	LAUNCH YEAR	PARTNER	PEAK SALES
ENDOSCOPY						
GI GENIUS (HEALTH TECH)	ARTIFICIAL INTELLIGENCE ENHANCED IMAGING DEVICE	LESION DETECTION (COLONOSCOPY)	LAUNCH (EU) LAUNCH (US)	2019 2021	MEDTRONIC (GLOBAL RIGHTS)	EUR 300+ MN
LUMEBLUE	COLONIC LESION STAINING DYE	LESION DETECTION (COLONOSCOPY)	LAUNCH (EU) PHASE III (US)	2021 2026	ALFASIGMA (EU)/CMS (CHINA) SEEK PARTNER BEFORE STARTING 2ND PHASE III (US)	EUR 100+ MN
ELEVIEW	LOW-VISCOSITY EMULSION	ENDOSCOPIC RESECTION CUSHION	MARKETED	2017	MEDTRONIC (GLOBAL RIGHTS) EXCL. CANADA (PENDOPHARM)	EUR 80+ MN
BYFAVO	FAST-ACTING BENZODIAZAPINE DERIVATIVE	PROCEDURAL SEDATION (E.G. COLONOSCOPY)	LAUNCH (US)	2020	EAGLE PHARMACEUTICALS (US ONLY) PAION (ORIGINATOR)	EUR 150+ MN
DERMATOLOGY						
WINLEVI	TOPICAL ANDROGEN RECEPTOR INHIBITOR	ACNE VULGARIS	LAUNCH (US) LAUNCH (EU)	2021 2025	US: SUN PHARMA EU/ROW: SEEK PARTNER(S)	EUR 400 MN
BREEZULA	TOPICAL ANDROGEN RECEPTOR INHIBITOR	ALOPECIA (HAIR LOSS)	PHASE IIB DR COMPLETED	2026	US: SEEK PARTNER EU/ROW: SEEK PARTNER(S)	EUR 400 MN
GASTROINTESTINAL DISORDERS						
AEMCOLO / RELAFALK	ANSAMYCIN ANTIBIOTIC	TRAVELER'S & INFECTIOUS DIARRHEA	LAUNCH	2019	REDHILL (US) DR. FALK (EU/AUS)	EUR 50 MN
AEMCOLO / RELAFALK	ANSAMYCIN ANTIBIOTIC	IRRITABLE BOWEL SYNDROME WITH DIARRHEA (IBS-D)	PHASE II	2026	REDHILL (US) DR. FALK (EU/AUS)	EUR 350+ MN
LIALDA / MEZAVANT (LEGACY PRODUCT)	5-ASA	ULCERATIVE COLITIS (INDUCTION & MAINTENANCE)	MARKETED	2007	TAKEDA (US, ROW) NOGRA (JAPAN)	EUR 700 MN
UCERIS / CORTIMENT (LEGACY PRODUCT)	ORAL GLUCOCORTICOSTEROID	ULCERATIVE COLITIS (INDUCTION)	MARKETED	2013	BAUSCH HEALTH (US) FERRING (ROW)	EUR 75 MN
CB-01-33 (COLESEVELAM)	BILE ACID SEQUESTRANT FORMULATION	BILE ACID DIARRHEA	PRECLINICAL	TBD		TBD
ONCOLOGY (NON-CORE)						
CB-03-10	ANDROGEN RECEPTOR ANTAGONIST	ONCOLOGY	PHASE I	TBD	PARTNER ON SUCCESSFUL PHASE I	TBD

ESTIMATES AS OF 3 MAY 2023 SOURCE: VALUATIONLAB, COSMO PHARMACEUTICALS

Uniquely positioned with 8 launched products covering GI disease and endoscopy
Cosmo's therapeutic focus is on the endoscopic oral and pharmaceutical treatment of colon disorders and dermatology. At present, Cosmo has eight products on the market, including Lialda/Mesavant and Uceris/Cortiment, for treating mild-to-moderate ulcerative colitis, Aemcolo/Relafalk for travelers' diarrhea (and potentially IBS-D), GI Genius, a novel artificial intelligence-enhanced imaging device for colonoscopy, Eleview, for endoscopic lesion resection, Byfavo, a fast-acting sedative ideally suited for colonoscopy, Lumeblue, an oral lesion staining dye for lesion detection in the entire colon, and most recently Winlevi, the novel topical androgen receptor inhibitor clascoterone for treating acne vulgaris. CB-03-10 is a non-core oncology compound derived from Cosmo's novel anti-androgen cortexolone,

which started a phase I trial in solid tumors in May 2022. After completing phase I, Cosmo plans to license CB-03-10 to a strong oncology player in return for upfront, clinical, regulatory, and sales milestone payments and royalties on sales. The company also sells the nutraceutical Zacol NMX, a dietary supplement in Italy.

In the following section, we will provide in-depth analyses and forecasts for Cosmo's key drivers for:

I) ENDOSCOPY

GI Genius – AI-enhanced colonoscopy imaging device

Product Analysis

GI Genius peak sales of EUR 300+ mn - rNPV of CHF 17/share

We conservatively forecast Cosmo's artificial intelligence (AI) enhanced colonoscopy device, GI Genius, to generate EUR 313 mn peak sales (booked by global partner Medtronic). GI Genius was launched by Medtronic in Europe in October 2019 and in the US in May 2021. Initial sales uptake was hampered by the pandemic. We assume the adoption rate for computer-aided (= artificial intelligence) detection in colonoscopy to rapidly increase to above 95% globally within 10 years from launch. As a first mover and global player, Medtronic is initially expected to have a dominant market share, which we conservatively assume will gradually decline to 30% market share in new AI devices in the US and 15% in the EU by rival systems, albeit in a larger market, as more AI players grow the market for AI-enhanced colonoscopy devices. Cosmo guides the net margin to be above 20%. We assume this consists of 22% royalties on sales and a net manufacturing income of EUR 600 per GI Genius device delivered to Medtronic. Medtronic provides GI Genius for free in return for an estimated fee per procedure ranging between an estimated EUR 45 (US) and EUR 15 (EU). We calculate an NPV of CHF 282 mn or CHF 17 per share with a WACC of 7% (see page 29).

NOTE: We have not included revenues for future upgrades for GI Genius, such as optical biopsy, procedural documentation & administration, or other GI indications, which provide substantial upside to our forecasts.

GI Genius & Medtronic: a game-changer in colonoscopy

The healthcare market is on the verge of revolutionary change with the arrival of artificial intelligence (AI) systems based on machine and deep learning combined with significant improvements in hardware (e.g., processing power) that will lead to better physician treatment outcomes. We believe Cosmo's AI colonoscopy device, branded GI Genius, combined with the global marketing muscle of Medtronic, the world's leading medical device company, will become a game-changer in how colonoscopy will be performed in the future. GI Genius provides physicians with a simple and effective interface – the operator is alerted in real-time by a dynamic green box around the lesion, like face or eye detection on digital cameras - to reduce the risk of missing a lesion and ultimately improve the detection rate during colonoscopy. Together with Lumeblue, a potential new gold standard image-enhancing staining agent for a colonoscopy that complements GI Genius, Cosmo is set for transformational change once both products are successfully launched globally in the next few years.

The most preventable cancer depends on the ADR and finding lesions early

Colorectal cancer is the third most common cause of cancer death worldwide. In the US, there are 150,000 new cases and 50,000 deaths yearly due to colorectal cancer. Colorectal cancer is considered a disease of older people, with more than 90% of patients being diagnosed after the age of 55 years. However, colorectal cancer is also considered one of

the most preventable cancers. Colonoscopy is the primary screening tool to prevent colorectal cancer by early detection and removal (resection) of precancerous lesions (adenomas) and cancerous lesions and polyps. Screening is advised typically for most people from age 50 years until age 75 years. If a colonoscopy does not find adenomas or cancer and there are no other risk factors, the next exam should be performed in ten years. If one or two small, low-risk adenomas are removed, the colonoscopy should be repeated in five to ten years.

Not all adenomas turn into cancer, but all colon cancers were previously adenomas
Colonoscopy aims to detect adenomas. Not all adenomas turn into cancers, but all cancers were previously adenomas. Therefore, the effectiveness of colonoscopy depends on the adenoma detection rate (ADR). Ultimately, the more adenomas are detected and extracted; the fewer cancers will subsequently develop. Most polyps look something like a mushroom growing from the colon wall and are easily seen and removed during the colonoscopy. Diminutive (tiny) polyps, measuring between 1 and 5mm, represent the vast majority of colorectal polyps observed during screening colonoscopy. There are also flat polyps that grow wide, spreading along the colon wall, usually in the right colon. Flat polyps are believed to make up about 9% of all polyps. But because they are challenging to find and remove altogether, they are believed to be responsible for most of the colon cancers that occur in people who are up to date with their colonoscopies.

Large variability in ADR increases the risk of interval colorectal cancer
Colonoscopists vary widely in their ability to find adenomas, with an ADR ranging from 7% to 54% with a mean of ~30%. Approximately 26% of diminutive polyps are missed. The detection rate for adenomas from flat polyps is even worse, with a national mean of 2%. Medicare expects a 25% ADR among women and 30% among men. The prevalence of adenomas is estimated to be >50%. If one or more adenomas are missed, the patient has an increased risk of developing colorectal cancer before their next colonoscopy. A large study by Corley et al. showed that every 1% increase in the adenoma detection rate was associated with a 3% decrease in the risk of colorectal cancer before the next exam.

Two main factors are considered to affect the low adenoma detection rate:

1. **Lesions that are difficult to spot:** this can be improved, for instance, by using high-definition wide-angle endoscopes with white light (HDWL), devices to clean and visualize the entire surface area, or image-enhancing dyes that mark difficult-to-spot (flat or tiny) adenomas (e.g., Lumeblue).
2. **Human error:** this is not easily overcome and is dependent on multiple factors such as motivation, training, manual skills, and intrinsic abilities such as observer-dependent visual acuity and pattern recognition.

Colonoscopy is an expensive screening tool with room to improve
Colonoscopy is also the costliest screening tool to prevent colorectal cancer. Any solution significantly increasing the adenoma detection rate (ADR) is expected to be integrated into the procedure and included in treatment guidelines. Particularly if the solution has proven efficacy and is simple to adopt. This is where computer-aided detection or artificial intelligence can play an important role. AI systems such as Cosmo's GI Genius can be added to a colonoscopy tower/stack, while implementation is simple with no extensive training needed.

GI Genius is a "second set of expert eyes" that never tire of assisting the operator
AI is an area of computer science that emphasizes the creation of intelligent machines that work and react like humans based on machine and deep learning. Machine learning uses algorithms to analyze data, learn from data, and make informed decisions based on what it has learned. A subfield of machine learning is deep learning, which structures algorithms in layers to an artificial neural network that can learn and make intelligent decisions on its own.

AI is rapidly making inroads in healthcare, with the most promising results in imaging (computer-aided detection) and diagnosis (computer-aided diagnosis, e.g., optical biopsy). Digital images provide vast amounts of high-quality data with complete data sets, which is crucial for AI and deep learning. AI processes the data and tries to replicate a physician's understanding of that data and determine what is normal and what may need to be addressed medically. Moreover, the human eye is often blind to some patterns that could be present in these images. As stated, in colonoscopy, reported miss rates of lesions range between 20-40% due to both polyp and operator characteristics.

Cosmo's GI Genius intends to provide the colonoscopy operator with a "second set of expert eyes" that never tire of reducing the rate of missed lesions and thereby improve the overall lesion detection rate. GI Genius provides physicians with a simple and effective interface to detect significantly more lesions during colonoscopy than the current gold standard HDWL (High-Definition endoscope with White Light). When a lesion is detected, GI Genius projects a dynamic green box around the lesion on the operator's screen in real-time. This convenient and straightforward interface highlights the lesion until it is removed. The device operates in real-time to assist the endoscopist in detecting lesions, is very simple to use, and is compatible with all endoscopes. Cosmo is the sole manufacturer. Medtronic is the exclusive worldwide distributor.

Highly accurate lesion detection rate demonstrated in several international trials
The accuracy of GI Genius is very high – as good as an expert colonoscopist - as demonstrated in several international trials (see Appendix, page 60).

> **Retrospective trials** have proven the system to be very accurate, with a true positive rate per polyp (sensitivity) of 99.7%. In comparison, the number of false positive frames in a full procedure (activation noise = false positives divided by the number of frames) amounted to 0.9%. In other words, the system was as good as an expert colonoscopist in detecting lesions and the extremely low number of false activations does not slow down or negatively alter the conventional colonoscopy procedure.
>
> **Investigator-initiated trial:** Positive results of the first prospective, completely independent, investigator-initiated clinical trial conducted at 3 Italian hospitals showed that GI Genius significantly increases the Adenoma Detection Rate (ADR) and the number of Adenomas Per Colonoscopy (APC) compared to standard colonoscopy, thereby providing additional efficacy of screening colonoscopy for colorectal cancer prevention.
>
> **"DETECT" trial:** conducted in eight centers across the US, Italy, and the United Kingdom, showed that using GI Genius in conjunction with colonoscopy significantly decreases the miss rate (2x) of colorectal polyps and adenomas compared to standard colonoscopy. Missed polyps are estimated to account for around half of all

cases of post-colonoscopy colorectal cancer and could be ultimately the difference between life and death when considered 90% of patients with colon cancer can survive when caught early.

Swift regulatory approval in major markets – GI Genius has at least 2-3 years lead
GI Genius was approved in the EU in October 2019 based on the retrospective trials Cosmo performed to establish the first proof of concept of the device in improving adenoma detection rates. The GI Genius Investigator-Initiated trial formed the basis for the rapid approval of GI Genius in the US ahead of time. GI Genius is the first of its kind to obtain FDA approval through the "de novo" application process in April 2021. Devices that are classified through the "de novo" process may be marketed and used as predicates for future 510(k) submissions. This provides a considerable barrier to entry for competitor devices, which must prove they are "substantially equivalent" to GI Genius. Moreover, Medtronic can set the price of GI Genius, being the first on market. We believe GI Genius has an estimated 2-3 years lead over competitor devices still in the experimental development stage.

GI Genius and Medtronic agreement to capitalize on emerging AI in colonoscopy
Cosmo plans to capitalize on the arrival of AI in colonoscopy through its GI Genius, which provides physicians a "second pair of expert eyes" that never tire, combined with Medtronic's global distribution platform. Medtronic is the world's leading medical device company with the knowledge, capital, drive, and marketing muscle to launch GI Genius successfully in colonoscopy. The key is establishing and locking in a customer base as soon as possible and leveraging this base with future upgrades such as optical biopsy, other GI applications, or procedural documentation modules. Medtronic will provide GI Genius for free, which can easily be fitted in the existing colonoscopy towers (stacks), in return for a modest fee per colonoscopy. Cosmo indicated that the annual subscription fee per GI Genius will amount to approximately USD 30,000 in the US and USD 20,000 in the EU/ROW.

AI cooperation with Medtronic extended to host an ecosystem of new apps for GI Genius and accelerate the development cycle
In March 2023, Cosmo's fully owned subsidiary Cosmo Intelligent Medical Devices (IMD) expanded its cooperation with Medtronic to accelerate the development of artificial intelligence (AI) applications in the healthcare system and bring new AI-based solutions into patient care. Other apps could include optical biopsy, detecting and monitoring inflammation in chronic gastrointestinal diseases, or augmented reality (see below).

GI Genius is the base technology platform for Medtronic to create an AI Access Platform, a set of solutions to enable and scale up the implementation of AI in the endoscopy suite. Simultaneously, Cosmo IMD will develop Cosmo's Innovation Center to provide Software as a Medical Device (SaMD) application developers with a sandbox, an isolated testing environment that allows software developers to design and test medical AI software applications using a virtual version of the GI Genius hardware. Software as a Medical Device (SaMD) is specific software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device.

The SaMD applications (apps) are intended to be uploaded and implemented on GI Genius, the hardware medical device, with the potential to accelerate AI innovation for better patient care. The SaMD apps from external as well as internal developers leverage the GI Genius technology platform and will be marketed by Medtronic, with Cosmo having a 20% of Medtronic sales impact on their profit.

Cosmo IMD will use NVIDIA Holoscan and NVIDIA IGX within Cosmo IMD's full-stack framework for SaMD development to offer leaner and more powerful development standards to speed up the medical device cycle and expand access to real-time AI in procedures, thereby attracting a larger community of developers. NVIDIA Holoscan, a domain-specific AI computing platform, delivers the full-stack infrastructure needed for scalable, software-defined, real-time processing of streaming data at the edge, so developers can build devices and deploy AI applications directly into clinical settings. NVIDIA IGX is an industrial-grade platform that combines enterprise-level hardware, software, and support. As a single, holistic platform, IGX allows companies to focus on application development and realize the benefits of AI faster. The opening of the architecture to external developers will accelerate the introduction of AI in every healthcare context.

The expanded collaboration will enable developers to work on Medtronic's GI Genius AI Access Platform and Cosmo's Innovation Center to efficiently train and validate SaMD apps by assisting with the hardware (GI Genius), AI software (NVIDIA Holoscan, IGX), science, data, regulatory authorities, and certification.

Future upgrades to the GI Genius could generate substantially higher revenues
Cosmo intends to improve GI Genius constantly through the distribution of new software upgrades regularly. New core functionalities are already under development, including:

Optical biopsy: Cosmo's high-quality data set is being used to train the deep neural network to classify colon polyps as adenomatous or non-adenomatous. The appropriate label is shown automatically next to the polyp detected by GI Genius, in real-time and without altering the clinical workflow. This feature, called CADx or optical biopsy, is clinically relevant to select optimal treatment regimens, avoiding inappropriate endoscopic resection, improving cost-effectiveness, and reducing the number of polypectomies.

Additional GI & other applications: The AI system can be used to detect and monitor inflammation in chronic gastrointestinal diseases such as IBD (inflammatory bowel disease), identify gastrointestinal bleeding, or even diagnose certain gastrointestinal infections.

Other implementations not yet mentioned by Cosmo could include:

Procedural documentation: While performing a colonoscopy, AI algorithms can observe and record all the elements that need to go into a procedural note such as time of insertion and withdrawal, findings, locations, and tools used according to medical insurance codes, thereby reducing the administrative burden for the colonoscopist, and converting documentation time to more patient (treatment) time.

Augmented reality: Augmented reality can superimpose computer-generated objects and data over existing real structures seen on the screen to improve the operator's ability to perform a task in real-time such as project the probability of malignancy for each polyp, detect the presence and type of polyposis according to the number and pattern of polyps that may become malignant, and provide a much more hands-on way for colonoscopists to begin training and for gastroenterologists to confirm a diagnosis.

These new applications (apps), which can be delivered through software upgrades, provide a substantial upside to our forecasts for GI Genius through additional fees, faster and higher adoption rates, and market share.

We conservatively forecast EUR 300+ mn peak sales for GI Genius

Although we believe Cosmo's GI Genius, together with the marketing muscle of Medtronic, will be a game-changer in colonoscopy, it is difficult to provide accurate forecasts for disruptive technologies in their early years. To complicate matters further, the number of colonoscopies dropped by an estimated ~80% in 2020 due to the COVID-19 pandemic. Although the number of colonoscopies seems to have recovered in 2021, it is difficult to predict by how much and when previous levels will be reached again. With experts now expecting the pandemic to turn into the endemic phase, we expect the number of colonoscopies to gradually recover beyond pre-pandemic levels due to the aging of the population and increased screening efforts.

We have based our GI Genius forecasts mainly on data provided by Medtronic (the number of US towers/stacks) and on US sources, which are more detailed and easily available, and extrapolated our findings to other regions. We only include forecasts for the higher-priced markets such as the US, Europe (excluding CEE), Japan, and Australia. Large markets such as CEE, Asia, or China could provide substantial upside to our forecasts. GI Genius was launched by Medtronic in the EU at the United European Gastroenterology Week in October 2019, approved in Australia in February 2020, and in the important and lucrative US market in April 2021.

US peak sales estimated to reach around EUR 250 mn

Medtronic estimates there are more than 30,000 stacks in the US alone. In 2019, an estimated 19 mn colonoscopies were performed in the US. Assuming 30,000 stacks, this amounts to approximately 630 colonoscopies performed on a single stack per year. Applying the guided USD 30,000 annual subscription fee per stack – the GI Genius will be provided for free by Medtronic – this amounts to an average fee of approximately USD 45 per colonoscopy or less than 2% of the total cost of a colonoscopy in the US. Assuming 250 net operational days (excluding weekends, holidays, and 10 maintenance days) we calculate that around 2.5 colonoscopies were performed per stack in 2019. We calculate this number dropped to 0.5 in 2020, heavily impacted by the COVID-19 pandemic. We estimate that the number of colonoscopies in the US will have doubled in 2021 and will gradually recover beyond pre-pandemic numbers due to the aging of the population.

Next to the number of colonoscopies performed, the adoption rate of computer-aided detection (CAD) in colonoscopy and the market share Medtronic captures will be critical for our forecasts. We initially forecast a low adoption rate of CAD devices in colonoscopy, as Medtronic will be the only player offering and promoting a commercial system. Going forward, we expect existing colonoscopy players such as Olympus and Fuji, but also AI tech companies outside colonoscopy (e.g., Google), to launch rival CAD systems and rapidly increase the CAD adoption rate. We assume the adoption rate to peak above 95% thanks to the ease of use, the accuracy of CAD systems spotting hard-to-detect lesions, the potential legal liability of not using such a system, and the relatively low-cost subscription model. Conversely, Medtronic is expected to have a dominant 100% market share in the first 3 years in the US, gradually declining to 30% of new stacks using CAD systems as new players enter the market.

We do not forecast a substantial increase in the number of colonoscopy stacks as we expect the CAD systems to gradually increase capacity utilization from an estimated 2.5 colonoscopies per day in 2019 (severely impacted by the COVID-19 pandemic) to an average of 3 procedures per day. Based on the above, with an annual subscription fee of USD 30,000, we calculate peak sales in the US to amount to EUR 245 mn, which Medtronic will book. Cosmo will retain a net margin of above 20%, consisting of a 22% royalty on sales and an estimated net manufacturing revenue of EUR 600 per device.

EU peak sales expected to reach EUR 70 mn

In the EU, we forecast a similar recovery in the number of colonoscopies after the pandemic (from an estimated 33 mn in 2019 to more than 40 mn in the next 10 years), a similar CAD adoption rate in colonoscopies and an initial dominant market share for Medtronic in the next 3 years gradually declining to 15% of new CAD systems. In the EU, we assume a yearly fee of USD 20,000. Based on the above, we expect GI Genius's peak sales in the EU to reach EUR 70 mn.

Forecasts & Sensitivity Analysis

GI GENIUS - FINANCIAL FORECASTS FOR AI-ENHANCED COLONOSCOPY IMAGING

INDICATION	COLONOSCOPY - ARTIFICIAL INTELLIGENCE ENHANCED ACCURATE AND CONVENIENT EARLY LESION DETECTION TO PREVENT COLON CANCER
DOSAGE	TO BE USED IN EVERY COLONOSCOPY
PRICING	WE CALCULATE A PER PROCEDURE FEE RANGING OF AROUND USD 45 IN THE US AND AROUND EUR 15 IN THE EU
STANDARD OF CARE	CURRENT GOLD STANDARD IS HIGH DEFINITION ENDOSCOPE WITH WHITE LIGHT (HDWL); OLYMPUS' ENDO-AID (EU / US LAUNCH: 2023E); FUJIFILM AI (EU / US LAUNCH: 2023E)
UNIQUE SELLING POINT	"SECOND SET OF EYES" THAT DETECTS LESIONS IN REAL TIME WITH EXTREME ACCURACY, MARKED BY A GREEN BOX, WHICH REDUCES FAILURE TO RECOGNIZE LESIONS

7Ps ANALYSIS

PATENT	WE CONSERVATIVELY ASSUME MARKET EXCLUSIVITY UNTIL 2039 AS THE ARTIFICIAL INTELLIGENCE TECHNOLOGY IS BASED ON PROPRIETARY DATA (TRADE SECRETS)
PHASE	EU; APPROVED WITH CE MARKING; LAUNCH OCT 2019; US: APPROVED APRIL 2021, LAUNCH MAY 2021; NOTE: 60-DAY TRIAL PERIOD BEFORE RECORDING SALES
PATHWAY	MEDICAL DEVICE REGULATORY PATHWAY; EU: APPROVED WITH CE MARKING; US: REGULATORY "DE NOVO" PATHWAY SETTING REQUIREMENTS FOR NEW AI DEVICES
PATIENT	HIGHER ADR DETECTION RATE LEADS TO LOWER PROBABILITY OF DEVELOPING COLORECTAL CANCER BEFORE NEXT COLOTECTAL EXAM
PHYSICIAN	"SECOND SET OF "EYES" THAT DETECTS LESIONS IN REAL TIME WITH EXTREME ACCURACY, MARKED BY A GREEN BOX, REDUCES FAILURE TO RECOGNIZE LESIONS
PAYER	SMALL ADDITIONAL COST TO PROCEDURE WHILE EARLY DETECTION OF COLON CANCER REDUCES LONG-TERM COSTS SUBSTANTIALLY
PARTNER	GLOBAL PARTNERING WITH MEDTRONIC; ANNUAL SUBSCRIPTION FEE PER DEVICE IN US (USD 30,000), IN EU (USD 20,000); GUIDED NET MARGIN FOR COSMO TO BE ABOVE 20%

REVENUE MODEL

UNITED STATES - SOLD BY MEDTRONIC	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
PEOPLE OF SCREEN-ELIGIBLE AGE (50-74 YEARS) (MN)	80	81	83	85	86	88	90	92	93	95	97
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PERCENTAGE COLONOSCOPIES (%)	20%	23%	23%	23%	23%	23%	23%	23%	23%	23%	23%
ANNUAL NUMBER OF COLONOSCOPIES (MN)	16	19	19	19	20	20	21	21	21	22	22
CHANGE (%)	104%	17%	2%	2%	2%	2%	2%	2%	2%	2%	2%
NUMBER OF COLONOSCOPY TOWERS (STACKS)	30,909	31,218	31,530	31,846	32,164	32,486	32,811	33,139	33,470	33,805	34,143
GROWTH (%)	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
NUMBER OF STACKS NEWLY ADOPTED WITH COMPUTER-AIDED DETECTION (%)	3%	10%	20%	30%	12%	2%	1%	1%	1%	1%	1%
NUMBER OF STACKS NEWLY ADOPTED WITH COMPUTER-AIDED DETECTION	773	3,122	6,306	9,554	3,860	650	328	331	335	338	341
GI GENIUS MARKET PENETRATION (%)	100%	60%	50%	40%	30%	30%	30%	30%	30%	30%	30%
NEW STACKS USING GI GENIUS	**773**	**1,873**	**3,153**	**3,821**	**1,158**	**195**	**98**	**99**	**100**	**101**	**102**
INSTALLED BASE OF STACKS USING COMPUTER-AIDED DETECTION	1,079	4,201	10,507	20,060	23,920	24,570	24,898	25,229	25,564	25,902	26,243
MARKET PENETRATION COMPUTER-AIDED DETECTION	3%	13%	33%	63%	74%	76%	76%	76%	76%	77%	77%
INSTALLED BASE OF STACKS USING GI GENIUS	**1,079**	**2,952**	**6,105**	**9,926**	**11,084**	**11,279**	**11,378**	**11,477**	**11,577**	**11,679**	**11,781**
GI GENUIS MARKET PENETRATION (%)	100%	70%	58%	49%	46%	46%	46%	45%	45%	45%	45%
ANNUAL FEE PER GI GENIUS (EUR)	28,644	27,586	27,586	27,586	27,586	27,586	27,586	27,586	27,586	27,586	27,586
ROLLOUT ADJUSTMENT FACTOR (YEAR 1)	0.38	0.38	0.38	0.38	0.38	0.38	0.38	0.38	0.38	0.38	0.38
SUBSCRIPTION SALES YEAR 1 (EUR MN)	8	20	33	40	12	2	1	1	1	1	1
SUBSCRIPTION SALES YEAR 2 (EUR MN)	12	21	52	87	105	32	5	3	3	3	3
SUBSCRIPTION SALES YEAR 3 (EUR MN)		11	21	52	87	105	32	5	3	3	3
ROLLOUT ADJUSTMENT FACTOR (YEAR 4)			0.85	0.62	0.62	0.62	0.62	0.62	0.62	0.62	0.62
SUBSCRIPTION SALES YEAR 4 (EUR MN)			10	13	32	54	65	20	3	2	2
INSTALLED BASE GI GENIUS SUBSCRIPTION RENEWALS			**306**	**1,079**	**2,952**	**6,105**	**9,926**	**11,084**	**11,279**	**11,378**	**11,477**
SALES INSTALLED BASE GI GENIUS AFTER SUBSCRIPTION RENEWAL (EUR MN)			1	3	8	17	27	31	31	31	32
SALES (EUR MN) - BOOKED BY MEDTRONIC	**20**	**52**	**117**	**195**	**245**	**210**	**131**	**59**	**41**	**40**	**40**
CHANGE (%)	1233%	160%	123%	67%	25%	-14%	-38%	-55%	-31%	-3%	1%
ROYALTY (%)	7%	22%	22%	22%	22%	22%	22%	22%	22%	22%	22%
ROYALTIES (USD MN)	1	13	28	47	59	50	31	14	10	9	10
ROYALTIES (~22%) (EUR MN)	1	12	26	43	54	46	29	13	9	9	9
MANUFACTURING REVENUE PER AI DEVICE (EUR)	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000
MANUFACTURING REVENUE (EUR MN)	4	11	19	23	7	1	1	1	1	1	1
COGS PER AI DEVICE (EUR)	-5,400	-5,400	-5,400	-5,400	-5,400	-5,400	-5,400	-5,400	-5,400	-5,400	-5,400
COGS (EUR MN)	-4	-10	-17	-21	-6	-1	-1	-1	-1	-1	-1
PROFIT BEFORE TAX (EUR MN)	**1**	**13**	**28**	**45**	**55**	**46**	**29**	**13**	**9**	**9**	**9**
TAXES (EUR MN)	0	-3	-6	-9	-11	-9	-6	-3	-2	-2	-2
PROFIT (EUR MN)	**1**	**10**	**22**	**36**	**44**	**37**	**23**	**11**	**7**	**7**	**7**

EUROPE (EXCL. CEE) / JAPAN / AUSTRALIA - SOLD BY MEDTRONIC	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
PEOPLE OF SCREEN-ELIGIBLE AGE (50-74 YEARS) (MN)	140	143	146	148	151	154	158	161	164	167	171
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PERCENTAGE COLONOSCOPIES (%)	20%	23%	23%	23%	23%	23%	23%	23%	23%	23%	23%
ANNUAL NUMBER OF COLONOSCOPIES (MN)	28	33	33	34	35	36	36	37	38	38	39
CHANGE (%)	104%	17%	2%	2%	2%	2%	2%	2%	2%	2%	2%
NUMBER OF COLONOSCOPY TOWERS (STACKS)	20,812	21,020	21,230	21,443	21,657	21,874	22,092	22,313	22,537	22,762	22,989
GROWTH (%)	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
NUMBER OF STACKS NEWLY ADOPTED WITH COMPUTER-AIDED DETECTION (%)	15%	30%	20%	15%	10%	2%	2%	1%	1%	1%	1%
NUMBER OF STACKS NEWLY ADOPTED WITH COMPUTER-AIDED DETECTION	3,122	6,306	4,246	3,216	2,166	437	442	223	225	228	230
GI GENIUS MARKET PENETRATION (%)	20%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
NEW STACKS USING GI GENIUS	**624**	**946**	**637**	**482**	**325**	**66**	**66**	**33**	**34**	**34**	**34**
INSTALLED BASE OF STACKS USING COMPUTER-AIDED DETECTION	4,469	10,775	15,021	18,237	20,403	20,840	21,282	21,505	21,731	21,958	22,188
MARKET PENETRATION COMPUTER-AIDED DETECTION	21%	51%	71%	85%	94%	95%	96%	96%	96%	96%	97%
INSTALLED BASE OF STACKS USING GI GENIUS	**944**	**1,890**	**2,527**	**3,009**	**3,334**	**3,400**	**3,466**	**3,499**	**3,533**	**3,567**	**3,602**
GI GENUIS MARKET PENETRATION (%)	21%	18%	17%	16%	16%	16%	16%	16%	16%	16%	16%
ANNUAL FEE PER GI GENIUS (EUR)	19,096	18,390	18,390	18,390	18,390	18,390	18,390	18,390	18,390	18,390	18,390
SUBSCRIPTION SALES YEAR 1 (EUR MN)	5	7	4	3	2	0	0	0	0	0	0
SUBSCRIPTION SALES YEAR 2 (EUR MN)	6	11	17	12	9	6	1	1	1	1	1
SUBSCRIPTION SALES YEAR 3 (EUR MN)	2	6	11	17	12	9	6	1	1	1	1
SUBSCRIPTION SALES YEAR 4 (EUR MN)	2	1	4	7	11	7	5	4	1	1	0
INSTALLED BASE GI GENIUS SUBSCRIPTION RENEWALS	**149**	**247**	**417**	**944**	**1,890**	**2,527**	**3,009**	**3,334**	**3,400**	**3,466**	**3,499**
SALES INSTALLED BASE GI GENIUS AFTER SUBSCRIPTION RENEWAL (EUR MN)	3	5	8	17	35	46	55	61	63	64	64
SALES (EUR MN) - BOOKED BY MEDTRONIC	**18**	**30**	**45**	**57**	**68**	**69**	**68**	**68**	**65**	**66**	**66**
CHANGE (%)	185%	67%	51%	28%	20%	1%	-1%	-1%	-3%	1%	0%
ROYALTIES (~22%) (EUR MN)	1	7	10	13	15	15	15	15	14	15	15
MANUFACTURING REVENUE (EUR MN)	3	6	4	3	2	0	0	0	0	0	0
COGS (EUR MN)	-3	-5	-3	-3	-2	0	0	0	0	0	0
PROFIT BEFORE TAX (EUR MN)	**1**	**7**	**10**	**13**	**15**	**15**	**15**	**15**	**14**	**15**	**15**
TAXES (EUR MN)	0	-1	-2	-3	-3	-3	-3	-3	-3	-3	-3
PROFIT (EUR MN)	**1**	**6**	**8**	**10**	**12**	**12**	**12**	**12**	**12**	**12**	**12**

	2022E	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
GLOBAL SALES (EUR MN)	**38**	**82**	**161**	**252**	**313**	**279**	**199**	**127**	**106**	**106**	**106**
CHANGE (%)	390%	116%	97%	56%	24%	-11%	-29%	-36%	-16%	-1%	1%
GLOBAL PROFIT (EUR MN)	**2**	**16**	**30**	**46**	**56**	**49**	**35**	**22**	**19**	**19**	**19**
CHANGE (%)	-47%	703%	91%	54%	20%	-12%	-29%	-36%	-16%	-1%	1%

WACC (%)	7%
NPV TOTAL PROFIT (CHF MN)	**282**
NUMBER OF SHARES (MN)	16.3
NPV PER SHARE (CHF)	**17**

PEAK SALES (EUR MN)	**WACC (%)**						
CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
470	27	26	25	25	24	23	23
420	24	23	23	22	21	21	20
370	21	21	20	19	19	18	18
320	18	18	17	**17**	16	16	15
270	16	15	15	14	14	13	13
220	13	12	12	12	11	11	11
170	10	9	9	9	9	8	8

ESTIMATES AS OF 3 MAY 2023

SOURCE: VALUATIONLAB ESTIMATES

Lumeblue – Colonic lesion detection dye

Product Analysis

Lumeblue peak sales of EUR 100+ mn - rNPV of CHF 5/share

We forecast peak sales of EUR 106 mn for Lumeblue in chromoendoscopy. Lumeblue was approved in the EU in August 2020, with the first launch in Italy in May 2022 by partner Alfa Sigma with more EU countries to follow soon. Following the Complete Response Letter (CRL) in May 2018, we expect the US launch to occur in 2026, assuming the second confirmatory phase III trial required by the FDA for US approval to start in 2022. We conservatively assume a slightly lower cost per procedure ranging between USD 60 (US) and EUR 20 (EU/ROW), anticipating a potential impact by the additional fee for GI Genius. We maintain our conservative market penetrations peaking at ~7% (EU/ROW) and ~5% (US). In February 2021, Alfasigma acquired the EU rights in return for EUR 4 mn upfront, double-digit royalties (we assume ~20%), and undisclosed sales milestones. Cosmo to discuss whether a second confirmatory phase III trial is needed in the US after CMS reported a second positive phase III trial in China. We assume a US commercialization partner to be contracted with Cosmo receiving a total of EUR 20 mn upfront and sales milestones and 20% sales royalties. Our rNPV amounts to CHF 82 mn, or CHF 5 per share, with an 82.5% success rate, the average of the EU (100% approved) and the US (65% phase III), and a WACC of 7% (see page 33).

What you see is what you get – an excellent fit with GI Genius

We believe Lumeblue (methylene blue MMX) can potentially become the new gold standard image-enhancing agent in colonoscopy. However, valuable time has been lost in the lucrative US market. In 2018, in a surprise move, the FDA turned down US approval on a single phase III trial despite the trial being successfully conducted under Special Protocol Assessment (SPA) and required a second confirmatory phase III trial. After partner CMS reported a second positive phase III trial in 1,800 patients in China in December 2022, Cosmo will discuss whether an additional confirmatory phase III trial is still required for US approval. A US commercialization partner will be contracted to launch Lumeblue in the US. We conservatively assume a second US trial will be needed, and the US launch to occur in 2026. Lumeblue was approved in the EU in August 2020 based on a single pivotal trial. Alfasigma acquired the EU (including Switzerland, UK, EAA, Russia, and Mexico) rights in February 2021 and launched Lumeblue in 2022. We conservatively forecast global peak sales of EUR 100+ mn with lower pricing and market penetration rates.

Simple but brilliant MMX reformulation of a messy and time-consuming blue dye

Lumeblue is a “simple” but brilliant MMX reformulation of liquid methylene blue dye. This dye was discovered in 1876 and was first used by Japanese gastroenterologists as a staining agent for polyps via a catheter almost 50 years ago. In spite of recommendations for increasing so-called chromoendoscopy (endoscopy with an image enhancing agent), this has never really taken off. Liquid methylene blue dye has turned out to be a time-consuming and "messy" procedure. Moreover, the detection of polyps and adenomas largely depends on the expertise of the endoscopist on when and where to spray the dye during the colonoscopy. As a result, methylene blue dye is used in less than 3% of colonoscopies, despite better detection rates. And detection rates of especially small polyps and adenomas are crucial in preventing colorectal cancer.

In 2010, Cosmo started developing a convenient oral formulation of methylene blue using its MMX formulation technology with the aim to deliver enough coloring agent along the entire length of the colon to increase the adenoma detection rate compared to gold standard white light high-definition endoscopy. Lumeblue penetrates the mucosal cells in such a way that significantly enhances the detection of adenomas by the endoscopist. The only adjustment to the entire treatment protocol is that the patient takes 8 oral Lumeblue tablets during or at the end of the bowel preparation (required in all colonoscopies) a day before the procedure and arrives with a fully dyed colon at the beginning of the procedure, with no further hassle for the endoscopist. No special equipment or training is needed. It is that simple.

This enables endoscopists to detect pre-cancerous (adenomas) and cancerous lesions and polyps throughout the entire colon, without the expertise and need to spray a dye for better detection. This saves the physician valuable time, and the hospital saves the cost of a spray catheter (approximately USD 80 – USD 150) that is no longer needed.

Excellent adenoma detection rate (ADR) demonstrated in several phase III trials
The efficacy of Lumeblue in detecting adenomas compared to standard High Definition endoscope with White Light (HDWL) has now been demonstrated in two separate phase III trials (see Appendix, page 62).

> **Phase III trial under SPA:** Positive pivotal phase III results were announced in 2016. Lumeblue was compared to the current gold standard HDWL (High-Definition endoscope with White Light). The primary endpoint was the number of patients with at least one histologically proven adenoma or carcinoma, or the difference in ADR (adenoma detection rate) compared to HDWL. The trial was conducted under Special Protocol Assessment (SPA) which enables the FDA to provide valuable input into the phase III trial design and streamline the approval process because the scientific and regulatory requirements have already been agreed upon. Usually, this eliminates the regulatory risk. Still, the FDA has the final decision if it believes the results are not sufficiently “robust”, as Cosmo experienced when it received the CRL in May 2018.
>
> **Phase III trial in China:** Lumeblue successfully completed a phase III trial in China sponsored by its partner, China Medical System Holdings Ltd. (CMS), in 2022. The trial met its primary endpoint - the detection rate of non-polypoid colorectal lesions - with very high statistical significance. The positive trial confirms the safety and efficacy of Lumeblue in earlier trials and should enhance regulatory approval in the vast Chinese and Asian markets.

Conclusion: a breakthrough in colorectal cancer prevention and saving lives
The increase in ADR has important clinical relevance. Scientific studies have shown that each 1% increase in ADR results in a 3% decline in the incidence of interval cancer and a 5% decline in the incidence of fatal colorectal cancer. Consequently, the use of Lumeblue in combination with HDWL endoscopy substantially increases the ADR and therefore provides a major contribution to colorectal cancer prevention, and ultimately saves lives.

GI Genius is as good as the eye sees – Lumeblue significantly improves contrast
The introduction of AI-enhanced colonoscopy with systems such as Cosmo’s GI Genius will radically change how lesions are detected with a “second set of expert eyes” that never get

tired, significantly reducing the chance of missing lesions and ultimately improving the detection rate. Nevertheless, GI Genius can only detect lesions as well as the human eye can see. Therefore, anything that improves the detection rate of the human eye, such as Lumeblue by staining lesions blue and significantly enhancing contrast, automatically improves the lesion detection rate of the GI Genius. Lumeblue with proven clinical efficacy in increasing the ADR (adenoma detection rate) compared to mainstay HDWL also enhances the GI Genius lesion detection rate and will be used frequently together in colonoscopy, in our view. To be conservative, we have lowered our pricing per procedure for Lumeblue to compensate for the additional fee for GI Genius of approximately USD 45 per procedure.

Alfasigma launched Lumeblue in the EU; EA Pharma contracted for Japan/S. Korea
In August 2020, the EMA approved Lumeblue in the EU based on the same single positive phase III trial the FDA initially required for US approval, again underlining the remarkable change of mind at the FDA. In February 2021, Alfasigma acquired the EU (including Switzerland, the UK, EEA, Russia, and Mexico) commercialization rights for Lumeblue. Cosmo received a EUR 4 mn upfront payment and is entitled to double-digit royalties and commercial milestones. The first EU launch by Alfasigma occurred in Italy in May 2022, with more countries to follow soon. An exclusive license agreement has already been signed with EA Pharma for Lumeblue (and Eleview) for Japan and South Korea for undisclosed upfront, development, and sales milestones and royalties on sales in 2019.

Will a second confirmatory phase III trial be needed in the US?
After CMS reported a second positive phase III trial in 1,800 patients in China in December 2022, the question is whether the FDA still requires an additional confirmatory phase III trial for US approval of Lumeblue. Cosmo will discuss the US clinical development plans for Lumeblue in the US with the FDA. Cosmo already presented a new clinical plan to the FDA with different endpoints that will consider the positive results of the first phase III trial. The COVID-19 pandemic has delayed discussions substantially. If another confirmatory trial is required, the phase III trial is expected to have slightly different features than the first without the need for a confounding (lower dose) treatment arm, leading to fewer patients that need to be enrolled (~800 patients), with an estimated cost of EUR 10-12 mn. The same clinical sites and systems will likely be used as in the first trial. Cosmo will only start the confirmatory phase III once it has contracted a US partner. We conservatively assume an additional confirmatory phase III trial will be required with a potential launch in 2026.

Peak sales of EUR 100+ mn, US development dependent on US partner
With the introduction of GI Genius ahead of the EU and the US launch of Lumeblue, we have conservatively lowered the pricing of Lumeblue to compensate for the additional fee for GI Genius. We assume a fee per procedure of EUR 20 in the EU/ROW and USD 60 for in the US. Maintaining our conservative peak market penetration rates at 7% (EU/ROW) and 5% (US), we forecast global Lumeblue peak sales of EUR 106 mn. We conservatively account for EUR ~12 mn development costs for an additional confirmatory phase III trial required for US approval, with a potential US approval in 2025 and launch in 2026. Note Cosmo will only start the phase III trial once a US out-licensing agreement is concluded. We assume EUR 20 mn cumulative upfront and sales milestones and 20% royalties on sales in the US.

Forecasts & Sensitivity Analysis

LUMEBLUE - FINANCIAL FORECASTS FOR CHROMOENDOSCOPY

INDICATION	CHROMOENDOSCOPY - EARLY LESION DETECTION TO PREVENT COLON CANCER BY ORAL METHYLENE BLUE MMX STAINING
DOSAGE	SINGLE 200 MG (8X 25 MG) ORAL DOSE DURING OR AT END OF THE INTAKE OF THE BOWEL CLEANSING PREPARATION
PRICING	PRICE PER PROCEDURE: US: USD 60; EU/ROW: EUR 20 (COSMO GUIDED: EUR 20-25)
STANDARD OF CARE	TIME CONSUMING AND "MESSY" METHYLENE BLUE DYE SPRAY
UNIQUE SELLING POINT	CONVENIENT TABLETS WITH ENHANCED STAINING TO DETECT POLYPS AND ADENOMAS IN THE ENTIRE COLON BACKED BY CLINICAL TRIAL RESULTS; NO COMPETITION

7Ps ANALYSIS

PATENT	SEP 2033 GRANTED GLOBAL USE PATENT - THREE GRANTED US PATENTS EXPIRE IN MARCH 2031; ONE GRANTED EU PATENT EXPIRES MARCH 2031
PHASE	POSITIVE PHASE III US (2016) AND CHINA (2022); US: CLR MAY 2018, 2ND US PHASE III TBD, LAUNCH 2027; EU: FILED FEB 2019, APPROVED AUG 2020, LAUNCH H1 2022
PATHWAY	PHARMACEUTICAL COMPOUND - REGULATORY PATHWAY DETERMINED IN CLOSE COOPERATION WITH EMA AND FDA
PATIENT	8 TABLETS TAKEN WITH BOWEL PREPARATION A DAY BEFORE PROCEDURE; HIGHER ADR DETECTION RATE, LOWER CHANCE OF DEVELOPING COLORECTAL CANCER
PHYSICIAN	INCREASE TIME EFFICIENCY OF COLONOSCOPIST, ENHANCED VISUALISATION OF SMALL POLYPS AND ADENOMAS, LOWER RISK OF MISSING SOMETHING
PAYER	SMALL ADDITIONAL COST TO COLONOSCOPY WHILE EARLY DETECTION OF COLON CANCER REDUCES LONG-TERM COSTS SUBSTANTIALLY
PARTNER	EU (INCL. CH, UK, EEA, RUSSIA, MEXICO): ALFASIGMA; CHINA: CMS; US: CONCLUDE US PARTNERING BEFORE START OF 2ND PHASE III TRIAL NEEDED FOR US APPROVAL

REVENUE MODEL

UNITED STATES - SOLD BY PARTNER (TBD)	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E
PEOPLE OF SCREEN-ELIGIBLE AGE (50-74 YEARS) (MN)	81	83	84	86	88	89	91	93	95	97	99
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
NUMBER OF COLONOSCOPIES (MN)	16	19	19	20	20	21	21	21	22	22	23
CHANGE (%)	104%	17%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PENETRATION (%)	0%	0%	0%	0%	1%	2%	3%	3%	4%	4%	5%
NUMBER OF COLONOSCOPIES WITH LUMEBLUE (MN)	0.0	0.0	0.0	0.0	0.1	0.3	0.5	0.6	0.8	0.9	1.0
COST PER PROCEDURE (EUR)	57	55	55	55	55	55	55	55	55	55	55
SALES (EUR MN) - BOOKED BY PARTNER (TBD)	**0**	**0**	**0**	**0**	**6**	**17**	**29**	**35**	**42**	**49**	**56**
CHANGE (%)						206%	70%	22%	19%	17%	15%
ROYALTY (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
ROYALTIES (EUR MN)	0	0	0	0	1	3	6	7	8	10	11
MANUFACTURING REVENUE (%)	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
MANUFACTURING REVENUE (EUR MN)	0	0	0	0	0	1	1	2	2	2	3
UPFRONT & MILESTONE PAYMENTS (EUR MN)	0	5	0	0	9	0	0	0	0	5	0
COGS (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
COGS (EUR MN)	0	0	0	0	0	0	-1	-1	-1	-1	-1
R&D COSTS (EUR MN)	-4	-4	-4	-1	0	0	0	0	0	0	0
PROFIT BEFORE TAX (EUR MN)	**-4**	**1**	**-4**	**-1**	**10**	**4**	**7**	**8**	**10**	**16**	**13**
TAX RATE (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
TAXES (EUR MN)	1	0	1	0	-2	-1	-1	-2	-2	-3	-3
PROFIT (EUR MN)	**-3**	**1**	**-3**	**-1**	**8**	**3**	**5**	**7**	**8**	**13**	**10**

EUROPE / REST OF WORLD - SOLD BY ALFASIGMA (EU) / CMS (CHINA)	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E
PEOPLE OF SCREEN-ELIGIBLE AGE (50-74 YEARS) (MN)	146	148	151	154	158	161	164	167	171	174	177
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
NUMBER OF COLONOSCOPIES (MN)	29	34	35	36	36	37	38	38	39	40	41
CHANGE (%)	104%	17%	2%	2%	2%	2%	2%	2%	2%		
PENETRATION (%)	0%	2%	4%	5%	6%	6%	6%	6%	6%	6%	6%
NUMBER OF COLONOSCOPIES WITH LUMEBLUE (MN)	0.0	0.7	1.4	1.8	2.2	2.2	2.3	2.3	2.4	2.4	2.5
COST PER PROCEDURE (EUR)	20	20	20	20	20	20	20	20	20	20	20
SALES (EUR MN) - BOOKED BY PARTNERS	**0**	**14**	**28**	**36**	**44**	**45**	**46**	**46**	**47**	**48**	**49**
CHANGE (%)		6720%	102%	27%	22%	2%	2%	2%	2%	2%	2%
ROYALTY (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
ROYALTIES (EUR MN)	0	3	6	7	9	9	9	9	9	10	10
MANUFACTURING REVENUE (%)	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
MANUFACTURING REVENUE (EUR MN)	0	1	1	2	2	2	2	2	2	2	2
UPFRONT & MILESTONE PAYMENTS (EUR MN)			5								20
COGS (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
COGS (EUR MN)	0	0	-1	-1	-1	-1	-1	-1	-1	-1	-1
PROFIT BEFORE TAX (EUR MN)	**0**	**3**	**11**	**8**	**10**	**10**	**10**	**11**	**11**	**11**	**31**
TAX RATE (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
TAXES (EUR MN)	0	-1	-2	-2	-2	-2	-2	-2	-2	-2	-6
PROFIT (EUR MN)	**0**	**3**	**9**	**7**	**8**	**8**	**8**	**9**	**9**	**9**	**25**

	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E
GLOBAL SALES (EUR MN)	**0**	**14**	**28**	**36**	**49**	**62**	**74**	**82**	**89**	**97**	**106**
CHANGE (%)		6720%	102%	27%	38%	25%	21%	10%	9%	9%	8%
GLOBAL PROFIT (EUR MN)	**-3**	**3**	**6**	**6**	**16**	**11**	**14**	**15**	**16**	**22**	**35**
CHANGE (%)	-300%	-209%	89%	-6%	181%	-31%	21%	10%	9%	31%	64%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**100**	
NUMBER OF SHARES (MN)	16.3	
NPV PER SHARE (CHF)	**6**	
SUCCESS PROBABILITY	82.5%	= AVERAGE EU (100% APPROVED) & US (65% SINGLE PHASE III) SUCCESS RATE
RISK ADJUSTED NPV PER SHARE (CHF)	**5**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	100%	7	7	7	6	6	6	6
	95%	7	6	6	6	6	6	5
	90%	6	6	6	6	5	5	5
SUCCESS PROBABILITY	82.5%	6	6	5	**5**	5	5	5
	75%	5	5	5	5	5	4	4
	70%	5	5	5	4	4	4	4
	65%	5	4	4	4	4	4	4

ESTIMATES AS OF 3 MAY 2023

SOURCE: VALUATIONLAB ESTIMATES

Eleview – Colonic lesion resection cushion

Product Analysis

Eleview peak sales of EUR 80+ mn - NPV of CHF 5 per share

We forecast global peak sales for Eleview in endoscopic lesion resection to amount to EUR 83 mn (booked by its commercialization partners). Medtronic sells Eleview globally, except for Canada (Pendopharm), replacing previous agreements with EA Pharma, Olympus, and Fujifilm. We assume a cost per vial between USD 81 (US) and EUR 35 (EU/ROW), 1.5 vials used per procedure, and a market penetration peaking at ~20% in the US and a more conservative ~10% in the EU/ROW. We assume Cosmo to receive an estimated ~3% royalty rate and ~20% manufacturing revenue from Medtronic while incurring COGS of 5% as an exclusive global supplier. Our NPV amounts to CHF 76 mn or CHF 5 per share with a WACC of 7% (see page 36).

First of a wave of colonoscopy products to reach the market

Eleview was the first of Cosmo's endoscopic product pipeline to reach the market, with its first approval in 2017. Eleview is an injectable solution designed and approved for gastrointestinal endoscopic procedures such as colonoscopies. It is targeted to replace the use of (unapproved) saline solutions in removing challenging lesions in these procedures. Eleview is a solution that is injected into the submucosal layer in the colon wall directly beneath a lesion such as an adenoma or polyp. Once injected, the solution reconfigures, creating an artificial net formed by polymer chains and traps water to immediately form a long-lasting, up to 45 minutes (methylene) blue-colored cushion. The cushion lifts the lesion and makes it easier for the physician to remove (resect) a challenging polyp. Moreover, the blue dye improves the visibility of the margins of the polyp, thereby decreasing the risk of gastrointestinal perforation and damage to the external muscular layer. This major complication requires immediate surgery. In clinical trials, Eleview decreased the time and volume needed to resect a lesion while reducing reinjections required and piecemeal excisions compared to saline injections.

Medtronic oversees global marketing, replacing Aries, Olympus, and Fujifilm

In 2019, Medtronic acquired the global commercialization rights for Eleview, except for Canada (Pendopharm) and Japan/South Korea (EA Pharma), effectively replacing its own US sales organization Aries Pharma, a US co-promotion agreement with Olympus America, and an exclusive distribution agreement with Fujifilm for Europe and South Africa. In May 2022, Medtronic acquired the commercialization rights for Japan and South Korea from EA Pharma, becoming the global commercialization partner for Eleview, except for Canada, where Pendopharm remains responsible for commercialization. Medtronic can now maximize Cosmo's returns through its marketing muscle with significant cost synergies by selling GI Genius, which helps detect lesions, and Eleview, which eases the removal of challenging lesions.

Only endoscopic lesion resection filler approved & backed by post-marketing trials

Eleview is the only endoscopic lesion resection filler specifically approved for this indication. The FDA and EMA approvals are based on trials comparing Eleview with standard-of-practice saline injections, providing a substantial barrier to entry. In May 2017, Cosmo announced the results of a "first-in-human" exploratory post-marketing trial comparing Eleview to a standard saline solution in patients undergoing endoscopic mucosal resection

of colonic lesions ≥20 mm (see Appendix, page 65). Even though the trial was not powered to show statistical significance, several endpoints were statistically significant, while others showed a numerical trend favoring Eleview. Eleview required less volume injected, less time, and fewer reinjections, and there were fewer resection pieces with Eleview.

Eleview sales hit by pandemic but expected to recover from 2023 onwards

Eleview sales were severely impacted by the COVID-19 pandemic, with a sharp drop in the number of colonoscopies. With the pandemic now expected to move into the endemic phase, we expect a gradual recovery from 2023 onwards. We forecast global peak sales to reach EUR 83 mn, with peak market penetrations ranging from ~10% (EU/ROW) to ~20% (US). Further upside to our forecasts could come from the recall of the competing product Orise from Boston Scientific in November 2022. We assume Cosmo receives a total of ~23% in royalties and manufacturing revenue with 5% COGS. We calculate an NPV for Eleview of CHF 76 mn or CHF 5 per share with a WACC of 7%.

Forecasts & Sensitivity Analysis

ELEVIEW - FINANCIAL FORECASTS FOR COLONIC LESION RESECTION

INDICATION	ENDOSCOPIC MUCOSAL RESECTION OF LARGE SESSILE POLYPS IN THE GASTROINTESTINAL TRACT
DOSAGE	SUBMUCOSAL INJECTION FORMULATION; 1-2 10 ML VIALS REQUIRED PER REMOVED LESION
PRICING	US: USD 92.50 PER VIAL / EU/ROW: EUR 30 PER VIAL; APPROXIMATELY 1 1/2 VIALS ARE REQUIRED PER ADENOMA
STANDARD OF CARE	SUBMUCOSAL SALINE INJECTIONS; SEIKAGAKU'S MUCOUP (JAPAN ONLY), LIFEEUROPE'S SIGMAVISC (EU ONLY) BOTH NO DYE; BOSTON SCIENTIFIC'S ORISE GEL (CONTAINS DYE)
UNIQUE SELLING POINT	FIRST INJECTABLE EMULSION CONTAINING A VISIBILITY ENHANCING DYE WITH LONG-LASTING CUSHION TO FACILITATE LESION RESECTION

7Ps ANALYSIS

PATENT	EXPIRY: NOV 2034; 3 GRANTED US PATENTS (US9226996; US9364580; US9522216) AND 1 GRANTED EU PATENT (EP2911707)
PHASE	APPROVED IN THE EU AND US IN MAY 2017; MARKETING TRIALS IN FOUR US SITES ONGOING (SPEED AND SAFETY VS. STANDARD CARE IN EMR)
PATHWAY	CLASSIFIED AS A CLASS II MEDICAL DEVICE IN US AND EU; CLINICAL TRIALS PROVIDE MARKETING ADVANTAGE AND BARRIER TO ENTRY
PATIENT	LESS RISK OF COLON PERFORATION THAT LEADS TO INVASIVE EMERGENCY REPAIR SURGERY AND LONG RECOVERY TIME
PHYSICIAN	EASIER AND FASTER REMOVAL OF LESIONSREDUCING THE RISK OF COLON PERFORATION AND ITS COMPLICATIONS
PAYER	SUBSTANTIAL COST SAVINGS DUE TO FASTER AND EASIER PROCEDURE AND LESS COSTLY COLON PERFORATIONS AND COMPLICATIONS
PARTNER	MEDTRONIC: GLOBAL RIGHTS EXCLUDING CANADA (PENDOPHARM) - WE ASSUME COSMO RETAINS A NET MARGIN OF AROUND 20%

REVENUE MODEL

UNITED STATES - SOLD BY MEDTRONIC	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
PEOPLE OF SCREEN-ELIGIBLE AGE (50-74 YEARS) (MN)	86	88	91	94	97	100	102	106	109	112	115
GROWTH (%)	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%
NUMBER OF COLONOSCOPIES (MN)	17	20	21	22	22	23	24	24	25	26	27
CHANGE (%)	106%	18%	3%	3%	3%	3%	3%	3%	3%		
PREVALENCE OF ADENOMATOUS POLYPS (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
COLONOSCOPIES WITH ADENOMATOUS POLYPS (MN)	5.2	6.1	6.3	6.5	6.7	6.9	7.1	7.3	7.5	7.7	8.0
NUMBER OF SIGMOIDOSCOPIES (MN)	3.4	4.1	4.2	4.3	4.4	4.6	4.7	4.9	5.0	5.2	5.3
PREVALENCE OF ADENOMATOUS POLYPS (%)	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%
SIGMOIDOSCOPIES WITH ADENAMATOUS POLYPS (MN)	0.3	0.4	0.4	0.4	0.4	0.5	0.5	0.5	0.5	0.5	0.5
TOTAL CASES WITH ADENOMOTOUS POLYPS (MN)	5.5	6.5	6.7	6.9	7.1	7.3	7.5	7.8	8.0	8.2	8.5
LIFTING AGENT REQUIRED (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
PROCEDURES WHERE LIFTING AGENT REQUIRED (MN)	**1.1**	**1.3**	**1.3**	**1.4**	**1.4**	**1.5**	**1.5**	**1.6**	**1.6**	**1.6**	**1.7**
PENETRATION (%)	2%	9%	12%	14%	15%	15%	16%	17%	18%	19%	19%
NUMBER OF PROCEDURES WITH ELEVIEW	26,369	117,127	160,854	193,293	206,202	219,712	233,847	256,401	280,099	304,988	314,138
COST PER VIAL (EUR)	57	55	55	55	55	55	55	55	55	55	55
NUMBER OF VIALS PER PROCEDURE	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
COST PER PROCEDURE (EUR)	143	138	138	138	138	138	138	138	138	138	138
SALES (EUR MN) - BOOKED BY MEDTRONIC	**4**	**16**	**22**	**27**	**28**	**30**	**32**	**35**	**39**	**42**	**43**
CHANGE (%)	86%	328%	37%	20%	7%	7%	6%	10%	9%	9%	3%
ROYALTY (%)	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%
ROYALTIES (EUR MN)	0	0	1	1	1	1	1	1	1	1	1
MANUFACTURING REVENUE (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
MANUFACTURING REVENUE (EUR MN)	1	3	5	5	6	6	7	7	8	9	9
COGS (%)	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
COGS (EUR MN)	0	-1	-1	-1	-1	-2	-2	-2	-2	-2	-2
PROFIT BEFORE TAX (EUR MN)	**1**	**3**	**4**	**5**	**5**	**6**	**6**	**7**	**7**	**8**	**8**
TAXES (EUR MN)	0	-1	-1	-1	-1	-1	-1	-1	-1	-2	-2
PROFIT (EUR MN)	**1**	**2**	**3**	**4**	**4**	**4**	**5**	**5**	**6**	**6**	**6**

EUROPE / ROW - SOLD BY MEDTRONIC (EX. CANADA)	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
PEOPLE OF SCREEN-ELIGIBLE AGE (50-74 YEARS) (MN)	154	159	164	169	174	179	184	190	196	201	207
GROWTH (%)	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%
NUMBER OF COLONOSCOPIES (MN)	31	37	38	39	40	41	42	44	45	40	41
CHANGE (%)	106%	18%	3%	3%	3%	3%	3%	3%	3%		
PREVALENCE OF ADENOMATOUS POLYPS (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
COLONOSCOPIES WITH ADENOMATOUS POLYPS (MN)	9.3	11.0	11.3	11.6	12.0	12.3	12.7	13.1	13.5	12.1	12.4
NUMBER OF SIGMOIDOSCOPIES (MN)	6.2	7.3	7.5	7.8	8.0	8.2	8.5	8.7	9.0	8.1	8.3
PREVALENCE OF ADENOMATOUS POLYPS (%)	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%
SIGMOIDOSCOPIES WITH ADENAMATOUS POLYPS (MN)	0.6	0.7	0.8	0.8	0.8	0.8	0.8	0.9	0.9	0.8	0.8
TOTAL CASES WITH ADENOMOTOUS POLYPS (MN)	37.0	43.9	45.2	46.6	47.9	49.4	50.9	52.4	54.0	48.3	49.8
LIFTING AGENT REQUIRED (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
PROCEDURES WHERE LIFTING AGENT REQUIRED (MN)	**7.4**	**8.8**	**9.0**	**9.3**	**9.6**	**9.9**	**10.2**	**10.5**	**10.8**	**9.7**	**10.0**
PENETRATION (%)	1%	5%	7%	8%	9%	10%	10%	10%	10%	10%	10%
NUMBER OF PROCEDURES WITH ELEVIEW	90,537	438,792	632,738	744,823	863,064	938,343	1,017,361	1,047,882	1,079,318	966,694	995,695
COST PER VIAL (EUR)	25	25	25	25	25	25	25	25	25	25	25
NUMBER OF VIALS PER PROCEDURE	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
COST PER PROCEDURE (EUR)	38	38	38	38	38	38	38	38	38	38	38
SALES EUROPE/ROW - BOOKED BY MEDTRONIC	**3**	**16**	**24**	**28**	**32**	**35**	**38**	**39**	**40**	**36**	**37**
CHANGE (%)	152%	385%	44%	18%	16%	9%	8%	3%	3%	-10%	3%
ROYALTY (%)	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%
ROYALTIES (EUR MN)	0	0	1	1	1	1	1	1	1	1	1
MANUFACTURING REVENUE (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
MANUFACTURING REVENUE (EUR MN)	1	3	5	6	7	7	8	8	8	7	8
COGS (%)	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
COGS (EUR MN)	0	-1	-1	-1	-2	-2	-2	-2	-2	-2	-2
PROFIT BEFORE TAX (EUR MN)	**1**	**3**	**4**	**5**	**6**	**6**	**7**	**7**	**7**	**7**	**7**
TAXES (EUR MN)	0	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1
PROFIT (EUR MN)	**0**	**2**	**3**	**4**	**5**	**5**	**6**	**6**	**6**	**5**	**5**

	2022E	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
GLOBAL SALES (EUR MN)	**7**	**33**	**46**	**55**	**61**	**65**	**70**	**75**	**79**	**78**	**81**
CHANGE (%)	112%	355%	41%	19%	11%	8%	8%	6%	6%	-1%	3%
GLOBAL PROFIT (EUR MN)	**1**	**5**	**7**	**8**	**9**	**10**	**10**	**11**	**12**	**12**	**12**
CHANGE (%)	113%	355%	41%	19%	11%	8%	8%	6%	6%	-1%	3%

WACC (%)	7%
NPV TOTAL PROFIT (CHF MN)	**76**
NUMBER OF SHARES (MN)	16.3
NPV PER SHARE (CHF)	**5**

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	115	8	7	7	7	7	7	6
	105	7	7	7	6	6	6	6
	95	6	6	6	6	6	5	5
PEAK SALES (EUR MN)	85	6	5	5	**5**	5	5	5
	75	5	5	5	5	4	4	4
	65	4	4	4	4	4	4	4
	55	4	4	3	3	3	3	3

ESTIMATES AS OF 3 MAY 2023

SOURCE: VALUATIONLAB ESTIMATES

II) DERMATOLOGY

Winlevi (acne)

Product Analysis

Winlevi peak sales of EUR 400 mn - rNPV of CHF 19 per share

We forecast global peak sales of EUR 396 mn for Winlevi in acne, with the US accounting for roughly 80% of global peak sales. The US commercial launch started in November 2021 by partner Sun Pharma. We assume US patent protection until 2030, an annual treatment cost of USD 550 (with initial heavy rebates), and a market penetration peaking at ~20%. We forecast up to EUR 103 mn in sales milestones, 15-20% tiered sales royalties, and ~5% manufacturing revenue from Sun Pharma with ~3% COGS. In the EU/ROW, we assume partnering in 2024, first launches in 2025, 10-year data exclusivity until 2035, and an annual treatment cost of EUR 250 with a peak market penetration of ~10%. We assume Cosmo will receive up to EUR 51 mn milestones, 20% sales royalties, 7% manufacturing revenue, and 5% COGS. Based on the above, our rNPV amounts to CHF 307 mn, or CHF 19 per share, applying a conservative 82.5% success probability, the average of US 100% (approved) and EU/ROW 65% (phase III), and a WACC of 7% (see page 41).

Winlevi first new acne drug based on new MOA in 40 years

Winlevi is Cosmo's most advanced dermatology product that became the first-ever topical anti-androgen to be approved and launched for acne based on a new mechanism of action (cortexolone-17) in almost forty years. In August 2020, Winlevi was approved for treating acne in the US, which affects up to 50 mn people annually in the US alone. Winlevi offers a non-antibiotic approach to people with acne by targeting the androgen receptors directly in the skin, filling a long-standing gap in acne treatment and complementing current treatments. The US approval was based on the two positive pivotal phase III trials, "Study 25" and "Study 26", and the long-term open-label phase III safety trial, "Study 27", where Winlevi demonstrated highly statistically significant improvements for all primary clinical endpoints including IGA (Investigator Global Assessment) score, non-inflammatory lesion counts, and inflammatory lesion counts compared to placebo with a favorable safety profile.

Sun Pharma launched Winlevi in the US and expanded its licensing agreement

Winlevi was launched in the US in a two-step approach. In September 2020, a market access launch was started to timely secure pricing, reimbursement, and formulary listing by major healthcare providers, which was followed by the commercial sales launch by partner Sun Pharma in early November 2021. Sun Pharma acquired exclusive licensing rights to commercialize Winlevi in the US and Canada, in July 2021. Cosmo will be the exclusive supplier of the product. A USD 45 mn upfront payment was received with Cosmo eligible for up to USD 190 mn commercial milestones and customary double-digit sales royalties. In June 2022, triggered by the flying start of Winlevi in the US, Cosmo and Sun Pharma expanded the exclusive licensing agreement to Japan, Australia, New Zealand, Brazil, Mexico, and Russia. Cosmo received an additional upfront payment of USD 7 mn with potential (undisclosed) regulatory and sales milestones and customary double-digit royalties on net sales.

Sun Pharma is the 9th largest pharma company in the US generics market with a strong presence in generics, branded prescription, and OTC drugs. Sun Dermatology will be responsible for commercialization and ranked 2nd by prescriptions in the US dermatology market with substantial marketing muscle.

USD 4.9 bn acne market limited to reformulations or combinations of old therapies

Current acne treatments are mostly limited to reformulations or single-product fixed-combinations of NCEs (new chemical entities) of which the last has been discovered in the mid 1990s when the topical retinoids Differin (adapalene) and Tazorac (tazarotene) were approved. Nevertheless, Winlevi targets a USD 4.9 bn acne market opportunity, where branded prescription acne products' average annual sales range between USD 250-400 mn. Major topical prescription acne drugs include Galderma's Epiduo (adapalene & benzoyl peroxide combo drug) and Allergan's Aczone (dapsone). Winlevi became the first and potentially only approved and launched topical anti-androgen for acne based on the very positive phase III top-line trial results announced in July 2018. However, without the systemic side effects that limit the use of existing oral alternatives, Winlevi should be expansive to the existing acne market. Winlevi can also be used in combination with other acne treatments, including Cosmo's own novel antibiotic CB-06-01 in phase II development for acne. Moreover, the company could potentially develop a higher-strength Winlevi formulation, given its excellent safety and tolerability. Development costs are relatively contained as dermatology drugs have relatively short clinical development timelines. Moreover, the US acne market is served by a relatively small number of dermatologists that can be effectively targeted by Sun Dermatology's dedicated sales force. Sun Dermatology could become the preferred US and Canadian partner for Cosmo's other dermatology pipeline projects. At the same time, commercial success in the US should attract commercialization partners outside the US at similar attractive terms, in our view.

Aim to be first effective & safe anti-androgen for acne without systemic side effects

Winlevi is a topical anti-androgen for treating acne containing the novel NCE clascoterone (cortexolone-17α-propionate), with strong local anti-androgen activity, discovered in Cosmo's labs. Winlevi aims to be the first effective and safe topical anti-androgen without systemic side effects. Increased androgen activity by hormones such as testosterone and its derivative dihydrotestosterone (DHT) leads to the overproduction of oily sebum by the sebaceous glands, the origin of acne. Oral anti-androgens such as spironolactone are available with proven efficacy, but use is limited by systemic side effects such as dizziness, headaches, diarrhea, and increased body hair growth, among others. Winlevi is a topically delivered small molecule that penetrates the skin to reach the androgen receptors of the sebaceous gland with strong local anti-androgen activity.

Winlevi acts on the overproduction of sebum that is at the top of the cascade of physiological events that lead to acne formation. It blocks the androgen hormones from the androgen receptors located at the sebaceous gland and hair follicle. This reduces the creation of the oily sebum that clogs the hair follicle with dead skin cells and the formation of comedones (blackheads and whiteheads), pimples, and deeper lumps (cysts or nodules) that occur on the face, neck, chest, back, shoulders, and upper arms. Consequently, the hair follicle is not clogged, preventing colonization and bacterial infection by P. acnes and subsequent inflammation. Once in the bloodstream, Winlevi metabolizes rapidly to cortexolone, a corticosteroid produced naturally by the body with negligible systemic anti-androgen activity and a known safety profile. Moreover, men and women can use Winlevi, which is not the case with other anti-androgen therapies.

Winlevi achieved all primary and secondary endpoints in both phase III acne trials
In 2018, positive phase III top-line results for Winlevi in acne were announced. Both pivotal phase III trials, the US "Study 25" and EU "Study 26", were "on spot" (pun intended) with highly statistically significant results for Winlevi compared to placebo across all three primary endpoints as well as secondary endpoints, indicating a strong treatment effect. Importantly, no treatment-related serious side effects with Winlevi were seen in the phase III trials underlining the very clean safety profile seen in previous clinical trials. In 2019, positive results from "Study 27", the long-term open-label phase III trial of Winlevi in acne, were announced, which confirmed that the drug is well tolerated with an acceptable safety profile without systemic side effects. The safety data completes the final clinical data set necessary for inclusion in the NDA (new drug application) filing for US approval (see Appendix, page 65).

Strong US uptake of Winlevi resulted in new licensing & supply agreements in 2022
The strong US uptake of Winlevi resulted in a new licensing and supply agreement with 3SBio in Greater China in July 2022, InfectoPharm in Germany, Italy, and Austria, in October 2022 and with Hyphens Pharma for Southeast Asia in December 2022.

3SBio is a leading biopharmaceutical company in China, listed on the Hong Kong stock exchange (1530.HK) with extensive expertise in researching, developing, manufacturing and marketing biopharmaceuticals, targeting cancer, ophthalmology, auto-immune and kidney disease, and dermatology. Under the terms of the license agreement, 3SBio received the exclusive right to develop and commercialize Winlevi in Greater China, while Cosmo will be the exclusive supplier of the API for the finished product for the initial commercialization period until such time as manufacturing has been transferred to 3SBio for sale in Greater China. Cosmo received an upfront payment of USD 6.5 mn, with potential development and sales milestones totaling up to USD 63.5 mn and customary ascending high single digit or double-digit royalties on net sales. The agreement also includes a right of first refusal for an exclusive license for Breezula to treat alopecia in Greater China. Over 95% of Chinese are suffering from acne in various degrees with more than 100 mn young people aging from 10 to 25 years old suffering from acne.

InfectoPharm is a well-established family-owned German company that operates internationally and enjoys a high reputation among physicians, pediatricians, and dermatologists. With sales of EUR 50 mn, the dermatological range is an important pillar of its business. Under the terms of the agreement, InfectoPharm will exclusively commercialize Winlevi in Germany, Italy, and Austria. Cosmo is responsible for the centralized procedure before the European Medicines Agency (EMA) aimed at obtaining a single Marketing Authorization for the product in the European Union and will be the exclusive supplier of Winlevi. Cosmo received an upfront payment of EUR 1 mn, with potential regulatory milestones totaling up to EUR 4.5 mn, and customary double-digit royalties on net sales.

Hyphens Pharma is listed on the Singapore stock exchange (SGX: 1J5). Under the terms of the agreement, Hyphens will receive the exclusive right to develop and commercialize Winlevi in 10 countries in Southeast Asia, including Singapore, Indonesia, Malaysia, the Philippines, Vietnam, Thailand, Brunei, Cambodia, Laos, and Myanmar, with Cosmo being the exclusive supplier of the product. Cosmo received an upfront payment of USD 1 mn, with potential regulatory and sales milestones totaling up to USD 4 mn and customary double-digit royalties on net sales. More than 600 mn people live in this region, with millions seeking treatment for acne.

Global peak sales of EUR 400 mn based on conservative assumptions

To account for regional differences, we have split our detailed forecasts into two regions:

1. **US** (Winlevi commercialized by partner Sun Dermatology with a specialist dermatology salesforce)
2. **EU/ROW** (commercialization partners in return for milestones and sales royalties)

We conservatively excluded regions such as CEE and BRIC (Brazil, Russia, India, China), given the affordability of Winlevi for the general population in these regions.

1) US peak sales of EUR 300+ mn

We conservatively estimate that 9.4% of the US population, or 30 mn people have acne. Some estimates reach up to 40-50 mn people. Although Winlevi is likely to be approved for all grades of acne, given its excellent safety and tolerability profile, we limit treatment to people with moderate to severe acne, which accounts for 20% of people with acne. Furthermore, we estimate that ~80% are on prescription drugs as most acne treatments are eligible for reimbursement. We assume an annual cost of therapy of USD 550 based on the extensive market research conducted by Cassiopea, which identified a WAC pricing corridor of between USD 300-700 that should provide broad payer access. However, we account for large rebates in the initial launch years of up to 60% and gradually declining to around 10%. Our pricing assumptions seem conservative compared to the annual cost of other branded topical acne treatments such as Galderma's Epiduo at around USD 1,200 (excluding rebates). Consequently, we expect the peak penetration in the target group to reach up to ~20%. US launch by Sun Dermatology occurred in early November 2021. Although many people will be motivated to continue treatment, as the symptoms of acne are visible and financially motivated by the co-payment cost, we conservatively assume a compliance rate of 45%, in line with compliance rates for long-term therapies. Based on the above, we forecast US peak sales to amount to EUR 316 mn or ~80% of global peak sales, underlining the importance of the US FDA approval and Sun Pharma exclusive licensing and supply agreement.

We account for the USD 45 mn upfront payment by Sun Pharma and conservatively up to EUR 126 mn additional commercialization milestones and tiered double-digit sales royalties starting at 15% and gradually increasing to 20%. We assume 5% manufacturing revenue with COGS gradually declining to 3%.

2) EU/ROW peak sales of around EUR 90 mn

Using the same 9.4% prevalence of acne in the EU/ROW, we calculate there are approximately 55 mn people with acne in this region. As in the US, we conservatively limit Winlevi use to people with moderate to severe acne and estimate that roughly 70% are on prescription treatment as most acne treatments are reimbursed. We assume first launches to occur in 2025 and peak penetration rates reach up to ~10% given the magnitude of countries and shorter patent life. Most acne treatments are reimbursed in Europe, often without a co-payment. However, treatment prices in this region are markedly lower than in the US. We conservatively assume an annual treatment cost per patient of EUR 250 or roughly half of the US cost. We also assume a slightly lower patient compliance rate of 40% due to the lack of co-payment and financial motivation. Based on the above, we forecast peak sales in the EU/ROW to amount to EUR 89 mn.

Forecasts & Sensitivity Analysis

WINLEVI - FINANCIAL FORECASTS FOR ACNE VULGARIS

INDICATION	TOPICAL TREATMENT FOR ACNE VULGARIS IN PEOPLE 12 YEARS AND OLDER
DOSAGE	1% CREAM APPLIED TWICE A DAY ON SKIN FOR APPROXIMATELY A YEAR
PRICING	ANNUAL TREATMENT PRICE PER PATIENT IN: EU/ROW: EUR 250; US: USD 550 (BASED ON CASSIOPEA US MARKET RESEARCH ACCEPTABLE WAC PRICE OF USD 300-700/YEAR)
STANDARD OF CARE	PRESCRIPTION TREATMENTS INCLUDE BENZOYL PEROXIDE CREAM, TOPICAL RETINOIDS, ORAL RETINOIDS OR SINGLE-PRODUCT COMBINATIONS OF THESE DRUGS
UNIQUE SELLING POINT	FIRST-IN-CLASS TOPICAL ANDROGEN RECEPTOR INHIBITOR FOR ACNE VULGARIS WITH NEGLIGIBLE SYSTEMIC BIOAVAILABILITY (EXCELLENT SAFETY & TOLERABILITY PROFILE)

7Ps ANALYSIS

PATENT	PROTECTED BY MEDICAL USE PATENT IN ACNE & ALOPECIA UNTIL 2022 (EU/ROW)/2023 (US) AND PATENT COVERING ALL CRYSTALLINE FORMS UNTIL 2028 (EU/ROW) AND 2030 (US)
PHASE	PHASE III STARTED 2015; POSITIVE RESULTS ACROSS ALL PRIMARY ENDPOINTS JUL 2018; APPROVED IN US IN AUG 2020; US COMMERCIAL LAUNCH 3 NOV 2021 BY SUN PHARMA
PATHWAY	SPA APPROVED JUL 2015; 2 PIVOTAL TRIALS (US & EU) 700 PTS. EACH; SAFETY AT LEAST 1,000 PTS.: 1 LT OPEN LABEL SAFETY TRIAL: 300+ PTS. 6 MONTHS; 100 PTS. 12 MONTHS
PATIENT	CONVENIENT TOPICAL CREAM WITH GOOD EFFICACY LACKING THE SIDE EFFECTS OF SYSTEMIC ANTI-ANDROGENS (E.G. MOOD CHANGES, LOSS OF LIBIDO, MALE BREASTS)
PHYSICIAN	CONVENIENT AND EFFECTIVE TOPICAL ACNE TREATMENT LACKING TYPICAL ANTI-ANDROGEN SIDE EFFECTS SHOULD ENHANCE PATIENT COMPLIANCE
PAYER	SIGNIFICANT COST-SAVINGS DUE TO THE LACK OF TYPICAL ANTI-ANDROGEN SIDE EFFECTS
PARTNER	US: SUN PHARMA: USD 45 MN UPFRONT, UP TO USD 190 MN MILESTONES, DOUBLE-DIGIT ROYALTIES, EXPANDED TO JAPAN AMONG OTHERS; EU/ROW: EXPECT SIMILAR AGREEMENTS

REVENUE MODEL

UNITED STATES - SOLD BY SUN PHARMA	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
PERSONS WITH ACNE (MN)	48	49	49	50	50	51	51	52	52	53	53
GROWTH (%)	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
MODERATE TO SEVERE ACNE (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
PERSONS WITH MODERATE TO SEVERE ACNE (MN)	10	10	10	10	10	10	10	10	10	11	11
ON PRESCRIPTION (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
PERSONS WITH MODERATE TO SEVERE ACNE ON RX (MN)	8	8	8	8	8	8	8	8	8	8	9
PENETRATION (%)	4%	8%	12%	15%	17%	18%	19%	19%	13%	3%	1%
PERSONS ON TREATMENT	308,775	623,725	944,944	1,192,992	1,365,578	1,460,365	1,515,940	1,531,100	1,082,487	273,328	69,015
GROSS COST OF THERAPY PER YEAR (EUR)	525	506	506	506	506	506	506	506	506	506	506
DISCOUNT RATE (%)	60%	45%	35%	25%	10%	10%	10%	10%	10%	10%	10%
NET COST OF THERAPY PER YEAR (EUR)	210	278	329	379	455	455	455	455	455	455	455
PATIENT COMPLIANCE (%)	45%	45%	45%	45%	45%	45%	45%	45%	45%	45%	45%
SALES (EUR MN) - BOOKED BY SUN PHARMA	**29**	**78**	**140**	**204**	**280**	**299**	**310**	**314**	**222**	**56**	**14**
CHANGE (%)	4459%	167%	79%	46%	37%	7%	4%	1%	-29%	-75%	-75%
ROYALTIES FROM SUN PHARMA (%)	13%	17%	20%	20%	20%	20%	20%	20%	20%	20%	20%
ROYALTIES FROM SUN PHARMA (EUR MN)	3.7	13	28	41	56	60	62	63	44	11	3
MANUFACTURING REVENUE (%)	11%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
MANUFACTURING REVENUE (EUR MN)	7.7	4	7	10	14	15	16	16	11	3	1
UPFRONT & MILESTONE PAYMENTS (EUR MN)	5	0	18	37	0	0	41	0	0	0	0
COGS (%)	15%	10%	5%	3%	3%	3%	3%	3%	3%	3%	3%
COGS (EUR MN)	-4	-8	-7	-6	-8	-9	-9	-9	-7	-2	0
PROFIT BEFORE TAX (USD MN)	**12**	**9**	**46**	**82**	**62**	**66**	**110**	**69**	**49**	**12**	**3**
TAXES (EUR MN)	-1	-2	-9	-16	-12	-13	-22	-14	-10	-2	-1
PROFIT (EUR MN)	**11**	**7**	**37**	**65**	**49**	**53**	**88**	**55**	**39**	**10**	**2**

EUROPE / REST OF WORLD - SOLD BY PARTNER (TBD)	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
PERSONS WITH ACNE (MN)	58	58	59	59	60	61	61	62	62	63	64
GROWTH (%)	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
MODERATE TO SEVERE ACNE (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
PERSONS WITH MODERATE TO SEVERE ACNE (MN)	12	12	12	12	12	12	12	12	12	13	13
ON PRESCRIPTION (%)	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
PERSONS WITH MODERATE TO SEVERE ACNE ON RX (MN)	8	8	8	8	8	8	9	9	9	9	9
PENETRATION (%)	0%	0%	0%	1%	5%	7%	9%	10%	10%	10%	10%
PERSONS ON TREATMENT	0	0	0	41,574	419,896	593,733	771,005	821,977	873,891	882,630	891,456
COST OF THERAPY PER YEAR (EUR)	250	250	250	250	250	250	250	250	250	250	250
PATIENT COMPLIANCE (%)	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%
SALES (EUR MN) - BOOKED BY PARTNER (TBD)	**0**	**0**	**0**	**4**	**42**	**59**	**77**	**82**	**87**	**88**	**89**
CHANGE (%)					910%	41%	30%	7%	6%	1%	1%
ROYALTIES FROM PARTNER (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
ROYALTIES FROM PARTNER (EUR MN)	0	0	0	1	8	12	15	16	17	18	18
MANUFACTURING REVENUE (%)	7%	7%	7%	7%	7%	7%	7%	7%	7%	7%	7%
MANUFACTURING REVENUE (EUR MN)	0	0	0	0	3	4	5	6	6	6	6
UPFRONT & MILESTONE PAYMENTS (EUR MN)	11	0	10	5	0	5	0	8	0	10	0
COGS (%)	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
COGS (EUR MN)	0	0	0	0	-2	-3	-4	-4	-4	-4	-4
R&D COSTS (EUR MN)	-2	-2	0	0	0	0	0	0	0	0	0
PROFIT BEFORE TAX (EUR MN)	**9**	**-2**	**10**	**6**	**9**	**18**	**17**	**26**	**19**	**29**	**20**
TAXES (EUR MN)	-1	0	-2	-1	-2	-4	-3	-5	-4	-6	-4
PROFIT (EUR MN)	**8**	**-1**	**8**	**5**	**7**	**14**	**14**	**20**	**15**	**24**	**16**

	2022E	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
GLOBAL SALES (EUR MN)	**29**	**78**	**140**	**208**	**322**	**358**	**388**	**396**	**309**	**144**	**103**
CHANGE (%)	4459%	167%	79%	49%	55%	11%	8%	2%	-22%	-53%	-28%
GLOBAL PROFIT (EUR MN)	**18**	**6**	**45**	**70**	**57**	**67**	**101**	**76**	**54**	**33**	**18**
CHANGE (%)	-52%	-66%	630%	55%	-19%	19%	51%	-25%	-28%	-39%	-46%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**372**	
NUMBER OF SHARES (MN)	16.3	
NPV PER SHARE (CHF)	**23**	
SUCCESS PROBABILITY	82.5%	= AVERAGE US APPROVED (100%) AND EU PHASE III (65%)
RISK ADJUSTED NPV PER SHARE (CHF)	**19**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF / SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	100%	24	24	23	23	22	22	21
	95%	23	23	22	22	21	21	20
	90%	22	21	21	20	20	19	19
	85%	21	20	20	19	19	18	18
SUCCESS PROBABILITY	82.5%	20	20	19	**19**	18	18	17
	80%	20	19	19	18	18	17	17
	70%	17	17	16	16	16	15	15
	65%	16	15	15	15	14	14	14
	60%	15	14	14	14	13	13	13

ESTIMATES AS OF 3 MAY 2023

SOURCE: VALUATIONLAB ESTIMATES

Breezula (androgenic alopecia – hair loss)

Product Analysis

Breezula peak sales of EUR 400 mn - rNPV of CHF 9 per share

We forecast peak sales of EUR 382 mn for Breezula (clascoterone solution) in male androgenic alopecia (AGA), the most common type of hair loss in men (and women), conservatively assuming first market launches in 2026, patent protection until 2036 (EU/ROW) and 2030 (US), an annual wholesale cost per patient of between EUR 350 (EU/ROW) and USD 1,200 (US), and a market penetration conservatively peaking at ~6% (US) and ~3% (EU/ROW) in the target population. We assume Cosmo will seek commercialization partners for Breezula in return for global upfront and sales milestones totaling EUR 203 mn with 20% sales royalties, 17% manufacturing revenue, and ~15% COGS. Our rNPV amounts to CHF 149 mn, or CHF 9 per share, with a 50% (phase II completed) success probability and a WACC of 7% (see page 45).

First and only topical anti-androgen treatment for hair loss

Breezula is a different formulation (anhydrous solution) and higher dosage strength (7.5x) of the same novel anti-androgen and new chemical entity (NCE), clascoterone, as used in Winlevi for acne. Breezula is a topical anhydrous clascoterone solution applied twice a day to the scalp to reduce hair thinning and hair loss in patients with androgenic alopecia. This is the most common type of hair loss in men and women and is caused by high concentrations of the hormone DHT (dihydrotestosterone), hence, the name androgenic (hormonal) alopecia (hair loss). In the US alone, an estimated 35 mn men and 21 mn women experience hair loss. Despite the high incidence of alopecia, Merck & Co's oral anti-androgen Propecia (finasteride) and Pfizer's topical vasodilator Rogaine (minoxidil), are the only two approved prescription drugs for hair loss in the US. Both drugs are now widely available as generics, while Rogaine is also available over the counter (OTC). The value of the non-surgical hair loss market has an estimated value of USD 2.8 bn. Hair restoration is a more invasive but relatively common treatment for alopecia, with an estimated value of USD 1.9 bn.

First and only topical anti-androgen treatment for men and women

Breezula could become the first and only topical anti-androgen treatment for alopecia for men and women, with the potential to be at least as effective as Propecia. However, without the systemic side effects such as sexual dysfunction that have hampered the uptake of this oral anti-androgen, which men can only use. Despite these limitations, global sales of Propecia peaked at USD 431 mn in 2009. In July 2018, positive top-line results were announced of a (6-month) interim analysis of a phase IIb dose-ranging trial in men with mild to moderate alopecia, followed by positive 12-month top-line results in April 2019. Phase III trials of Breezula in men are expected to start in Q2 2023. We assume Cosmo to seek commercialization partners for Breezula after approval in return for upfront and commercialization milestones and sales royalties.

Breezula blocks DHT, the root cause of hair loss, without systemic effects

Androgenic alopecia is multifactorial and is caused by a combination of genetics and the effects of androgens such as the male hormone testosterone and its derivative dihydrotestosterone (DHT). High concentrations of DHT at the hair follicle shorten the hair growth cycle. DHT causes overproduction of the oily substance sebum (also the cause of

acne) that clogs the hair follicles on the scalp hampering the growth of the hair shaft and leading to skin inflammation. As the hair follicles gradually shrink, they produce progressively smaller and thinner hairs until eventually, they are no longer able to produce hair. In most cases, these DHT-dependent effects are reversible as seen with Propecia which blocks 5-alpha-reductase, which converts free testosterone into DHT.

Breezula acts similar to Propecia in that it blocks the formation of DHT. Breezula also reduces the skin's production of prostaglandin D2, a hormone-like compound, which in high levels can inhibit hair growth, too. However, because Breezula is a topical anti-androgen, it acts predominantly at the cutaneous level on the scalp. Once in the bloodstream, Breezula metabolizes rapidly to cortexolone, a corticosteroid produced naturally by the body with negligible systemic anti-androgen activity and a known safety profile. Breezula, therefore, does not interfere with the hormonal and androgenic profile of patients such as is the case with Propecia, an oral anti-androgen, with a wide range of sexual side effects such as erectile dysfunction and libido disorders. Moreover, Propecia is not approved in women because it can cause birth defects.

Although Breezula is given at 7.5 times higher dosage strength of clascoterone than Winlevi, because the scalp is less permeable than facial skin, the systemic penetration of both products is basically the same. Therefore, Breezula should have a similar excellent safety and tolerability profile as seen with Winlevi and can be given both to men and women. This is a major competitive advantage over Propecia with the potential to expand its commercial opportunity substantially.

Phase IIb trials show the effect of Breezula in men and only in a subgroup of women
In 2017, a phase IIb dose-ranging trial was started in up to 400 men with mild to moderate androgenic alopecia treated with Breezula for 12 months with an interim analysis scheduled after 6 months. In July 2018, positive (6-month) interim analysis top-line results were reported with positive topline results in April 2019 after 12-month treatment with Breezula reported in April 2019 (see Appendix, page 68). Following the positive results in men, a phase IIb dose-ranging trial of Breezula was started in women with alopecia in November 2019. In September 2021, topline results were reported, with positive POC results only seen in a subgroup of women under 30 years of age (see Appendix, page 72). The data will be analyzed to identify the female subgroups potentially benefiting from Breezula treatment. We have conservatively excluded Breezula forecasts for women. Therefore, successful development in a subgroup of women could provide a substantial upside to our forecasts.

Phase III development in male alopecia to start in Q2 2023
Phase III development of Breezula in male alopecia is expected to start in Q2 2023. The phase III program has been finalized under SPA (Special Protocol Assessment) following FDA feedback on the PRO (Patient Reported Outcome) questionnaire. Assuming a similar phase III development program as Winlevi in acne (~1,400 patients, two pivotal phase III trials in the US and EU, 6 months treatment duration), top-line results could become available in 2025. Assuming a normal review (~10 – 12 months), approval is expected in H2 2026 and launch in H1 2026.

US peak sales of around EUR 350 mn

It is estimated that approximately 57 mn men suffer from androgenic alopecia in the US or approximately 16% of the population. As alopecia treatment is typically not reimbursed by health insurers and must be paid out of pocket by patients, we expect that a relatively low amount of people, we estimate 20%, are on prescription medication for alopecia. We assume a US launch in H1 2026 with a peak penetration of up to 6%. This may prove conservative if Breezula lives up to the attractive profile seen in the phase IIb dose-ranging trials. We assume an annual treatment cost of USD 1,200 per person, comparable to the cost of Merck & Co's branded Propecia (finasteride). Applying a long-term patient compliance rate of 40% and patent protection until 2036, we forecast Breezula peak sales in the US to amount to EUR 348 mn. We assume Cassiopea to commercialize Breezula through a partner in return for upfront and commercialization milestones of EUR 172 mn, 20% sales royalties, 17% manufacturing revenue, and 15% COGS.

EU/ROW peak sales of EUR 60+ mn

Applying the same ~16% prevalence rate, we estimate that around 93 mn men suffer from alopecia in the EU/ROW region. In this region, we believe an even lower percentage of people, we estimate 15%, are on prescription medication for alopecia. Here too, most alopecia prescription drugs are not reimbursed. Most prescription drugs In Europe are included in formularies and are fully reimbursed. Consequently, many people are not used to paying out of pocket for prescription drugs. Hence, we assume a low peak penetration rate of 4%, which, together with a markedly lower annual treatment cost per patient of EUR 250, a slightly lower 35% patient compliance rate, and patent protection until 2036 amounts to peak sales of EUR 67 mn for Breezula in the EU/ROW. We assume upfront and sales milestones from commercialization partners of EUR 30 mn and similar royalties on sales, manufacturing income, and COGS percentages as in the US.

Forecasts & Sensitivity Analysis

BREEZULA - FINANCIAL FORECASTS FOR MALE ALOPECIA

INDICATION	ANDROGENIC ALOPECIA (MOST COMMON TYPE OF HAIR LOSS) IN MEN AND WOMEN
DOSAGE	WE ASSUME 7.5% TOPICAL ANHYDROUS SOLUTION APPLIED TWICE A DAY ON SCALP; CHRONIC TREATMENT REQUIRED TO MAINTAIN THE EFFECT
PRICING	ANNUAL TREATMENT COST PER PATIENT IN: EU/ROW: EUR 350; US: USD 1,200 (SIMILAR TO MERCK & CO'S BRANDED PROPECIA)
STANDARD OF CARE	PRESCRIPTION (RX) DRUGS INCLUDE SYSTEMIC (TABLETS) PROPECIA (FINASTERIDE), AVODART (DUTASTERIDE), PROGESTERONE; RX & OTC: TOPICAL ROGRAINE (MINOXIDIL)
UNIQUE SELLING POINT	FIRST-IN-CLASS TOPICAL ANDROGEN RECEPTOR INHIBITOR FOR ALOPECIA WITH GOOD EFFICACY AND AN EXCELLENT SAFETY AND TOLERABITY PROFILE FOR MEN AND WOMEN

7Ps ANALYSIS

PATENT	PROTECTED BY MEDICAL USE PATENT IN ACNE & ALOPECIA UNTIL 2022 (EU/ROW)/2023 (US) AND PATENT COVERING ALL CRYSTALLINE FORMS UNTIL 2028 (EU/ROW) AND 2030 (US)
PHASE	PHASE IIB TRIAL STARTED 2017 (404 MALES 18-55 YEARS, 5 ARMS, 12 MONTHS TREATMENT), POSITIVE 6-MONTHS (INTERIM) AND 12-MONTHS RESULTS; START PHASE III Q2 2023
PATHWAY	2 PIVOTAL PHASE III TRIALS (US & EU) EACH ~500 PTS.; SAFETY AT LEAST 1,000 PTS.: 1 LT OPEN LABEL SAFETY TRIAL: 300+ PTS. 6 MONTHS; 100 PTS. 12 MONTHS
PATIENT	POTENTIALLY IMPROVED EFFICACY OVER CURRENT TREATMENTS, LACKS SYSTEMIC EFFECTS, CAN ALSO BE GIVEN TO WOMEN (PROPECIA NOT INDICATED FOR WOMEN)
PHYSICIAN	NEW, WELL TOLERATED TREATMENT WITH NEW MECHANISM (TOPICAL ANTI-ANDROGEN) WITH POTENTIALLY IMPROVED EFFICACY THAN CURRENT TREATMENTS
PAYER	LIMITED IMPACT - MOST HAIR LOSS TREATMENTS ARE NOT REIMBURSED AND PAID OUT-OF-POCKET BY PATIENTS
PARTNER	US: LIKELY PARTNER WITH SUN PHARMA (THAT SELLS WINLEVI IN US, CANADA, JAPAN AMONG OTHERS); EU/ROW: SEEK PARTNER(S) ON POSITIVE PHASE III OR ON US APPROVAL

REVENUE MODEL

UNITED STATES - SOLD BY PARTNER (TBD)	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
MALES AFFECTED BY ALOPECIA (MN)	59	60	62	63	64	65	67	68	69	71	72
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
ON PRESCRIPTION (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
MALES ON PRESCRIPTION (MN)	11.8	12.1	12.3	12.6	12.8	13.1	13.3	13.6	13.9	14.1	14.4
PENETRATION (%)	0%	0%	0%	0%	3%	4%	5%	6%	3%	2%	0%
MALES ON TREATMENT	0	0	0	0	422,861	562,020	706,577	788,700	482,684	246,169	25,109
COST OF THERAPY PER YEAR (EUR)	1,146	1,103	1,103	1,103	1,103	1,103	1,103	1,103	1,103	1,103	1,103
PATIENT COMPLIANCE (%)	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%
SALES (EUR MN) - BOOKED BY CASSIOPEA	**0**	**0**	**0**	**0**	**187**	**248**	**312**	**348**	**213**	**109**	**11**
CHANGE (%)						33%	26%	12%	-39%	-49%	-90%
ROYALTIES FROM PARTNER (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
ROYALTIES FROM PARTNER (EUR MN)	0	0	0	0	37	50	62	70	43	22	2
MANUFACTURING REVENUE (%)	17%	17%	17%	17%	17%	17%	17%	17%	17%	17%	17%
MANUFACTURING REVENUE (EUR MN)	0	0	0	0	32	42	53	59	36	18	2
UPFRONT & MILESTONE PAYMENTS (EUR MN)	0	0	0	51	28	37	0	46	0	0	0
COGS (%)	0%	0%	20%	18%	15%	15%	15%	15%	15%	15%	15%
COGS (EUR MN)	0	0	0	0	-28	-37	-47	-52	-32	-16	-2
PROFIT BEFORE TAX (EUR MN)	**0**	**0**	**0**	**51**	**69**	**91**	**69**	**123**	**47**	**24**	**2**
TAXES (EUR MN)	0	0	0	-10	-14	-18	-14	-25	-9	-5	0
PROFIT (EUR MN)	**0**	**0**	**0**	**40**	**55**	**73**	**55**	**98**	**37**	**19**	**2**

EUROPE / REST OF WORLD - SOLD BY PARTNER (TBD)	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
MALES AFFECTED BY ALOPECIA (MN)	106	109	111	113	115	118	120	122	125	127	130
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
ON PRESCRIPTION (%)	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
MALES ON PRESCRIPTION (MN)	16.0	16.3	16.6	16.9	17.3	17.6	18.0	18.3	18.7	19.1	19.5
PENETRATION (%)	0%	0%	0%	0%	2%	3%	2%	2%	1%	1%	1%
MALES ON TREATMENT	0	0	0	0	362,918	546,451	390,166	278,578	198,905	142,018	101,401
COST OF THERAPY PER YEAR (EUR)	350	350	350	350	350	350	350	350	350	350	350
PATIENT COMPLIANCE (%)	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%
SALES (EUR MN) - BOOKED BY PARTNER(S)	**0**	**0**	**0**	**0**	**44**	**67**	**48**	**34**	**24**	**17**	**12**
CHANGE (%)						51%	-29%	-29%	-29%	-29%	-29%
ROYALTIES FROM PARTNER (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
ROYALTIES FROM PARTNER (EUR MN)	0	0	0	0	9	13	10	7	5	3	2
MANUFACTURING REVENUE (%)	17%	17%	17%	17%	17%	17%	17%	17%	17%	17%	17%
MANUFACTURING REVENUE (EUR MN)	0	0	0	0	8	11	8	6	4	3	2
UPFRONT & MILESTONE PAYMENTS (EUR MN)	0	0	0	20		10					
COGS (%)	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
COGS (EUR MN)	0	0	0	0	-7	-10	-7	-5	-4	-3	-2
R&D COSTS (EUR MN)	-2	-8	-8	-2	0	0	0	0	0	0	1
PROFIT BEFORE TAX (EUR MN)	**-2**	**-8**	**-8**	**18**	**10**	**25**	**11**	**8**	**5**	**4**	**4**
TAXES (EUR MN)	0	2	2	-4	-2	-5	-2	-2	-1	-1	-1
PROFIT (EUR MN)	**-2**	**-6**	**-6**	**14**	**8**	**20**	**8**	**6**	**4**	**3**	**3**

	2022E	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
GLOBAL SALES (EUR MN)	**0**	**0**	**0**	**0**	**231**	**315**	**360**	**382**	**237**	**126**	**24**
CHANGE (%)						36%	14%	6%	-38%	-47%	-81%
GLOBAL PROFIT (EUR MN)	**-2**	**-6**	**-6**	**55**	**63**	**93**	**63**	**104**	**42**	**22**	**5**
CHANGE (%)	-60%	220%	0%	-957%	14%	48%	-32%	64%	-60%	-47%	-78%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**297**	
NUMBER OF SHARES (MN)	16.3	
NPV PER SHARE (CHF)	**18**	
SUCCESS PROBABILITY	50%	= PHASE II COMPLETED
RISK ADJUSTED NPV PER SHARE (CHF)	**9**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF / SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	100%	20	19	19	18	18	17	17
	95%	19	18	18	17	17	16	16
	90%	18	17	17	16	16	15	15
	85%	17	16	16	15	15	15	14
SUCCESS PROBABILITY	80%	16	15	15	14	14	14	13
	75%	15	14	14	14	13	13	13
	70%	14	13	13	13	12	12	12
	65%	13	12	12	12	11	11	11
	50%	10	10	9	**9**	9	9	8

ESTIMATES AS OF 3 MAY 2023

SOURCE: VALUATIONLAB ESTIMATES

III) GASTROINTESTINAL

Aemcolo/Relafalk – Travelers' disease & IBS-D

Product Analysis

I) Travelers' diarrhea peak sales EUR 50 mn - NPV of CHF 3/share

We forecast peak sales of EUR 47 mn for Aemcolo/Relafalk in travelers' diarrhea after being launched in the US and EU in 2019 with an estimated (3-days) treatment cost of USD 150 (US) and EUR 48 (EU/ROW), and a market penetration conservatively peaking at around 10% (EU/ROW) and 12% (US) of treated patients. In the US, RedHill markets Aemcolo through a traditional specialist sales force and a novel online DTC business model directly to US travelers, which could provide substantial upside to our US forecasts. Cosmo receives high twenties sales royalties and up to USD 100 mn in regulatory and sales milestones (including other indications) while exclusively supplying Aemcolo to RedHill. In the EU/ROW, where Dr. Falk is largely responsible for commercialization, we assume royalties of ~12%, manufacturing income of 10%, and COGS of 1%. Our NPV amounts to CHF 44 mn, or CHF 3 per share, with a WACC of 7% (see detailed forecasts on page 51).

II) IBS-D peak sales of EUR 350+ mn - rNPV of CHF 11/share

In IBS-D (irritable bowel syndrome predominantly with diarrhea), we forecast peak sales of EUR 375 mn assuming the first market launches in 2026, a (14-day) treatment cost of USD 1,575 (US), and EUR 504 (EU/ROW), and a global market penetration conservatively peaking at around 6%. Assuming comparable sales royalty assumptions as for travelers' diarrhea and higher regulatory and sales milestones, our rNPV amounts to CHF 182 mn, or CHF 11 per share for IBS-D with a 50% (phase II completed) success rate (see page 53).

Developing a "better" Xifaxan - patience & patients still needed

Rifamycin SV MMX (branded Aemcolo in the US and Relafalk in the Dr. Falk territories) is the third gastrointestinal prescription drug to reach the market based on Cosmo's proprietary MMX formulation technology. It is another underestimated product in the company's pipeline. The compound appears to have an improved profile compared to Bausch Health's competing antibiotic Xifaxan (rifaximin), with 2022 global sales of USD 1.78 bn. For Cosmo to enjoy Aemcolo/Relafalk's full potential, patience is still required. The COVID-19 pandemic seriously affected the antibiotic's global rollout in its first indication, travelers' diarrhea, with global travel plummeting in 2020 and 2021, while the clinical development program for IBS-D (irritable bowel syndrome – diarrhea-predominant), a large target indication, was also significantly delayed. With the pandemic expected to move into the endemic phase, the global travel market is expected to recover gradually from 2022 onwards. The start the pivotal phase III trials of Aemcolo/Relafalk in IBS-D by its development partners is in planning. First launches in IBS-D could occur in 2026. Aemcolo has marketing exclusivity in the US until 2028 based on QIDP (Qualified Infectious Disease Product) and NCE (new chemical entity) designations. Relafalk enjoys 10-years of data exclusivity until 2028 in the EU.

TD a small indication with potential surprise – IBS-D a large indication in late-stage
The US and EU approval of Aemcolo/Relafalk in its first indication of travelers' diarrhea in November 2018, marks the first new gastrointestinal disease-specific antibiotic in ~15 years. In October 2019, RedHill Biopharma (ticker code: RDHL) acquired the exclusive US development and commercialization rights for Aemcolo in the US. Aemcolo will now be launched through RedHill's specialist sales force and through a novel online DTC business model directly targeting travelers. The EU launch of Relafalk by Dr. Falk's sales force started in Q4 2019. The pandemic severely impacted global sales uptake. We conservatively forecast global peak sales of EUR 50+ mn in travelers' diarrhea related to the short 3-day treatment course. Substantial upside to our US travelers' diarrhea forecasts could occur if a novel online DTC business model directly targeting the yearly 46 mn US travelers succeeds. The novel antibiotic is also being developed for treating IBS-D (irritable bowel syndrome – diarrhea-predominant) an indication with a far higher peak sales potential of EUR 350+ mn thanks to a longer 14-day treatment regimen. In January 2021, positive topline results of the phase II proof-of-concept (POC) trial of Aemcolo in IBS-D were reported; however, they were significantly delayed by the pandemic. The phase III trials in IBS-D are in planning.

RedHill becomes Cosmo's strategic partner to sell Aemcolo in the US
Cosmo concluded an exclusive license agreement for Aemcolo with RedHill Biopharma (NASDAQ ticker: RDHL) in return for a high twenty percent royalty on US sales, potential regulatory and commercial milestones of up to USD 100 mn. Cosmo will be the exclusive supplier of Aemcolo to RedHill. Both companies also entered into a share subscription agreement that provides for an investment of USD 36.6 mn by Cosmo in RedHill ADSs (American Depository Shares), with Cosmo taking a 19.56% strategic stake in RedHill, becoming their largest shareholder, and entitled to appoint one board member. This agreement follows Cosmo's "equity for product" investment strategy, which substantially reduces its development and, marketing & sales costs while retaining long-term upside in the value creation by RedHill through its current 14.8% strategic equity stake. RedHill is a US gastrointestinal specialty biopharmaceutical company. It has 3 FDA-approved prescription drugs, including Talicia (omeprazole magnesium, amoxicillin, and rifabutin delayed-release capsules) for H. pylori infection in adults, Movantik (naloxegol tablets) for opioid-induced constipation in adults with chronic non-cancer pain, and Aemcolo (rifamycin SV MMX delayed-release tablets) for travelers' diarrhea, and 6 late-stage clinical compounds.

I) Travelers' diarrhea – timing is vital, a small market share could generate huge sales

Cosmo estimates approximately 46 mn Americans are traveling every year to "at-risk" countries where the ISTM (International Society of Travel Medicine) recommends traveling with an antibiotic as a precaution. Additionally, the ISTM specifically mentions Aemcolo as a first-line antibiotic for a travel kit for self-treatment in case of infection. To succeed, travelers must be targeted while making their travel plans, and it must be made easy for them to buy Aemcolo, a prescription drug that cannot be bought over the counter (OTC). This asks for a different approach than traditionally targeting physicians, as most travelers do not visit their doctor before traveling. Important to note is that over a third of travelers do seek health advice mostly online before leaving, paying out of pocket for OTC products such as Imodium (loperamide) for diarrhea or travel vaccines. In the case of travelers' diarrhea, cheap OTC diarrhea products such as Imodium decrease the motility of the colon, thus stopping diarrhea. However, they do not treat the underlying infection. Consequently, these

treatments can exacerbate the underlying infection, which sometimes persists upon return or even leads to lasting complications.

Ordering Aemcolo is as simple as pushing an online button with home delivery
When travelers book a trip abroad online, an Aemcolo ad pops up, informing the traveler of the need for Aemcolo to treat travelers' diarrhea. The key message is that travelers' diarrhea can destroy the traveler's costly business trip or vacation and can keep the traveler on the toilet for up to a week. Aemcolo can heal in 24 hours and should be part of a travel kit as a precaution when traveling to "at-risk" countries. A button links the traveler to an online telemedicine provider offering an online consultation with a healthcare practitioner who can write an e-prescription to a pharmacy, where Aemcolo can be delivered at home. Cosmo has teamed up with renowned companies such as Ogilvy Health, an experienced marketing partner with a strong international team with direct experience in travelers' health, and UpScriptHealth, a strong end-to-end execution partner with expertise in telemedicine through warehousing, pharmacy dispensing, and home delivery. We expect RedHill to maintain a similar online prescription option.

A small penetration in travelers could lead to a substantial upside in Aemcolo sales
Pricing in the US is targeted at USD 150 for a 3-days treatment. We conservatively base our forecasts on the penetration of patients treated for travelers' diarrhea and not as a precaution that is bought ahead of traveling to "at-risk" countries. A small penetration in travelers could lead to a substantial upside to our current sales forecasts of EUR 50 mn.

The traditional launch outside the US by Dr. Falk was also affected by the pandemic
Dr. Falk, which has development and commercialization rights for Europe (excluding Italy), selective Eastern European countries, and Australia, markets the antibiotic under the brand Relafalk by traditionally targeting physicians that treat patients with travelers' diarrhea. We assume Cosmo will receive royalties on sales in the low mid-teen range. Cosmo will manufacture Aemcolo exclusively for Dr. Falk and receive a manufacturing fee. In November 2018, the antibiotic was approved for travelers' diarrhea in the EU through the European Decentralized Procedure in Germany, the UK, Spain, Portugal, Sweden, Norway, Denmark, Finland, Greece, Hungary, Poland, and Bulgaria, while first launches by Dr. Falk started in Q4 2019. Unfortunately, their rollout coincided with the pandemic. With global travel expected to recover from 2022 onwards gradually, we expect to see a sharp sales uptake upon the expected relaunch in 2023.

Broad use in colon infections likely replicating Bausch Health's Xifaxan success
Aemcolo/Relafalk is a reformulation of the generic broad-spectrum, semi-synthetic, orally non-absorbable antibiotic rifamycin using Cosmo's MMX technology. The MMX technology allows the antibiotic to be delivered directly into the colon, avoiding unwanted effects on beneficial bacterial flora living in the upper gastrointestinal tract. Aemcolo/Relafalk has the potential to be used in a range of bacterial colon infections, such as travelers' diarrhea, infectious diarrhea, infectious colitis, IBS-D, and diverticulitis, among others, which affect millions of people every year.

The hallmark of colon infections is that they are typically treated based on symptoms, of which diarrhea caused by the underlying bacterial infection is one of the main reasons for patients to seek treatment. Most physicians treat patients empirically, without a specific diagnosis, as the results of pathogen testing typically take too long and it is critical to treat

the infection as soon as possible. A broad-spectrum antibiotic is often sufficient to treat the infection and relieve symptoms.

For instance, the success of Bausch Health's antibiotic Xifaxan (rifaximin), is related to the broad use for colon infections outside its approved indications, such as travelers' diarrhea and IBS-D. Aemcolo/Relafalk appears to have an improved efficacy, safety, and tolerability profile compared to Xifaxan. Therefore, we believe the initial uptake of Aemcolo/Relafalk may be underestimated as it is likely that it will also be prescribed empirically outside its first approved indications. Critical will be approval for IBS-D as the treatment course consists of a 14-day pack compared to a short 3-day pack for travelers' diarrhea.

Travelers' diarrhea and IBS-D are targeted as the first indications
Cosmo currently targets travelers' diarrhea (we forecast EUR 50+ mn peak sales) and IBS-D (EUR 350+ mn peak sales) as the first indications. Aemcolo/Relafalk completed phase III development for travelers' diarrhea, where it demonstrated superiority compared to placebo and non-inferiority compared to ciprofloxacin in two separate pivotal phase III trials.

Key QIDP & Fast Track designations in travelers' diarrhea underline the importance
In the US, Aemcolo received QIDP (Qualified Infectious Disease Product) and Fast Track designations for travelers' diarrhea, which underlines the importance of treating colon infections with new antibiotics. The increasing rise in antibiotic resistance makes current antibiotic treatments redundant. Aemcolo is eligible for additional five years of market exclusivity from the day of approval in the US, based on the GAIN (Generating Antibiotic Incentives Now) Act of 2012. The US NDA (new drug application) filing occurred in March 2018. Thanks to the priority review Aemcolo received its first approval in the US in November 2018, just ahead of the EU approval.

Current treatments for travelers' diarrhea have certain limitations
Travelers' diarrhea is the most common travel-related illness affecting millions of international travelers annually. It can occur anywhere, but the highest-risk destinations are in most of Asia (except for Japan) and the Middle East, Africa, Mexico, and Central and South America. Travelers' diarrhea is a digestive tract disorder that commonly causes loose stools, abdominal cramps, and dehydration. Eating contaminated food or drinking contaminated water causes travelers' diarrhea. The most common cause is enterotoxigenic Escherichia coli (ETEC) bacteria. These bacteria attach themselves to the lining of the intestine and release a toxin that causes diarrhea and abdominal cramps, causing discomfort. In healthy adults, diarrhea is rarely serious or life-threatening; symptoms typically resolve after several days. However, in certain high-risk populations, such as people with weakened immune systems, diabetes, inflammatory bowel disease, cirrhosis of the liver, or people who take acid blockers or antacids, symptoms may become severe. Treatments include broad-spectrum antibiotics such as Bayer's Cipro (ciprofloxacin), which is generically available, and Bausch Health's Xifaxan. However, bacterial resistance to current antibiotics is increasing, and Cipro and Xifaxan have certain limitations compared to Aemcolo, including a "black box" warning (Cipro) or are less potent (Xifaxan).

Positive phase III trial results in travelers' diarrhea show an attractive profile
Aemcolo successfully completed its phase III development in 2016 when the results of two pivotal phase III with different trial designs were announced. The antibiotic demonstrated an attractive and competitive profile in travelers' diarrhea. Aemcolo has been administered in

more than 600 patients in phase III alone and was well tolerated, with only 5.5% of adverse events possibly drug-related (see Appendix, page 73).

A competitive advantage compared to competitor drugs in travelers' diarrhea

In preclinical and clinical trials, Aemcolo/Relafalk demonstrated to have a competitive advantage compared to key competitor antibiotics in travelers' diarrhea (and IBS-D). First, Aemcolo/Relafalk has no systemic absorption, which is important in avoiding bacterial resistance. Thanks to Cosmo's MMX technology, Aemcolo/Relafalk is delivered topically only in the colon where the main infection is, avoiding earlier delivery in the upper gastrointestinal tract with unnecessary destruction of beneficial saprophytic flora. Specific competitive advantages with respect to competitor drugs include:

- **Ciprofloxacin:** has a so-called FDA "black box" warning, flagging an increased risk of tendinitis and tendon ruptures in all ages, limiting its use to severe bacterial infections. The risk is further increased in older patients (>60 years of age), patients taking corticosteroids, and patients with kidney, heart, or lung transplants.
- **Xifaxan** (rifaximin)**:** Bausch Health's Xifaxan (2022 sales +5% to USD 1.78 bn) is also a key competitor to Aemcolo/Relafalk and has been approved in travelers' diarrhea, IBS-D, and hepatic encephalopathy. Aemcolo/Relafalk showed non-inferiority versus Xifaxan in TLUS and treatment success rates in a double-blind phase II clinical trial. Aemcolo/Relafalk also has a clear edge in anti-inflammatory properties. Based on the EC_{50} values, Aemcolo/Relafalk is 100 times more potent than Xifaxan and at least 1,000 times more potent at stimulating PXR transcriptional activity in a cell line engineered to express a fusion human PXR protein than Xifaxan. In terms of the maximum possible stimulation of PXR activity, Xifaxan at 30 µM only activates up to 60% of the maximum activity with Aemcolo/Relafalk at 0.3 µM.

Forecasts & Sensitivity Analysis

AEMCOLO / RELAFALK - FINANCIAL FORECASTS FOR TRAVELERS' DIARRHEA

INDICATION	TRAVELERS' DIARRHEA CAUSED BY NON-INVASIVE STRAINS OF ESCHERICHIA COLI (E.COLI)
DOSAGE	388 MG (TWO TABLETS) ORALLY TWICE DAILY (IN THE MORNING AND EVENING) FOR THREE DAYS: TOTAL OF 12 TABLETS PER TREATMENT
PRICING	3 DAYS TREATMENT PER PATIENT; US: USD 12.50/TABLET = USD 50/DAY = USD 150/TREATMENT; EU/ROW: EUR 4/TABLET = EUR 16/DAY = EUR 48/TREATMENT
STANDARD OF CARE	VALEANT'S XIFAXAN (RIFAXIMIN); BAYER'S CIPROBAY (CIPROFLOXACIN) WHICH IS AVAILABLE GENERICALLY
UNIQUE SELLING POINT	WELL TOLERATED ANTIBIOTIC WITH SHORTER TREATING PERIOD & LESS SUSCEPTABILITY TO ANTIBIOTIC RESISTANCE (WITHOUT A BLACK BOX WARNING)

7Ps ANALYSIS

PATENT	EXPIRY: EU: 2028E (10 YEAR DATA EXCLUSIVITY); US: 2028 (NCE + QIDP EXCLUSIVITY); 4 GRANTED US PATENTS & 1 GRANTED EU PATENT EXPIRE IN MAY 2025
PHASE	EU TRIAL (NON-INFERIORITY VS CIPRO) & US TRIAL (SUPERIORITY VS PLACEBO) PRIMARY ENDPOINTS MET; APPROVED NOV 2018 IN US & EU; LAUNCH 2019
PATHWAY	NORMAL REVIEW IN EU; EXPEDITED REVIEW IN US DUE TO QIDP (QUALIFIED INFECTIOUS DISEASE PRODUCT) DESIGNATION
PATIENT	WELL TOLERATED ANTIBIOTIC WITH FASTER TIME TO RECOVERY
PHYSICIAN	WELL TOLERATED ANTIBIOTIC WITH LESS PROPENSITY TO ANTIBIOTIC RESISTANCE
PAYER	COST EFFECTIVE ANTIBIOTIC DUE TO FASTER RECOVERY TIME AND ABSENCE OF ANTIBIOTIC RESISTANCE MAKING MANY CURRENT TREATMENTS REDUNDANT
PARTNER	EU (EX. ITALY) & AUS.: DR. FALK (BRANDED RELAFALK); US: (BRANDED AEMCOLO) REDHILL BIOPHARMA FROM MID-OCT 2019 (ONLINE DTC SALES BY OGILVY & UPSCRIPT HEALTH)

REVENUE MODEL

UNITED STATES - SOLD BY REDHILL BIOPHARMA	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
PATIENTS WITH TRAVELERS' DIARRHEA (MN)	9	10	11	11	11	11	11	12	12	12	12
GROWTH (%)	150%	15%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PERCENTAGE DIAGNOSED (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
PATIENTS DIAGNOSED (MN)	3	3	3	3	3	3	3	3	4	4	4
PERCENTAGE TREATED (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
PATIENTS TREATED	2,161,007	2,485,158	2,534,861	2,585,558	2,637,270	2,690,015	2,743,815	2,798,692	2,854,666	2,911,759	2,969,994
PENETRATION (%)	0%	3%	6%	8%	9%	10%	9%	1%	0%	0%	0%
NUMBER OF PATIENTS	1,945	76,791	154,373	209,172	239,728	257,972	249,975	25,497	2,601	265	27
COST OF TREATMENT (EUR)	143	138	138	138	138	138	138	138	138	138	138
SALES (EUR MN) - BOOKED BY REDHILL	**0**	**11**	**21**	**29**	**33**	**36**	**34**	**4**	**0**	**0**	**0**
CHANGE (%)	408%	3703%	101%	35%	15%	8%	-3%	-90%	-90%	-90%	-90%
ROYALTY (%)	27%	27%	27%	27%	27%	27%	27%	27%	27%	27%	27%
ROYALTIES (EUR MN)	0	3	6	8	9	10	9	1	0	0	0
MANUFACTURING REVENUE (%)	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
MANUFACTURING REVENUE (EUR MN)	0	0	0	0	0	0	0	0	0	0	0
UPFRONT & MILESTONE PAYMENTS (EUR MN)	0	0	5	0	0	9	0	0	0	0	0
COGS (%)	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
COGS (EUR MN)	0	0	0	0	0	0	0	0	0	0	0
PROFIT BEFORE TAX (EUR MN)	**0**	**3**	**10**	**8**	**9**	**19**	**9**	**1**	**0**	**0**	**0**
TAX RATE (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
TAXES (EUR MN)	0	-1	-2	-2	-2	-4	-2	0	0	0	0
PROFIT (EUR MN)	**0**	**2**	**8**	**6**	**7**	**15**	**7**	**1**	**0**	**0**	**0**

EUROPE / REST OF WORLD - SOLD BY DR. FALK	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
PATIENTS WITH TRAVELERS' DIARRHEA (MN)	11	12	13	13	13	13	14	14	14	15	15
GROWTH (%)	150%	15%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PERCENTAGE DIAGNOSED (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
PATIENTS DIAGNOSED (MN)	3	4	4	4	4	4	4	4	4	4	4
PERCENTAGE TREATED (%)	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
PATIENTS TREATED	2,269,057	2,609,416	2,661,604	2,714,836	2,769,133	2,824,516	2,881,006	2,938,626	2,997,399	3,057,347	3,118,494
PENETRATION (%)	0%	2%	4%	6%	7%	8%	6%	3%	2%	1%	0%
NUMBER OF PATIENTS	1,475	53,884	108,194	164,655	195,639	227,797	185,883	94,800	48,348	24,658	12,575
COST OF TREATMENT (EUR)	48	48	48	48	48	48	48	48	48	48	48
SALES (EUR MN) - BOOKED BY DR. FALK	**0**	**3**	**5**	**8**	**9**	**11**	**9**	**5**	**2**	**1**	**1**
CHANGE (%)	-84%	3553%	101%	52%	19%	16%	-18%	-49%	-49%	-49%	-49%
ROYALTY (%)	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%
ROYALTIES (EUR MN)	0	0	1	1	1	1	1	1	0	0	0
MANUFACTURING REVENUE (%)	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%
MANUFACTURING REVENUE (EUR MN)	0	0	1	1	1	1	1	0	0	0	0
UPFRONT & MILESTONE PAYMENTS (EUR MN)											
COGS (%)	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
COGS (EUR MN)	0	0	0	0	0	0	0	0	0	0	0
R&D COSTS (EUR MN)	0	0	0	0	0	0	0	0	0	0	0
PROFIT BEFORE TAX (EUR MN)	**0**	**1**	**1**	**2**	**2**	**2**	**2**	**1**	**0**	**0**	**0**
TAXES (EUR MN)	0	0	0	0	0	0	0	0	0	0	0
PROFIT (EUR MN)	**0**	**0**	**1**	**1**	**2**	**2**	**2**	**1**	**0**	**0**	**0**

	2022E	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
GLOBAL SALES (EUR MN)	**0**	**13**	**26**	**37**	**42**	**47**	**43**	**8**	**3**	**1**	**1**
CHANGE (%)	-29%	3672%	101%	39%	16%	10%	-7%	-81%	-67%	-54%	-50%
GLOBAL PROFIT (EUR MN)	**0**	**3**	**9**	**8**	**9**	**17**	**9**	**2**	**0**	**0**	**0**
CHANGE (%)	-16%	3678%	235%	-17%	15%	93%	-47%	-83%	-69%	-56%	-51%

WACC (%)	7%
NPV TOTAL PROFIT (CHF MN)	**44**
NUMBER OF SHARES (MN)	16.3
NPV PER SHARE (CHF)	**3**

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	80	4	4	4	4	4	4	4
	70	4	4	4	4	4	4	3
	60	3	3	3	3	3	3	3
PEAK SALES (EUR MN)	50	3	3	3	**3**	3	3	2
	40	2	2	2	2	2	2	2
	30	2	2	2	2	2	2	1
	20	1	1	1	1	1	1	1

ESTIMATES AS OF 3 MAY 2023

SOURCE: VALUATIONLAB ESTIMATES

II) IBS-D is a common GI disorder largely underdiagnosed and untreated

Aemcolo/Relafalk's potential second indication, which we have included in our forecasts, targets patients with irritable bowel syndrome – diarrhea-predominant (IBS-D). IBS is the most common functional gastrointestinal disorder that can cause abdominal pain, bloating, and altered bowel function, causing diarrhea (IBS-D), constipation (IBS-C), or both (IBS-M), the three major subtypes of IBS. Studies show that the prevalence of IBS may range from 10% to 25% and frequently occurs in young adulthood. Prevalence rates in women are approximately 1.5 to 3-fold higher than in men. Although IBS may occur at any age, about half of the people with IBS experienced initial symptoms before the age of 35 years. IBS tends to be underdiagnosed because people with symptoms of IBS often do not seek medical attention, as there is a significant stigma associated with IBS, and are often not properly diagnosed. It has been reported that only 30% of people with symptoms of IBS, mainly IBS-D, will consult with a physician. Most people with IBS experience symptoms for an average of 8.1 days/month, had approximately two times as many days off work as the general population, and experienced more days in bed or felt less productive at work because of their symptoms. It is estimated that IBS costs USD 1.6 bn per year in health-related spending in the US alone.

Aemcolo/Relafalk targets bacterial overgrowth but without systemic side effects

The precise cause of IBS is not known. Factors that appear to play a role include muscle contractions in the intestine, abnormalities in the nerves of the digestive system (poorly controlled signals between brain and intestines), inflammation of the intestines, severe infection (associated with a surplus of bacteria in the intestines called "bacterial overgrowth"), and changes in "good" bacteria in the gut (microflora). IBS patients are often treated with a range of antibiotics to reduce bacterial overgrowth. However, these often have systemic side effects and impact the microflora. Aemcolo has a wide spectrum of activity against the microbes implicated in bacterial overgrowth. Because it is non-absorbed, it should lack systemic side effects seen with current antibiotics with a low propensity to resistance.

Positive POC results reported in 2021 after a significant delay due to the pandemic

In 2017, a phase IIa proof-of-concept (POC) trial of Aemcolo/Relafalk in patients with IBS-D was started. However, the trial was severely impacted by the COVID-19 pandemic. Positive topline results were finally reported in January 2021. The trial was very successful, notwithstanding the decision by Cosmo to reduce the envisaged patient number by 20% due to COVID-19 restrictions. The results show the achievement of statistical significance in all the trial populations, including ITT, Full Analysis Set (FAS), modified-FAS, and Per Protocol (PP) population for the composite primary endpoint (substantial pain and diarrhea decrease) [OR 3.26 (1.39 – 7.67); p-value 0.0066], and for most secondary endpoints such as adequate relief of IBS-related symptoms [OR 2.18 (1.12 – 4.26); p-value 0.0227], and IBS-related bloating at the end of the treatment period [OR 2.13 (1.11 – 4.07); p-value 0.0223] (see Appendix, page 73).

Phase III trials in planning with first launches expected in 2026

Cosmo, together with its licensees, is in discussions with the US and EU regulatory agencies with a view to starting the phase III clinical trials required for marketing authorization. The pivotal phase III trials are expected to have a trial duration of approximately 18 months. We assume the first launches in the US and EU for Aemcolo/Relafalk in IBS-D to occur in 2026.

AEMCOLO / RELAFALK - FINANCIAL FORECASTS IRRITABLE BOWEL SYNDROME WITH DIARRHEA (IBS-D)

INDICATION	IRRITABLE BOWEL SYNDROME PREDOMINANTLY WITH DIARRHEA (IBS-D)
DOSAGE	582 MG (3 TABLETS) THREE TIMES DAILY FOR 14 DAYS: TOTAL OF 126 TABLETS PER TREATMENT - TBD
PRICING	14 DAYS TREATMENT ASSUMED: US: USD 12.50/TABLET = USD 112.50/DAY = USD 1,575/TREATMENT; EU/ROW: EUR 4/TABLET = EUR 36/DAY = EUR 504/TREATMENT
STANDARD OF CARE	NOVARTIS' ZELNORM (TEGASEROD) HOWEVER NOT INDICATED FOR MEN; BAUSCH HEALTH'S XIFAXAN (RIFAXIMIN) APPROVED IN 2015
UNIQUE SELLING POINT	WELL TOLERATED AND EFFECTIVE ANTIBIOTIC WITH LIKELY SHORTER TREATMENT COURSE, LOW PROPENSITY TO ANTIBIOTIC RESISTANCE (WITHOUT BLACK BOX WARNING)

7Ps ANALYSIS

PATENT	EXPIRY: EU: 2028E (10 YEAR DATA EXCLUSIVITY); US: 2028 (NCE + QIDP EXCLUSIVITY); 4 GRANTED US PATENTS & 1 GRANTED EU PATENT EXPIRE IN MAY 2025
PHASE	POSITIVE PHASE II IBS-D RESULTS JANUARY 2021; PHASE III START TBD, RESULTS 2024, FILING 2025, ASSUMING NORMAL REVIEW FIRST LAUNCHES EXPECTED IN 2026
PATHWAY	NORMAL REVIEW IN EU; EXPEDITED REVIEW IN US DUE TO QIDP (QUALIFIED INFECTIOUS DISEASE PRODUCT) DESIGNATION
PATIENT	WELL TOLERATED ANTIBIOTIC WITH FASTER TIME TO RECOVERY
PHYSICIAN	WELL TOLERATED ANTIBIOTIC WITH LESS SUSCEPTABILITY TO ANTIBIOTIC RESISTANCE
PAYER	COST EFFECTIVE ANTIBIOTIC DUE TO FASTER RECOVERY TIME AND ABSENCE OF ANTIBIOTIC RESISTANCE MAKING MANY CURRENT TREATMENTS REDUNDANT
PARTNER	EU (EX. ITALY) & AUS.: DR. FALK (BRANDED RELAFALK); US: (BRANDED AEMCOLO) REDHILL BIOPHARMA FROM MID-OCT 2019

REVENUE MODEL

UNITED STATES - SOLD BY REDHILL BIOPHARMA	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
NUMBER OF IBS PATIENTS (MN)	40	41	42	43	43	44	45	46	47	48	49
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
IBS PATIENTS WITH IBS-D (%)	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
IBS PATIENTS WITH IBS-D (MN))	20.1	20.5	20.9	21.3	21.7	22.1	22.6	23.0	23.5	24.0	24.5
IBS PATIENTS CONSULTING PHYSICIAN (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
IBS PATIENTS CONSULTING PHYSICIAN (MN)	6.0	6.1	6.3	6.4	6.5	6.6	6.8	6.9	7.1	7.2	7.3
PENETRATION (%)	0%	0%	0%	0%	2%	6%	6%	5%	5%	4%	4%
NUMBER OF PATIENTS (MN)	0.0	0.0	0.0	0.0	0.1	0.4	0.4	0.4	0.3	0.3	0.3
COST OF THERAPY PER DAY (EUR)	107	103	103	103	103	103	103	103	103	103	103
NUMBER OF TREATMENT DAYS	14	14	14	14	14	14	14	14	14	14	14
COST OF TREATMENT (EUR)	1,504	1,448	1,448	1,448	1,448	1,448	1,448	1,448	1,448	1,448	1,448
COMPLIANCE (%)	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%
SALES (EUR MN) - BOOKED BY REDHILL	**0**	**0**	**0**	**0**	**75**	**231**	**224**	**208**	**192**	**175**	**157**
CHANGE (%)						206%	-3%	-7%	-8%	-9%	-10%
ROYALTY (%)	27%	27%	27%	27%	27%	27%	27%	27%	27%	27%	27%
ROYALTIES (EUR MN)	0	0	0	0	20	62	60	56	52	47	42
MANUFACTURING REVENUE (%)	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
MANUFACTURING REVENUE (EUR MN)	0	0	0	0	1	3	3	2	2	2	2
UPFRONT & MILESTONE PAYMENTS (EUR MN)	0	0	0	14	0	14	0	23	28	0	0
COGS (%)	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
COGS (EUR MN)	0	0	0	0	-1	-2	-2	-2	-2	-2	-2
PROFIT BEFORE TAX (EUR MN)	**0**	**0**	**0**	**14**	**20**	**76**	**61**	**80**	**80**	**48**	**43**
TAX RATE (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
TAXES (EUR MN)	0	0	0	-3	-4	-15	-12	-16	-16	-10	-9
PROFIT (EUR MN)	**0**	**0**	**0**	**11**	**16**	**61**	**49**	**64**	**64**	**38**	**34**

EUROPE / REST OF WORLD - SOLD BY DR. FALK	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
NUMBER OF IBS PATIENTS (MN)	72	74	75	77	78	80	81	83	85	86	88
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
IBS PATIENTS WITH IBS-D (%)	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
IBS PATIENTS WITH IBS-D (MN))	36	37	38	38	39	40	41	41	42	43	44
PATIENTS CONSULTING PHYSICIAN (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
PATIENTS CONSULTING PHYSICIAN (MN)	11	11	11	11	12	12	12	12	13	13	13
PENETRATION (%)	0%	0%	0%	0%	2%	6%	5%	4%	3%	3%	2%
NUMBER OF PATIENTS (MN)	0.0	0.0	0.0	0.0	0.2	0.7	0.7	0.5	0.4	0.4	0.3
COST OF THERAPY PER DAY (EUR)	36	36	36	36	36	36	36	36	36	36	36
NUMBER OF TREATMENT DAYS	14	14	14	14	14	14	14	14	14	14	14
COST OF TREATMENT (EUR)	504	504	504	504	504	504	504	504	504	504	504
COMPLIANCE (%)	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%
SALES (EUR MN) - BOOKED BY DR. FALK	**0**	**0**	**0**	**0**	**47**	**145**	**133**	**108**	**88**	**72**	**59**
CHANGE (%)						206%	-8%	-18%	-18%	-18%	-18%
ROYALTY (%)	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%
ROYALTIES (EUR MN)	0	0	0	0	6	17	16	13	11	9	7
MANUFACTURING INCOME (%)	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%
MANUFACTURING INCOME (EUR MN)	0	0	0	0	5	14	13	11	9	7	6
UPFRONT & MILESTONE PAYMENTS (EUR MN)	0	0	0	6	5	7	11	0	0	0	0
COGS (%)	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
COGS (EUR MN)	0	0	0	0	0	-1	-1	-1	-1	-1	-1
R&D COSTS (EUR MN)	0	0	0	0	0	0	0	0	0	0	0
PROFIT BEFORE TAX (EUR MN)	**0**	**0**	**0**	**6**	**15**	**38**	**39**	**23**	**19**	**15**	**12**
TAX RATE (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
TAXES (EUR MN)	0	0	0	-1	-3	-8	-8	-5	-4	-3	-2
PROFIT (EUR MN)	**0**	**0**	**0**	**4**	**12**	**30**	**31**	**18**	**15**	**12**	**10**

	2022E	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
GLOBAL SALES (EUR MN)	**0**	**0**	**0**	**0**	**123**	**375**	**356**	**316**	**280**	**247**	**216**
CHANGE (%)						206%	-5%	-11%	-11%	-12%	-13%
GLOBAL PROFIT (EUR MN)	**0**	**0**	**0**	**15**	**28**	**91**	**80**	**82**	**79**	**50**	**44**
CHANGE (%)	-100%				81%	226%	-13%	3%	-4%	-36%	-12%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**365**	
NUMBER OF SHARES (MN)	16.3	
NPV PER SHARE (CHF)	**22**	
SUCCESS PROBABILITY	50%	(PHASE II COMPLETED SUCCESS PROBABILITY)
RISK ADJUSTED NPV PER SHARE (CHF)	**11**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	100%	25	24	23	22	21	21	20
	90%	22	22	21	20	19	19	18
	80%	20	19	18	18	17	17	16
SUCCESS PROBABILITY	70%	17	17	16	16	15	14	14
	60%	15	14	14	13	13	12	12
	50%	12	12	12	**11**	11	10	10
	40%	10	10	9	9	9	8	8

ESTIMATES AS OF 3 MAY 2023

SOURCE: VALUATIONLAB ESTIMATES

LEGACY BUSINESS

Lialda / Mezavant (ulcerative colitis)

Generic erosion has only a minor impact on Cosmo revenues

The approval of Lialda/Mezavant in 2007 was the first validation of Cosmo's proprietary MMX colon delivery technology. It was also the company's first prescription drug to reach the market for treating ulcerative colitis, a chronic relapsing-remitting illness where the colon and rectum become inflamed, for which no known cure exists. Still, patients can manage their symptoms with appropriate treatment. Lialda/Mezavant contains generic mesalamine in a novel oral tablet formulation that utilizes the company's MMX technology. It was the first convenient once-a-day formulation of mesalamine on the market with the highest amount of mesalamine per tablet, which significantly reduces the frequency of dosing (once instead of 3-4 times a day) and the pill burden (2-4 tablets instead of 6-16) compared to competitor mesalamine products, which led to its success.

Early licensing agreements funded other research projects at far better terms

Lialda/Mezavant was globally out-licensed to Giuliani and Shire Pharmaceuticals (acquired by Takeda in 2019) in 2001, in the early stage of Cosmo's existence and clinical development of the drug. This aligned with the company's strategy to share the risk and not overstretch its financial reach. As a result, the licensing terms were rather poor, with royalty revenues on sales of 3.5% (with a cumulative cap of USD 95 mn on global sales - the US and EU cumulative cap of USD 80 mn was reached in 2014) and manufacturing revenues of 3% of sales. Takeda has the right to manufacture up to 20% of Lialda/Mezavant capacity, but this has proven difficult, and Takeda has not succeeded. This highlights Cosmo's manufacturing expertise and state-of-the-art facilities. On the positive side, Lialda/Mezavant's cash flows were used to fund other MMX projects such as Uceris/Cortiment, Aemcolo/Relafalk, and Lumeblue and allowed the company to take on more risk over time by out-licensing these projects at a later stage of development with significantly better economics.

Stellar rise of Lialda thanks to its best-in-class profile, but generics spoil the party

In 2007, Lialda/Mezavant was initially approved for induction of remission in patients with active, mild-to-moderate ulcerative colitis, followed by maintenance treatment in 2011. The convenient once-a-day dosing, with considerably fewer tablets, has been the key driver of growth and market penetration, achieving peak sales of USD 792 mn in 2016. Lialda was expected to enjoy protection for a few more years until 2020 when the MMX composition of matter patent would expire. However, after years of patent battles, the last legal barrier between Shire and a generic version of Lialda fell and the FDA approved a generic from the Indian generic manufacturer Zydus Cadila in June 2017. Zydus, which launched its generic, acquired “first-to-file” rights providing 6 months of exclusivity. This class of drugs has proven extremely difficult to manufacture. For instance, there are still no generics for Takeda’s own ulcerative colitis drug Pentasa (mesalamine), which lost patent protection a decade ago. Cosmo is less affected as Lialda revenues are largely manufacturing revenue from Takeda, which are expected to decline less than pricing and sales.

In 2022, Lialda reported a 6% growth in revenues to EUR 29.6 mn (2021: EUR 27.8 mn), mainly due to increased volumes in the US and Japan.

LIALDA / MEZAVANT - FINANCIAL FORECASTS FOR ULCERATIVE COLITIS	
INDICATION	INDUCTION AND MAINTENANCE OF REMISSION FOR PATIENTS WITH ULCERATIVE COLITIS FO MILD TO MODERATE SEVERITY
DOSAGE	2.4 GRAMS/DAY (MAINTENANCE) OR 2.4-4.8 GRAMS/DAY (INDUCTION)
PRICING	US: 2 TABLETS PER DAY FOR 120 DAYS = USD 1,473 PER PATIENT; EU/ROW 2 TABLETS PER DAY FOR 120 DAYS = EUR 454 PER PATIENT
STANDARD OF CARE	GENERIC MESALAMINE / ASACOL (WARNER CHILCOTT)
UNIQUE SELLING POINT	ONLY ONCE-A-DAY DOSING (2-4 TABLETS), OTHER MESALAMINES REQUIRE 3-4 TIMES A DAY DOSING (6-16 TABLETS)
7Ps ANALYSIS	
PATENT	EXPIRY 2020 ("MMX" FORMULATION PATENT (USPTO: 7,431,943 - JUNE 2020)); INDIAN COMPANY ZYDUS RECEIVED US FDA APPROVAL FOR ITS GENERIC IN JUNE 2017
PHASE	LAUNCHED IN THE US BY SHIRE IN 2007 AND ROLLED OUT LATER IN THE EU; WE EXPECT NOGRA PHARMA TO LAUNCH IN JAPAN IN 2018
PATHWAY	ESTABLISHED REGULATORY PATHWAY - "MMX" SUSTAINED RELEASE FORMULATION OF GENERIC MESALAMINE
PATIENT	CONVENIENT ONCE-A-DAY DOSING SCHEDULE AND LOWER PILL LOAD COMPARED TO COMPETITORS
PHYSICIAN	BETTER PATIENT COMPLIANCE DUE TO ONCE-A-DAY DOSING SCHEDULE POTENTIALLY ENHANCING EFFICACY
PAYER	COST EFFECTIVE TREATMENT DUE TO IMPROVED PATIENT COMPLIANCE AND EFFICACY
PARTNER	US: TAKEDA (ACQUIRED SHIRE IN 2019) I EU: GIULIANI SPA / LEHNER SA (TAKEDA HAS EXCLUSIVE SELLING RIGHTS) I JAPAN: NOGRA PHARMA

REVENUE MODEL

BASED ON SHIPPED TABLETS	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E
NUMBER OF TABLETS SHIPPED BY COSMO (MN)	**428**	**437**	**441**	**441**	**441**	**441**	**441**	**441**	**441**	**441**	**441**
CHANGE (%)	6%	2%	1%	0%	0%	0%	0%	0%	0%	0%	0%
COSMO REVENUE PER TABLET (EUR)	0.069	0.069	0.069	0.069	0.069	0.069	0.069	0.069	0.069	0.069	0.069
COSMO MANUFACTURING REVENUE (EUR MN)	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**
CHANGE (%)	6%	2%	1%	0%	0%	0%	0%	0%	0%	0%	0%
COSMO COST PER TABLET (EUR)	0.007	0.007	0.007	0.007	0.007	0.007	0.007	0.007	0.007	0.007	0.007
COGS (EUR MN)	-3	-3	-3	-3	-3	-3	-3	-3	-3	-3	-3

	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E
LIALDA REVENUES (EUR MN)	**27**	**27**	**27**	**27**	**27**	**27**	**27**	**27**	**27**	**27**	**27**
CHANGE (%)	6%	2%	1%	0%	0%	0%	0%	0%	0%	0%	0%

WACC (%)	7%
NPV TOTAL PROFIT (CHF MN)	**207**
NUMBER OF SHARES (MN)	16.3
NPV PER SHARE (CHF)	**13**

ESTIMATES AS OF 3 MAY 2023

SOURCE: VALUATIONLAB ESTIMATES

Uceris/Cortiment (ulcerative colitis)

Uceris impacted by generics – Cortiment continues to grow

Uceris/Cortiment was Cosmo's second drug to reach the market using Cosmo's proprietary MMX colon delivery technology, with a peak sales potential in ulcerative colitis that could have rivaled Lialda's peak sales before generics entered the US market. The drug is branded Uceris in the US and Cortiment outside the US, where Ferring is largely responsible for commercialization. In the US, Bausch Health (formerly Valeant Pharmaceuticals) is responsible for the commercialization of Uceris.

First convenient, oral, locally active corticosteroid for treating ulcerative colitis

Up to 30% of patients with mild or moderate ulcerative colitis do not respond to aminosalicylate (5-ASA) drugs such as Lialda sufficiently and require a different or add-on therapy. Patients refractive to 5-ASA treatment typically receive a course of a systemically absorbed corticosteroid, which success may be limited by side effects. Uceris is the first convenient, oral, locally active corticosteroid using Cosmo's proprietary MMX formulation of generic budesonide to be approved for induction of active, mild, or moderate ulcerative colitis. In the US, systemic corticosteroids such as prednisone are prescribed off-label for mild or moderate ulcerative colitis. Still, they have been used scarcely due to dreaded long-term side effects (e.g., stunted growth, weight gain, "moon" face, bruising).

Awareness of Uceris high thanks to widespread use of Astra Zeneca's Entocort EC

Outside the US, budesonide, given by enema, is used to treat ulcerative colitis patients. Due to the inconvenient administration, budesonide enema is not used extensively. Physicians are also familiar with a budesonide extended-release formulation for the small intestine, branded Entocort EC by AstraZeneca. This drug was approved globally for treating Crohn's disease, a type of inflammatory bowel disease that may affect any part of the gastrointestinal tract, but most commonly the last part of the small intestine (the terminal ileum). Entocort EC was on the brink of reaching USD 400 mn in sales just before the patent expired in 2011. Many physicians know budesonide as an effective treatment for IBD; however, limited by side effects.

US uptake hampered by multiple acquisitions and "at-risk" generic launches

In early 2013, Uceris was approved and launched by Santarus, Cosmo's original US commercialization partner. Uceris was off to a flying start in the US, triggering consecutive acquisitions. In late 2013, Salix acquired Santarus. In 2015, Valeant acquired Salix. In 2018, Valeant was renamed Bausch Health to distance itself from the public outrage associated with massive price increases of several of its products. In July 2018, the FDA approved Actavis' (Teva) generic version of Uceris, with Actavis launching its " at-risk " version and an authorized generic by Bausch Health shortly after. In November 2017, the US District Court for the District of Delaware ruled a non-infringement of Actavis' generic version of Uceris. Bausch Health appealed the District Court's ruling.

Global rollout by Ferring is well on its way, approved in more than 45 countries

Outside the US (except in Japan and Asia), Ferring is responsible for selling Cortiment and has obtained approval in more than 45 countries, including the major EU countries and several countries in South and North America and the Far East. Unfortunately, pricing in the EU is a fraction of the US price. In recent years, Cortiment has been growing steadily, around 10% annually. We assume growth to continue at a similar rate in the future, with net manufacturing revenue of ~18% of sales after COGS.

UCERIS / CORTIMENT - FINANCIAL FORECASTS FOR ULCERATIVE COLITIS

INDICATION	INDUCTION OF REMISSION FOR PATIENTS WITH ACTIVE ULCERATIVE COLITIS OF MILD TO MODERATE SEVERITY
DOSAGE	A SINGLE 9 MG ORAL TABLET ONCE DAILY FOR UP TO 8 WEEKS
PRICING	8 WEEKS TREATMENT DURATION: US: USD 40/DAY = USD 2,240; EU: EUR 10/DAY = EUR 560
STANDARD OF CARE	GENERIC MESALAMINE /ASACOL (WARNER CHILCOTT) / LIALDA (COSMO) / ENTOCORT EC/ENEMA (ASTRAZENECA)
UNIQUE SELLING POINT	FIRST ORAL STEROID FOR ULCERATIVE COLITIS ON US MARKET - BETTER RESPONSE RATES THAN SALYCILATES, SAFER THAN SYSTEMIC STEROIDS (E.G. PREDNISON)
7Ps ANALYSIS	
PATENT	EXPIRY SEP 2031; 12 GRANTED US PATENTS (COM, METHOD OF USE); 1 GRANTED EU PATENT (EP1183014); ACTAVIS GENERIC APPROVED & LAUNCHED "AT RISK" IN JUL 2018
PHASE	US: APPROVED JANUARY 2013 / EU: APPROVED OCTOBER 2014; LAUNCHED IN 22 COUNTRIES, APPROVED IN 47, PENDING REGISTRATION IN 13, FILINGS PLANNED FOR 29
PATHWAY	ESTABLISHED REGULATORY PATHWAY - "MMX" SUSTAINED RELEASE FORMULATION OF GENERIC BUDESONIDE
PATIENT	SIMPLE SINGLE ORAL TABLET VS ENTOCORT ENEMA (RECTAL ADMINISTRATION)
PHYSICIAN	HIGHER RESPONSE RATES THAN ASACOL, LIALDA AND ENTOCORT
PAYER	HIGHER PATIENT COMPLIANCE AND RESPONSE RATES LEAD TO LOWER TOTAL TREATMENT COSTS
PARTNER	FERRING GLOBAL RIGHTS EX-US; US: LICENSED TO BAUSCH HEALTH (FORMERLY VALEANT PHARMACEUTICALS)

REVENUE MODEL

UNITED STATES - SOLD BY BAUSCH HEALTH	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
NUMBER OF PATIENTS (MN)	1.2	1.3	1.3	1.3	1.4	1.4	1.5	1.5	1.5	1.6	1.6
PATIENT WITH MILD-TO-MODERATE DISEASE (85%)	1.0	1.1	1.1	1.1	1.2	1.2	1.2	1.3	1.3	1.4	1.4
PENETRATION (%)	1%	1%	1%	0%	0%	0%	0%	0%	0%	0%	0%
NUMBER OF PATIENTS (MN)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
COST OF THERAPY PER YEAR (EUR)	2,139	2,060	2,060	2,060	2,060	2,060	2,060	2,060	2,060	2,060	2,060
SALES (EUR MN) - BOOKED BY BAUSCH HEALTH	**23**	**19**	**15**	**13**	**10**	**9**	**7**	**6**	**5**	**4**	**3**
CHANGE (%)	10%	-21%	-18%	-18%	-18%	-18%	-18%	-18%	-18%	-18%	-18%
MANUFACTURING REVENUE (~14%) (EUR MN)	3	3	2	2	1	1	1	1	1	1	0
COGS (~2%) (EUR MN)	0	0	0	0	0	0	0	0	0	0	0
PROFIT BEFORE TAX (EUR MN)	**3**	**2**	**2**	**2**	**1**	**1**	**1**	**1**	**1**	**0**	**0**
TAXES (EUR MN)	-1	0	0	0	0	0	0	0	0	0	0
PROFIT (EUR MN)	**2**	**2**	**1**	**1**	**1**	**1**	**1**	**1**	**0**	**0**	**0**

EUROPE / REST OF WORLD - SOLD BY FERRING	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
NUMBER OF PATIENTS (MN)	1.3	1.4	1.4	1.5	1.5	1.6	1.6	1.6	1.7	1.7	1.8
PATIENT WITH MILD-TO-MODERATE DISEASE (85%)	1.1	1.2	1.2	1.2	1.3	1.3	1.4	1.4	1.4	1.5	1.5
PENETRATION (%)	3%	3%	4%	4%	5%	6%	7%	7%	6%	3%	1%
NUMBER OF PATIENTS (MN)	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.0
COST OF THERAPY PER YEAR (EUR)	560	560	560	560	560	560	560	560	560	560	560
SALES (EUR MN) - BOOKED BY FERRING	**20.6**	**24**	**29**	**35**	**43**	**51**	**60**	**69**	**57**	**29**	**15**
CHANGE (%)	4%	18%	19%	20%	22%	19%	17%	15%	-18%	-49%	-49%
MANUFACTURING REVENUE (~20%) (EUR MN)	4	5	6	7	8	10	12	13	11	6	3
UPFRONT & MILESTONE PAYMENTS (EUR MN)	9					5					
COGS (~2%) (EUR MN)	0	0	-1	-1	-1	-1	-1	-1	-1	-1	0
PROFIT BEFORE TAX (EUR MN)	**13**	**4**	**5**	**6**	**7**	**14**	**10**	**12**	**10**	**5**	**3**
TAXES (EUR MN)	-3	-1	-1	-1	-1	-3	-2	-2	-2	-1	-1
PROFIT (EUR MN)	**10**	**3**	**4**	**5**	**6**	**11**	**8**	**10**	**8**	**4**	**2**

	2022E	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
GLOBAL SALES (EUR MN)	**44**	**43**	**44**	**47**	**53**	**59**	**67**	**75**	**61**	**33**	**18**
CHANGE (%)	7%	-3%	3%	7%	12%	12%	12%	12%	-18%	-46%	-45%
GLOBAL PROFIT (EUR MN)	**12**	**5**	**6**	**6**	**7**	**12**	**9**	**10**	**8**	**4**	**2**
CHANGE (%)	140%	-58%	7%	10%	14%	71%	-24%	13%	-18%	-47%	-46%
WACC (%)	6%										
NPV TOTAL PROFIT (CHF MN)	**54**										
NUMBER OF SHARES (MN)	16.3										
NPV PER SHARE (CHF)	**3**										

ESTIMATES AS OF 3 MAY 2023

SOURCE: VALUATIONLAB ESTIMATES

Income Statement

COSMO PHARMACEUTICALS								SHARE PRICE (CHF) 54.70			
IFRS											
INCOME STATEMENT (EUR MN)	**2022**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
PRODUCT SALES (INCL. PARTNER SALES)	**472**	**609**	**799**	**989**	**1,551**	**1,951**	**1,948**	**1,851**	**1,556**	**1,224**	**1,045**
CHANGE (%)	36%	29%	31%	24%	57%	26%	0%	-5%	-16%	-21%	-15%
TOTAL MANUFACTURING:	**66**	**80**	**94**	**143**	**156**	**173**	**181**	**156**	**129**	**97**	**88**
CHANGE (%)	52%	21%	42%	53%	67%	11%	16%	-14%	-17%	-25%	-10%
1) MANUFACTURING OF OWN PRODUCTS	**53**	**66**	**80**	**129**	**142**	**159**	**165**	**141**	**114**	**81**	**71**
CHANGE (%)	62%	25%	50%	62%	78%	12%	17%	-15%	-19%	-29%	-12%
2) MANUFACTURING GENERICS, SPECIALTY DRUGS & RELATED SERVICES	**13**	**14**	**14**	**14**	**15**	**15**	**15**	**15**	**16**	**16**	**16**
CHANGE (%)	4%	5%	2%	2%	2%	2%	2%	2%	2%	2%	2%
LICENCE AND UPFRONT FEES AND MILESTONES	**24.3**	**5**	**43**	**146**	**55**	**87**	**52**	**76**	**28**	**15**	**20**
ROYALTIES TO COSMO	**10**	**38**	**78**	**116**	**229**	**304**	**300**	**276**	**219**	**158**	**125**
CHANGE (%)	15%	288%	689%	49%	195%	32%	31%	-8%	-21%	-28%	-21%
OTHER REVENUES FROM SALES	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**
CHANGE (%)	19%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
TOTAL REVENUES (COSMO)	**102**	**125**	**216**	**407**	**442**	**566**	**534**	**510**	**377**	**271**	**234**
CHANGE (%)	57%	22%	73%	88%	9%	28%	-6%	-5%	-26%	-28%	-14%
COGS	**-40**	**-52**	**-56**	**-78**	**-125**	**-150**	**-162**	**-154**	**-118**	**-81**	**-60**
CHANGE (%)	47%	29%	39%	40%	123%	20%	29%	-5%	-24%	-31%	-26%
GROSS PROFIT	**62**	**72**	**160**	**328**	**317**	**416**	**373**	**356**	**260**	**191**	**175**
CHANGE (%)	92%	18%	120%	106%	-3%	31%	-10%	-5%	-27%	-27%	-8%
MARGIN (%)	60%	58%	74%	81%	72%	73%	70%	70%	69%	70%	75%
R&D	**-16**	**-21**	**-20**	**-11**	**-11**	**-12**	**-12**	**-13**	**-13**	**-14**	**-14**
CHANGE (%)	37%	35%	-6%	-44%	0%	5%	5%	5%	5%	5%	-2%
S,G&A	**-20**	**-20**	**-20**	**-20**	**-20**	**-20**	**-21**	**-21**	**-21**	**-21**	**-21**
CHANGE (%)	90%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
AS % OF REVENUES	19.5%	16.1%	9.3%	5.0%	4.6%	3.6%	3.8%	4.1%	5.5%	7.7%	9.0%
OTHER OPERATING INCOME / (EXPENSES)	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**
NET OPERATING EXPENSES	**-34**	**-39**	**-38**	**-29**	**-29**	**-30**	**-31**	**-32**	**-32**	**-33**	**-33**
CHANGE (%)	60%	17%	-3%	-23%	0%	2%	2%	2%	2%	2%	-1%
EBIT	**28**	**33**	**122**	**299**	**288**	**386**	**342**	**324**	**227**	**158**	**142**
CHANGE (%)	153%	18%	266%	146%	-4%	34%	-11%	-5%	-30%	-31%	-10%
MARGIN (%)	27.5%	26.7%	56.3%	73.5%	65.0%	68.1%	64.0%	63.6%	60.3%	58.1%	60.5%
EBITDA	**35**	**41**	**130**	**308**	**298**	**397**	**354**	**337**	**241**	**172**	**158**
CHANGE (%)	92%	16%	216%	137%	-3%	33%	-11%	-5%	-28%	-28%	-8%
MARGIN (%)	35%	33%	60%	76%	67%	70%	66%	66%	64%	64%	67%
SHARE OF RESULT OF ASSOCIATES	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
LOSS FROM REMEASUREMENT PREVIOUSLY HELD INVESTMENT ASSOCIATE											
NET FINANCIAL INCOME / (EXPENSES)	**-4**	**-5**	**7**	**9**	**12**	**17**	**20**	**26**	**31**	**39**	**50**
PROFIT BEFORE TAXES	**24**	**28**	**128**	**308**	**300**	**403**	**362**	**351**	**258**	**197**	**192**
CHANGE (%)	2%	15%	355%	140%	-3%	34%	-10%	-3%	-26%	-24%	-3%
TAXES	-6.968	-8	-25	-57	-64	-88	-81	-81	-58	-41	-35
TAX RATE (%)	28.5%	28.0%	19.7%	18.4%	21.4%	21.9%	22.4%	23.1%	22.5%	20.9%	18.0%
NET PROFIT/(LOSS)	**18**	**20**	**103**	**251**	**236**	**315**	**281**	**270**	**200**	**156**	**157**
CHANGE (%)	-19%	16%	408%	144%	-6%	34%	-11%	-4%	-26%	-22%	1%
MARGIN (%)	17.1%	16.3%	47.8%	61.8%	53.3%	55.7%	52.6%	52.9%	53.0%	57.5%	67.1%
PROFIT/(LOSS) PER SHARE (IN EUR)	**1.05**	**1.16**	**5.88**	**14.33**	**13.44**	**17.95**	**16.03**	**15.36**	**11.40**	**8.89**	**8.96**
PROFIT/(LOSS) PER SHARE (IN CHF)	1.04	1.15	5.86	14.29	13.40	17.90	15.98	15.31	11.36	8.86	8.93

ESTIMATES AS OF 3 MAY 2023 SOURCE: VALUATIONLAB ESTIMATES

FY 2023 guidance:

- **Total revenue:** EUR 110 mn (+7.7%) to EUR 120 mn (+17.5%)
- **Total revenue (excl. milestones):** EUR 110 mn (+41.4%) to EUR 120 mn (+54.2%)
- **Operating profit:** EUR 25 mn (-10.7%) to EUR 35 mn (+25%)

Ratios & Balance Sheet

COSMO PHARMACEUTICALS										SHARE PRICE (CHF)	54.70
IFRS											
RATIOS	**2022**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
P/E		47.4x	9.3x	3.8x	4.1x	3.1x	3.4x	3.6x	4.8x	6.2x	6.1x
P/S		7.7x	4.5x	2.4x	2.2x	1.7x	1.8x	1.9x	2.6x	3.5x	4.1x
P/NAV		2.0x	1.6x	1.1x	0.9x	0.7x	0.6x	0.5x	0.4x	0.4x	0.4x
EV/EBITDA		17.5x	5.5x	2.3x	2.4x	1.8x	2.0x	2.1x	3.0x	4.2x	4.6x
PER SHARE DATA (CHF)	**2022**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
EARNINGS	**1.04**	**1.15**	**5.86**	**14.29**	**13.40**	**17.90**	**15.98**	**15.31**	**11.36**	**8.86**	**8.93**
CHANGE (%)	-25%	10%	408%	144%	-6%	34%	-11%	-4%	-26%	-22%	1%
CASH	**14.61**	**5.80**	**13.58**	**31.62**	**49.24**	**72.76**	**94.00**	**114.63**	**130.08**	**142.11**	**153.91**
CHANGE (%)	2%	-60%	134%	133%	56%	48%	29%	22%	13%	9%	8%
DIVIDENDS	**0.95**	**1.05**	**1.17**	**1.29**	**1.44**	**1.59**	**1.77**	**1.96**	**2.18**	**2.42**	**2.69**
YIELD (%)	2%	2%	2%	2%	3%	3%	3%	4%	4%	4%	5%
NET ASSET VALUE	**28.11**	**27.51**	**33.36**	**47.65**	**61.05**	**78.94**	**94.92**	**110.23**	**121.59**	**130.45**	**139.39**
CHANGE (%)	-15%	-2%	21%	43%	28%	29%	20%	16%	10%	7%	7%
BALANCE SHEET (EUR MN)	**2022**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
NET LIQUID FUNDS	**241**	**102**	**239**	**557**	**867**	**1,281**	**1,654**	**2,018**	**2,289**	**2,501**	**2,709**
TOTAL ASSETS	**760**	**621**	**758**	**1,075**	**1,385**	**1,799**	**2,173**	**2,536**	**2,808**	**3,020**	**3,227**
TOTAL SHAREHOLDERS' EQUITY	**464**	**484**	**587**	**839**	**1,074**	**1,389**	**1,671**	**1,940**	**2,140**	**2,296**	**2,453**
- CHANGE IN %	-10%	4%	21%	43%	28%	29%	20%	16%	10%	7%	7%
- RETURN ON EQUITY	4%	4%	18%	30%	22%	23%	17%	14%	9%	7%	6%
TOTAL EQUITY	**464**	**484**	**587**	**839**	**1,074**	**1,389**	**1,671**	**1,940**	**2,140**	**2,296**	**2,453**
FINANCIAL DEBT	**174**	**156**	**141**	**127**	**114**	**103**	**92**	**83**	**75**	**67**	**61**
EMPLOYEES	295	298	301	304	307	310	313	316	319	323	326
- CHANGE IN %	*7%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*
CASH FLOW STATEMENT (EUR MN)	**2022**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
PROFIT / (LOSS) BEFORE TAXES	24	28	128	308	300	403	362	351	258	197	192
DEPRECIATION & AMORTIZATION	7	8	9	9	10	11	12	13	14	15	16
OTHER NON-CASH ITEMS	1	0	0	0	0	0	0	0	0	0	0
CASH FLOWS FROM OPERATING ACTIVITIES	**33**	**36**	**137**	**317**	**310**	**414**	**374**	**363**	**272**	**212**	**208**
CASH FLOWS FROM INVESTING ACTIVITIES	2	0	0	0	0	0	0	0	0	0	0
FREE CASH FLOW	**35**	**36**	**137**	**317**	**310**	**414**	**374**	**363**	**272**	**212**	**208**
CASH FLOWS FROM FINANCING ACTIVITIES	-46	-175	0	0	0	0	0	0	0	0	0
NET FOREIGN EXCHANGE DIFFERENCES	-2										
CHANGE IN LIQUID FUNDS	**-11**	**-139**	**137**	**317**	**310**	**414**	**374**	**363**	**272**	**212**	**208**

ESTIMATES AS OF 3 MAY 2023 — SOURCE: VALUATIONLAB ESTIMATES

Cash & cash equivalents of EUR 241 mn (31 December 2022) and sustainable cash flows is sufficient to fund all development programs and, if needed, pay back the EUR 175 mn convertible bonds in 2023.

APPENDIX

I) PARTNERSHIPS:

Cosmo has established a global sales infrastructure through strategic partnerships for almost all its major products (except for Lumeblue in the US). Cosmo commercializes its products through selective players in exchange for:

- **Equity, milestones, and royalties:** Aemcolo in the US (14.8% stake in RedHill)
- **Equity stakes and milestones:** Byfavo in the US (0.7% stake in Eagle Pharmaceuticals, which acquired Acacia in June 2022) and a 7.3% stake in PAION), with Cosmo eligible for up to EUR 105 mn sales milestones
- **Milestones and royalties:** Lialda (Shire/Takeda/Giuliani); Uceris US (Bausch Health); Cortiment ROW (Ferring); Relafalk ROW (Dr. Falk); Lumeblue EU (Alfasigma), Lumeblue China (China Medical System Holdings), Winlevi US, Japan, Australia, New Zealand, Brazil, Mexico, Russia (Sun Pharma), Winlevi Greater China (3SBio), Winlevi Germany, Italy, Austria (InfectoPharm), Winlevi Southeast Asia (Hyphens Pharma)
- **Revenue split:** GI Genius, Eleview, and all upcoming medical devices (Medtronic)

MAJOR PARTNERSHIPS

PRODUCT	INDICATION	PEAK SALES (EUR MN)	PARTNER	YEAR	REGION	TERMS
WINLEVI	ACNE VULGARIS	396	SUN PHARMA	2021	US	USD 45 MN UPFRONT PAYMENT, UP TO USD 190 MN ADDITIONAL SALES MILESTONES, DOUBLE-DIGIT ROYALTIES ON SALES, EXCLUSIVE SUPPLY AGREEMENT; EXPANDED TO JAPAN, AUSTRALIA, NEW ZEALAND, BRAZIL, MEXICO AND RUSSIA IN JULY 2022 WITH ADDITIONAL UPFRONT PAYMENT OF USD 7 MN (WE ASSUME TIERED ROYALTIES OF 15-20%, 5% MANUFACTURING REVENUE, 3% COGS)
				2022	JAPAN, AUSTRALIA, NEW ZEALAND, BRAZIL, MEXICO, RUSSIA	
			3SBIO	2022	GREATER CHINA	USD 6.5 MN UPFRONT PAYMENT, DEVELOPMENT AND SALES MILESTONES UP TO USD 63.5 MN, ASCENDING HIGH SINGLE-DIGIT OR DOUBLE-DIGIT SALES ROYALTIES; EXCLUSIVE SUPPLY AGREEMENT FOR CHINA, TAIWAN, HONG KONG, AND MACAO
			INFECTOPHARM	2022	GERMANY, ITALY, AUSTRIA	EUR 1 MN UPFRONT PAYMENT, UP TO EUR 4.5 MN REGULATORY MILESTONES, DOUBLE-DIGIT ROYATIES ON NET SALES (WE ASSUME 20% ROYALTIES AND 7% MANUFACTURING REVENUE)
			HYPHENS PHARMA	2022	SOUTHEAST ASIA	USD 1 MN UPFRONT PAYMENT, UP TO USD 4 MN REGULATORY AND SALES MILESTONES, DOUBLE-DIGIT ROYALTIES ON NET SALES
LUMEBLUE	LESION DETECTION DYE	106	ALFASIGMA	2021	EUROPE	WE ASSUME 20% NET ROYALTIES, UP TO EUR 33 MN MILESTONES
			CMS	2020	CHINA	
			TBD	2026E	US	CONCLUDE US PARTNERINGBEFORE STARTING SECOND PHASE III TRIAL; WE ASSUME 20% NET ROYALTIES, UP TO EUR 53 MN MILESTONES
			PENDOPHARM	2018	CANADA	HIGH DOUBLE-DIGIT ROYALTIES, UNDISCLOSED MILESTONES
			EA PHARMA	2018	JAPAN SOUTH KOREA	UNDISCLOSED UPFRONT PAYMENT, MILESTONES AND SALES ROYALTIES
AEMCOLO / RELAFALK	TD* / IBS-D**	422	REDHILL	2019	US	USD 36.3 MN COSMO INVESTMENT TO ACQUIRE 19.56% REDHILL STAKE; COSMO ELIGIBLE FOR HIGH 20% ROYALTIES, REGULATORY & SALES MILESTONES UP TO USD 100 MN; COSMO SUPPLIES AEMCOLO
			DR. FALK	2008	EU (EX. ITALY) & AUSTRALIA	UNDISCLOSED; WE ASSUME ~12% ROYALTIES AND ~10% MANUFACTURING REVENUE
			PENDOPHARM	2018	CANADA	HIGH DOUBLE-DIGIT ROYALTIES, UNDISCLOSED MILESTONES
GI GENIUS	AI ENHANCED COLONOSCOPY	313	MEDTRONIC	2019	GLOBAL	COSMO RETAINS NET MARGIN ABOVE 20%; COSMO SUPPLIES GI GENIUS DEVICE TO MEDTRONIC
BYFAVO	PROCEDURAL SEDATION	164	EAGLE PHARMACEUTICALS	2022	US	UP TO USD 105 MN SALES MILESTONES (NOTE: ORIGINAL AGREEMENT WAS WITH ACACIA THAT WAS ACQUIRED BY EAGLE IN JUNE 2022)
			PAION	2016	US	PAION ENTITLED TO UP TO EUR 42.5 MN MILESTONES AND TIERED ROYALTIES RANGING FROM 20% UP TO 25% FROM EAGLE
ELEVIEW	LESION RESECTION CUSHION	83	MEDTRONIC	2019	GLOBAL (EXCL. CANADA)	UNDISCLOSED; IN MAY 2021 MEDTRONIC ACQUIRED THE RIGHTS TO JAPAN AND SOUTH KOREA, WHICH EA PHARMA HELD SINCE 2018; WE ASSUME COSMO RETAINS A NET MARGIN OF AROUND 20%
			PENDOPHARM	2018	CANADA	CAD 5 MN UPFRONT; HIGH DOUBLE-DIGIT ROYALTIES, UNDISCLOSED SALES MILESTONES
UCERIS / CORTIMENT	ULCERATIVE COLITIS	75	BAUSCH HEALTH	2008	US	TIERED ROYALTIES OF 12-14% AND 10% MANUFACTURING REVENUE
			FERRING	2015	ROW (EX. ASIA)	TIERED ROYALTIES OF 12-15% AND 7% MANUFACTURING REVENUE, UNDISCLOSED MILESTONES
LIALDA / MEZAVANT	ULCERATIVE COLITIS	709	TAKEDA	2001	US	3.5% ROYALTIES (CUMULATIVE CAP OF USD 95 MN GLOBAL SALES); 3% MANUFACTURING REVENUE
		(GENERIC)	GIULIANI / LEHNER	2001	EU	
			MOCHIDA	2009	JAPAN	LOW SINGLE DIGIT ROYALTIES UP TO A CUMULATIVE TOTAL OF USD 15 MN

* TD = TRAVELERS' DIARRHEA; ** IBS-D = IRRITABLE BOWEL SYNDROME - DIARRHEA PREDOMINANT

SOURCE: VALUATIONLAB, COSMO PHARMACEUTICALS

In the US, Cosmo plans to sign on a US partner before starting the second phase III confirmatory trial required by the FDA for US approval of Lumeblue.

"Equity-for-products" stakes valued at EUR 22 mn with substantial equity upside

As can be seen in the table below, the value of Cosmo's equity-for-product stakes in its commercialization partners amounts to EUR 22 mn. Cosmo benefits from milestones and royalties of its partnered products and the long-term value creation of its partner's entire product and pipeline portfolio, which should boost the value of its equity stakes even further.

EQUITY-FOR-PRODUCT INVESTMENTS

COMPANY	YEAR	PRODUCT (INDICATION)	PARTNER RIGHTS	STATUS	PEAK SALES	STAKE (%)	VALUE (EUR MN)	COMMENT
REDHILL BIOPHARMA (ISRAEL)	2019	**AEMCOLO** (TD *)	US	MARKETED	EUR 50+ MN	14.8%	14	USD 48.3 MN CASH AND DOWN-PAYMENT FOR 19.56% STAKE; COSMO RECEIVES SALES ROYALTIES IN THE HIGH TWENTIES INCLUDING SUPPLY OF PRODUCT AND UP TO USD 100 MN SALES MILESTONES. AUG 2020: COSMO TO CO-DEVELOP NEXT-GENERATION H. PYLORI COMPOUND, EXCLUSIVE EUROPEAN RIGHTS, PAY 30% DEVELOPMENT COSTS, USD 7 MN ON SIGNING, USD 2 MN ON EU APPROVAL, 30% ROYALTIES, FUND PHASE III RHB-204, PAY USD 5 MN UPFRONT, USD 7 MN MILESTONES, 15% ROYALTIES; FEB 2021: PARTNERSHIP EXPANDED TO MANUFACTURE MOVANTIK, RHB-204 AND OPAGANIB FOR REDHILL
		AEMCOLO (IBS **)	US	PHASE IIB	EUR 350+ MN			
		TALICIA (H. PYLORI INFECTION)		*MARKETED*	*USD 100 MN*			
		*MOVANTIK (OIC***)*		*MARKETED*	*USD 350+ MN*			
		OPAGANIB (COVID-19)		*COMPASSIONATE USE*	*TBD*			
		RHB-204 (NTM^ INFECTIONS)	*GLOBAL*	*PHASE III*	*TBD*			
		NEXT-GEN H. PYLORI COMPOUND	*EU*	*NA*	*TBD*			
EAGLE PHARMA (US)	2020 / 2022	**BYFAVO** (PROCEDURAL SEDATION)	US	APPROVED: JULY 2020	EUR 150+ MN	0.7%	3	EAGLE ACQUIRED ACACIA IN JUNE 2022 THAT PREVIOUSLY ACQUIRED THE US RIGHTS FOR BYFAVO FROM COSMO IN 2020; COSMO RECEIVED FOR ITS 19.7% ACACIA STAKE EUR 13.3 MN CASH AND 96,040 NEW EAGLE SHARES (0.7% STAKE)
		BARHEMSYS (PONV^^)		*MARKETED*	*EUR 350+ MN*			
		VASOPRESSIN (VASODILATORY SHOCK)		*MARKETED*	*NA*			
		PEMFEXY (LUNG CANCER)		*MARKETED*	*NA*			
PAION (GERMANY)	2016	**BYFAVO** (SEDATION/ANESTHESIA)	US	APPROVED: JULY 2020	EUR 150+ MN	6.8%	3	EUR 10 MN UPFRONT PAYMENT FOR 9.1% STAKE; PAION ENTITLED UP TO EUR 42.5 MN MILESTONES (EUR 15 MN ON US APPROVAL); TIERED ROYALTIES FROM 20% UP TO 25% (NOW PAID BY ACACIA WHICH ACQUIRED THE US RIGHTS OF BYFAVO IN JULY 2020)
		BYFAVO (SEDATION/ANESTHESIA - ROW)			*EUR 450+ MN*			

BOLD = COSMO PRODUCTS; *ITALIC* = PARTNER KEY PRODUCTS; *TD = TRAVELERS' DIARRHEA; **IBS = IRRITABLE BOWEL SYNDROME; ***OIC = OPIOID-INDUCED CONSTIPATION; ^NTM = NONTUBERCULOUS MYCOBACTERIA; ^^PONV = POST-OPERATIVE NAUSEA AND VOMITING

ESTIMATES AS OF 3 MAY 2023 SOURCE: VALUATIONLAB ESTIMATES

Cosmo reacquired Cassiopea through a public exchange offer in December 2021

In July 2015, Cosmo spun off its dermatology franchise into the newly formed company Cassiopea, which was listed on the Swiss Stock Exchange (ticker: SKIN). Cosmo received EUR 258 mn net offering proceeds of the IPO and retained a 46.5% stake in Cassiopea to benefit from the long-term upside potential of its differentiated dermatology pipeline through for instance a trade sale or US listing.

In August 2020, Cassiopea's lead pipeline compound Winlevi (clascoterone) in acne was approved in the US to become the first topical anti-androgen on the market with global peak sales of EUR 400+ mn. Unfortunately, Cassiopea was unsuccessful in finding a potential buyer at attractive terms despite reviewing more than 20 potential term sheets. Instead, the company signed an exclusive US commercialization agreement for Winlevi with Sun Pharmaceuticals at attractive terms, including a USD 45 mn upfront payment, up to USD 190 mn commercial milestones, and customary double-digit royalties on net sales, in July 2021. Apparently, the financial markets were unfazed by the Sun Pharmaceuticals' agreement and disappointed that the value of Cassiopea was not immediately unlocked by a trade sale, leading to a decline in Cassiopea's stock price.

In an opportunistic move to unlock the value of Cassiopea, Cosmo offered to reacquire the remaining outstanding Cassiopea shares it did not own through a public exchange offer, which was successfully concluded in December 2021. As a result, Winlevi now launched for acne in the US, and Breezula soon in late-stage development for hair loss, will become important pipeline assets for Cosmo, fully contributing to its future growth.

II) CLINICAL DATA:

1) GI Genius (AI-enhanced lesion detection):

In retrospective trials, GI Genius has proven to be very accurate, with a true positive rate per polyp (sensitivity) of 99.7%, while the number of false positives frames in a full procedure (activation noise = false positives divided by the number of frames) amounted to 0.9%. In other words, the system was as good as an expert colonoscopist in detecting lesions and the extremely low number of false activations does not slow down or negatively alter the conventional colonoscopy procedure.

Positive GI Genius Investigator-Initiated trial formed the base of US approval

In February 2020, Cosmo reported positive results of the first prospective, completely independent, investigator-initiated clinical trial of GI Genius in detecting colorectal polyps. The abstract, titled "Real-Time Computer-aided Diagnosis for Detection of Colorectal Neoplasia at Colonoscopy," was presented at Digestive Disease Week (DDW) in Chicago on 4 May 2020. The trial showed that GI Genius significantly increases the Adenoma Detection Rate (ADR) and the number of Adenomas Per Colonoscopy (APC) compared to standard colonoscopy, thereby providing additional efficacy of screening colonoscopy for colorectal cancer prevention. The trial was conducted at 3 Italian hospitals and enrolled 685 patients aged 40 to 80 years undergoing colonoscopy for colorectal cancer primary screening or surveillance and was performed by highly experienced endoscopists. Patients were randomized 1:1 between High-Definition endoscopy with White Light (HDWL) colonoscopy with GI Genius and standard HDWL colonoscopy alone. The trial endpoints included the ADR and the APC according to morphology, size, site, histology, and withdrawal time (WT). A minimum WT of 6 minutes was set to ensure maximum trial quality under American and European endoscopy guidelines.

- **The ADR was significantly higher in the GI Genius group at 56.9**% than in the control group at 40.9%; OR [95% CI]: 1.9 [1.4, 2.57]; p<0.001
- **The APC was significantly higher in the GI Genius group at 1.13±1.63** compared to 0.73±1.12 for the control group; OR [95% CI]: 2.1 [1.6 to 2.72]; p<0.001

The increase in ADR has important clinical relevance. Scientific studies have shown that each 1% increase in ADR results in a 3% decline in the incidence of interval cancer and a 5% decline in the incidence of fatal colorectal cancer.

The main reason for the difference between the two groups was the performance of GI Genius in the detection of small lesions (<10 mm: 1.39±1.71 vs 1.07±1.31; p<0.0001) and flat lesions (1.8±1.9 vs. 1.19±1.5; p<0.0001). No difference in withdrawal time was observed (GI Genius: 417±101 seconds versus control group: 435±149 seconds; p=0.1).

The first US trial "DETECT" shows a 50% reduction in missed polyps with GI Genius

In March 2022, Medtronic published the results of the first US trial dubbed "DETECT" in Gastroenterology, the official medical journal of the American Gastroenterology Association (AGA). The findings confirm the topline results of the DETECT trial from November 2021 that both AMR and polyp miss rate (PMR) significantly improve when GI Genius is used during a colonoscopy. The trial showed that using GI Genius in conjunction with colonoscopy significantly decreases the miss rate (2x) of colorectal polyps and adenomas compared to standard colonoscopy. The DETECT trial was conducted in eight centers across the US, Italy, and the United Kingdom, in university hospitals and community clinics. Subjects included male and female patients aged 45 or older undergoing a screening or surveillance colonoscopy for colorectal cancer. Overall, 249 subjects were randomized (1:1) in the trial, of whom 230 subjects completed the trial and were included in the analysis, undergoing two consecutive colonoscopies that were randomly assigned in order of which they were conducted: one with GI Genius and a colonoscopy with white light endoscopy.

In colonoscopies performed as part of the trial, the adenoma miss rate (AMR) was significantly lower when GI Genius was used as compared to a non-AI-assisted colonoscopy (15.5% vs. 32.4%; p-value <0.001). These findings demonstrate that using GI Genius during colonoscopy significantly decreases the miss rate of both adenomas and polyps, further

confirming the benefit GI Genius adds to colonoscopy procedures. The trial further found that false-negative rates when a GI Genius-assisted colonoscopy detected adenoma(s) after an initial standard colonoscopy did not were much lower than that of non-AI-assisted colonoscopies (6.8% vs. 29.6%). In this trial, a false negative indicates patients with an initial standard colonoscopy where no adenoma was detected were subsequently found to have at least one adenoma during a second AI-assisted colonoscopy. Missed polyps are estimated to account for around half of all cases of post-colonoscopy colorectal cancer. They could ultimately be the difference between life and death when considering that 90% of patients with colon cancer survive when caught early.

2) LumeBlue (lesion detection dye):

Phase III trial under SPA:
Positive pivotal phase III results were announced at Cosmo's special R&D event in Zurich on November 29th, 2016. Lumeblue was compared to the current gold standard HDWL (High-Definition endoscope with White Light). The primary endpoint was the number of patients with at least one histologically proven adenoma or carcinoma or the difference in ADR (adenoma detection rate) compared to HDWL.

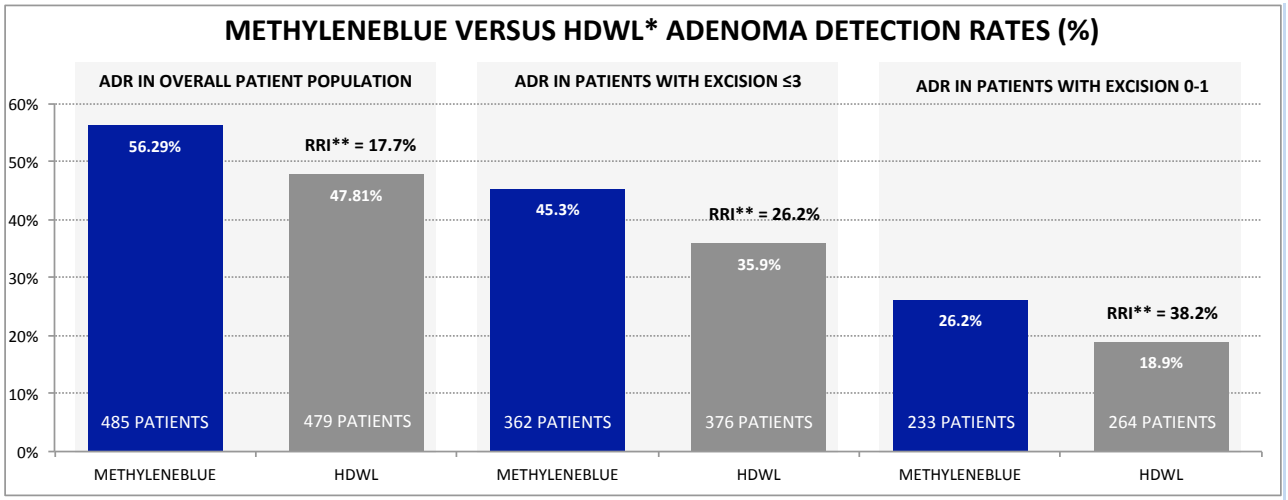
Lumeblue's pivotal phase III trial was conducted in 18 centers in 8 countries in North America and Europe. Cosmo enrolled 1,249 patients, the ITT (intent to treat) population. This resulted in a FAS (full analysis set) of 1,205 patients, a Per Protocol population (patients who completed the procedure according to the trial protocol) of 1,137 and a safety population of 1,208 patients. The endpoints were determined according to the FAS.

Due to the nature of Lumeblue, a blue-colored dye, the pivotal trial could not be blinded, which is usually needed to gain approval. It was agreed with the FDA that the trial would be randomized in three arms in a ratio of 2:1:2, a 200 mg Lumeblue + HDWL, HDWL (placebo), and 100 mg Lumeblue + HDWL confounding arm (a control group to exclude potential bias).

The patient breakdown per treatment arm FAS population:

1. **200 mg Lumeblue treatment arm:** 479 patients; 61.6% males; 47.8% first time screening colonoscopies; 6.3% surveillance colonoscopies performed < 2 years; 45.9% surveillance colonoscopies performed > 2 years from first colonoscopy
2. **HDWL (placebo) arm:** 485 patients; 60.6% males; 48% first time screening colonoscopies; 5.8% surveillance colonoscopies performed < 2years; 46.2% surveillance colonoscopies performed > 2 years from first colonoscopy
3. **100 mg Lumeblue confounding arm:** 241 patients (not statistically powered)

Two central histolabs, one in the US and one in Europe, conducted histological analysis, while five endoscopy centers were randomly assigned videos for review.
Primary and secondary endpoints were achieved across several patient populations



* HDWL = HIGH DENSITY WHITE LIGHT; ** RRI = RELATIVE RISK INCREASE

SOURCE: COSMO PHARMACEUTICALS, VALUATIONLAB

As can be seen in the chart above, Lumeblue was superior in all patient subgroups based on the FAS (Full Analysis Set) population:

- Lumeblue achieved its primary endpoint in the overall patient population, achieving a higher ADR than HDWL. Lumeblue identified 17.7% more patients with adenomas and carcinomas than HDWL, with a p-value of 0.009, indicating a highly statistically significant result
- Lumeblue was also statistically superior and clinically meaningful in the segment of patients with 0-3 excisions, where 75%-80% of the patients are. 26.2% more patients were identified with Lumeblue than with HDWL, with a high statistical p-value of 0.0107
- The largest difference in ADR was in patients with 0-1 excisions amounting to 38.2% in favor of Lumeblue.
- No major drug-related adverse events were reported

The FPR (false positive rate), an important secondary endpoint, in the Lumeblue treatment arm was 21.5% lower than in the HDWL arm, with a high statistically significant p-value of < 0.001. A false positive is a resected lesion that is initially recognized as an adenoma or carcinoma but, after histological analysis, proves not to be the case. In the Lumeblue arm, 356 out of 485 patients had an excision. 83 excisions, or 23.3%, were false positives. In the HDWL arm, 326 out of 479 patients had an excision, of which 97 excisions, or 29.7%, were false positives.

METHYLENEBLUE FLAGS MORE DIMINUTIVE ADENOMAS

	WLHD*	METHYLENE BLUE
PATIENTS WITH DIMINUTIVE ADENOMAS	144	178
PERCENTAGE OVERALL POPULATION	30.06%	36.70%
RELATIVE RISK RATE		1.221
P-VALUE		0.0342
ODDS RATIO		1.35 (1.02, 1.76)

METHYLENEBLUE FLAGS MORE NON-POLYPOID LESIONS

	WLHD*	METHYLENE BLUE
PATIENTS WITH NON-POLYPOID LESIONS	168	213
PERCENTAGE OVERALL POPULATION	35.07%	43.92%
RELATIVE RISK RATE		1.252
P-VALUE		0.0056
ODDS RATIO		1.45 (1.12, 1.88)

* WLHD = WHITE LIGHT WITH HIGH DEFINITION ENDOSCOPE

SOURCE: COSMO PHARMACEUTICALS, VALUATIONLAB

Further analysis of the pivotal trial showed that Lumeblue identified more patients with hard to detect lesions than HDWL, such as diminutive adenomas (5 mm or less in diameter) and non-polypoid (flat or depressed) lesions, as can be seen in the tables above.

Phase III trial in China:
In December 2022, positive phase III trial results of Lumeblue in China were reported, sponsored by Cosmo's partner China Medical System Holdings Limited (CMS). Lumeblue was compared to a placebo in white light colonoscopy to assess its safety and efficacy in improving histologically confirmed non-polypoid colorectal lesions in subjects undergoing screening or surveillance colonoscopy for colorectal cancer (CRC).

The phase III trial was a randomized, double-blind, placebo-controlled trial (placebo being, in this case, the standard of care) in 22 sites across China. All patients were prepped with Fortrans 3-liter split dose, two liters the day before the procedure and one liter the day of the procedure. 1,802 subjects were randomized, 897 in the Lumeblue arm and 905 in the placebo arm. Of those, 872 in the Lumeblue arm and 879 in the placebo arm were in the primary efficacy population (FAS: Full Analysis Set).

The trial met the **primary endpoint** - the detection rate of non-polypoid colorectal lesions, defined as "*the proportion of subjects with at least one histologically confirmed non-polypoid colorectal lesion*" - with very high statistical significance. In the overall FAS, the proportion of patients with at least one histologically confirmed non-polypoid colorectal lesion was significantly higher in the Lumeblue group (445/872 subjects; 51.0%) as compared with placebo (362/879, 41.2%); (adjusted OR [95% CI]: 1.55 [1.27, 1.89]; P< 0.0001). No severe side effects were reported.

The study also confirmed the superiority of Lumeblue versus placebo in several clinically meaningful endpoints (in the FAS) including the:

a) **Number of histologically confirmed non-polypoid colorectal lesions per patient:** The per-patient number of histologically confirmed non-polypoid colorectal lesions in the Lumeblue group was 0.9, as compared to 0.7 in the placebo group (difference between groups [95%CI]: 0.18 [0.07, 0.30] P=0.0022).
b) **Number of histologically confirmed non-polypoid adenomas or cancers per patient:** The per-patient number of histologically confirmed non-polypoid adenomas or cancers in the Lumeblue group was 0.6 as compared to 0.5 in the placebo group (difference between groups [95%CI] 0.12 ([0.03, 0.22] P=0.0125).
c) **Detection rate of non-polypoid adenoma or cancer (NP-ADR):** 341 out of 872 patients (39.1%) were detected with at least one histologically confirmed non-polypoid adenoma in the Lumeblue arm, as compared with 274 out of 879 patients in the placebo group (31.2%) (OR [95%CI]: 1.43 [1.17, 1.75] P=0.0004).
d) **Proportion of patients with at least one histologically confirmed <10 mm non-polypoid colorectal lesion:** Non-polypoid histologically confirmed colorectal lesions less than <10 mm were found in 415 out of 872 patients (47.6%) in the Lumeblue group versus 350 out of 879 patients (39.8%) in the placebo group (OR [95%CI] 1.43 [1.17, 1.74] P= 0.0003).
e) **Number of histologically confirmed <10 mm non-polypoid colorectal lesions per patient:** The per-patient number of histologically confirmed non-polypoid colorectal lesions <10 mm was 0.9 in the Lumeblue group versus 0.7 in the placebo group (difference between groups [95%CI]: 0.15 [0.03, 0.26] P=0.0110).
f) **Number of histologically confirmed non-polypoid adenomas or cancers <10 mm per patient:** Overall, the per-patient number of histologically confirmed non-polypoid adenomas or cancers <10 mm was 0.6 in the Lumeblue test group versus

0.5 in the placebo group (difference between groups [[95 %CI]: 0.11 [0.02, 0.20] P=0.0199).

3) Eleview (lesion resection cushion):

Eleview's pivotal trial enrolled in total 226 patients with complex lesions, of which 211 patients completed the trial according to the protocol and were used in the primary analysis set. The lesions' size and location varied greatly. The mean lesion size in the Eleview arm was 31.64 mm (ranging from 20 mm to 100 mm). The mean lesion size in the comparator arm (standard saline solution) was 32.31 mm (ranging from 20 mm to 70 mm). The location varied from the caecum (beginning of the colon) to the rectum, with the majority in the right section of the colon (typically the most difficult to reach and challenging for polyp removal).

PRIMARY ENDPOINTS ALL IN FAVOR OF ELEVIEW

PRIMARY ENDPOINT	STATISTICS	ELEVIEW (N=102)	REFERENCE COMPARATOR (SALINE) (N=109)
1) MEAN TOTAL INJECTED VOLUME TO COMPLETE EMR* PROCEDURE (ML)	**MEAN (± SD)**	**16,1 (± 9.8) ****	**31.6 (± 32.1)**
	RANGE (MIN - MAX)	3.0 - 41.0	4.0 - 248.0
	% DIFFERENCE	**-49.1% ****	
	P-VALUE	< 0.001	
2) TOTAL INJECTED VOLUME PER LESION SIZE (ML/MM)	**MEAN (± SD)**	**0.53 (±0.32) ****	**0.92 (± 0.65)**
	RANGE (MIN - MAX)	0.09 - 1.75	0.20 - 4.96
	% DIFFERENCE	**-42.4% ****	
	P-VALUE	< 0.001	
3) TIME TO RESECT THE LESION (MINUTES)	**MEAN (± SD)**	**19.15 (± 16.80) *****	**29.70 (± 69.18)**
	RANGE (MIN - MAX)	1 - 100	0.20 - 4.96
	% DIFFERENCE	**-35.5% *****	
	P-VALUE	0.326	

* EMR = ENDOSCOPIC MUCOSAL RESECTION; ** STATISTICALLY SIGNIFICANT; *** FAVORABLE NUMERICAL DIFFERENCE

SOURCE: COSMO PHARMACEUTICALS, VALUATIONLAB

1) Mean total injected volume to complete EMR procedure in the Eleview arm was 16.1 ml (range 3-41). In the comparator arm 49.2% more liquid had to be injected with the mean volume reaching 31.6 ml (range 4-248).

2) Total injected volume per lesion size was 0.53 ml per mm (range 0.09-1.75). In the comparator arm 42.4% more volume per mm was needed with the volume per lesion size reaching 0.92 ml per mm (0.2-4.96). Both these endpoints reached statistical significance (p <0.001).

3) Time to resect the lesion was notably lower in the Eleview arm with mean time taking 19.15 minutes (1-100) while it took 35.5% longer in the comparator arm taking 29.7 minutes with ranges of 2-687 minutes, therefore showing that lesion removal with Eleview took one third less time.

4) Winlevi (acne):

The phase III program consisted of three trials, including two pivotal phase III trials, one in the US ("Study 25") and one in the EU ("Study 26"), and one open-label long-term safety trial ("Study 27") where patients who have participated in the phase III trials are rolled over to evaluate long-term safety. The FDA requires at least 1,000 patients treated for safety evaluation.

Each pivotal phase III trial was a multicenter, double-blind, placebo-controlled trial evaluating ~700 patients from 9 years of age and older with moderate to severe facial acne

vulgaris (IGA grades 3 and 4) to be randomized to Winlevi 1% cream applied twice daily or placebo cream, for a treatment duration of 12 weeks. Therapeutics Inc. was selected as the CRO provider in the US, and Innopharma S.r.l. for the EU.

Primary endpoints include the:

- **Success rate in IGA score:** proportion of subjects in each treatment group achieving success defined as clear (score 0) or almost clear (score 1) and at least a two-point reduction in IGA score at week 12 compared to baseline.
- **Change from baseline in non-inflammatory lesion counts:** absolute change from baseline in non-inflammatory lesion counts in each treatment group at week 12.
- **Change from baseline in inflammatory lesion counts:** absolute change from baseline in inflammatory lesion counts in each treatment group at week 12.

Secondary endpoints include the:

- **Change from baseline in total lesion counts:** absolute change from baseline in total lesion counts for each treatment group at week 12.
- **Percentage change from baseline in total lesion counts:** percent change from baseline in total lesion counts for each treatment group at week 12.
- **Percentage change from baseline in non-inflammatory lesion counts:** percent change from baseline in non-inflammatory lesion counts for each treatment group at week 12.
- **Percentage change from baseline in inflammatory lesion counts:** percent change from baseline in inflammatory lesion counts for each treatment group at week 12.

Winlevi achieved all primary and secondary endpoints in both phase III acne trials

In July 2018, positive phase III top-line results for Winlevi in acne were announced. As can be seen in the tables below, both pivotal phase III trials, the US "Study 25" and EU "Study 26", were "on spot" (pun intended) with highly statistically significant results for Winlevi compared to placebo across all three primary endpoints as well as secondary endpoints, indicating a strong treatment effect. Importantly, no treatment-related serious side effects with Winlevi were seen in the phase III trials underlining the very clean safety profile seen in previous clinical trials.

PRIMARY ENDPOINTS (AT WEEK 12)	**STUDY 25** (US PHASE III TRIAL; N=708)							
	INTENT-TO-TREAT (ITT) POPULATION (N=708)				**PER PROTOCOL (PP) POPULATION** (N=531)			
	WINLEVI (2X DAILY)	**PLACEBO** (2X DAILY)	**IMPROVEMENT OVER PLACEBO**	**P-VALUE**	**WINLEVI** (2X DAILY)	**PLACEBO** (2X DAILY)	**IMPROVEMENT OVER PLACEBO**	**P-VALUE**
1) SUCCESS RATE IN IGA* SCORE (SUCCESS = CLEAR (SCORE O) OR ALMOST CLEAR (SCORE 1); AT LEAST TWO-POINT REDUCTION IGA SCORE)	16.1%	7.0%	130%	0.0008	20.4%	7.3%	179%	<0.0001
2) CHANGE FROM BASELINE IN NON-INFLAMMATORY LESION COUNTS (ABSOLUTE CHANGE FROM BASELINE IN EACH TREATMENT GROUP)	-19.4	-13.1	48%	0.0016	-20.0	-11.5	74%	0.0001
3) CHANGE FROM BASELINE IN INFLAMMATORY LESION COUNTS (ABSOLUTE CHANGE FROM BASELINE IN EACH TREATMENT GROUP)	-19.4	-15.5	25%	0.0029	-20.7	-16.1	29%	0.0005

* IGA = INVESTIGATOR ASSESSMENT SCORE

SOURCE: CASSIOPEA, VALUATIONLAB

As can be seen in the table above, "Study 25" demonstrated statistically significant higher improvements over placebo across all three co-primary endpoints in the ITT population (all patients who were enrolled in the trial) as well as the PP population (those patients who fully complied with the trial protocol).

PRIMARY ENDPOINTS (AT WEEK 12)	STUDY 26 (EU PHASE III TRIAL; N=732)							
	INTENT-TO-TREAT (ITT) POPULATION (N=732)				PER PROTOCOL (PP) POPULATION (N=560)			
	WINLEVI (2X DAILY)	PLACEBO (2X DAILY)	IMPROVEMENT OVER PLACEBO	P-VALUE	WINLEVI (2X DAILY)	PLACEBO (2X DAILY)	IMPROVEMENT OVER PLACEBO	P-VALUE
1) SUCCESS RATE IN IGA* SCORE (SUCCESS = CLEAR (SCORE 0) OR ALMOST CLEAR (SCORE 1); AT LEAST TWO-POINT REDUCTION IGA SCORE)	18.7%	4.7%	298%	<0.0001	22.2%	5.5%	304%	<0.0001
2) CHANGE FROM BASELINE IN NON-INFLAMMATORY LESION COUNTS (ABSOLUTE CHANGE FROM BASELINE IN EACH TREATMENT GROUP)	-19.4	-10.9	78%	<0.0001	-21.7	-11.6	87%	<0.0001
3) CHANGE FROM BASELINE IN INFLAMMATORY LESION COUNTS (ABSOLUTE CHANGE FROM BASELINE IN EACH TREATMENT GROUP)	-20.0	-12.6	59%	<0.0001	-21.5	-13.4	60%	<0.0001

* IGA = INVESTIGATOR ASSESSMENT SCORE

SOURCE: CASSIOPEA, VALUATIONLAB

A similar, albeit more pronounced effect, was seen in “Study 26”, where the placebo rates were generally lower than in “Study 25”.

SECONDARY ENDPOINTS (AT WEEK 12)	STUDY 25 (US PHASE III TRIAL; N=708)			
	INTENT-TO-TREAT (ITT) POPULATION (N=708)			
	WINLEVI (2X DAILY)	PLACEBO (2X DAILY)	IMPROVEMENT OVER PLACEBO	P-VALUE
ABSOLUTE REDUCTION OF TOTAL LESION COUNTS	-39.2	-28.9	36%	0.0002
PERCENTAGE REDUCTION OF TOTAL LESIONS COUNTS	-37.1%	-28.5%	30%	0.0016
PERCENTAGE REDUCTION OF NON-INFLAMMATORY LESION COUNTS	-30.7%	-21.9%	40%	0.0141
PERCENTAGE REDUCTION OF INFLAMMATORY LESION COUNTS	-44.8%	-36.6%	22%	0.0070

SOURCE: CASSIOPEA, VALUATIONLAB

SECONDARY ENDPOINTS (AT WEEK 12)	STUDY 26 (EU PHASE III TRIAL; N=732)			
	INTENT-TO-TREAT (ITT) POPULATION (N=732)			
	WINLEVI (2X DAILY)	PLACEBO (2X DAILY)	IMPROVEMENT OVER PLACEBO	P-VALUE
ABSOLUTE REDUCTION OF TOTAL LESION COUNTS	-40.3	-23.7	70%	<0.0001
PERCENTAGE REDUCTION OF TOTAL LESIONS COUNTS	-37.7%	-22.2%	70%	<0.0001
PERCENTAGE REDUCTION OF NON-INFLAMMATORY LESION COUNTS	-29.3%	-15.8%	85%	<0.0001
PERCENTAGE REDUCTION OF INFLAMMATORY LESION COUNTS	-47.0%	-29.8%	58%	<0.0001

SOURCE: CASSIOPEA, VALUATIONLAB

Winlevi was safe and well-tolerated with side effects similar to placebo

In “Study 25”, the percentage of TEAE (Treatment-Emergent Adverse Effects) for the Winlevi group amounted to 11.3% (40 subjects with 56 TEAE) versus 11.5% (41 subjects with 52 TEAE) for placebo. The percentage of severe, moderate, and mild TEAE for the Winlevi group was 0% (4% placebo), 21% (35% placebo), and 79% (62% placebo), respectively, with only one SAE (Serious Adverse Event) in the placebo group. Four subjects on Winlevi had 5 related AEs all (of them mild), compared to 9 with 11 for placebo; 2 of them, each with 1 AE continued treatment (application site pain, application site dryness), while 2 of them with 3 AEs withdrew from Winlevi treatment (application site hypersensitivity, oropharyngeal pain).

A similar safety and tolerability pattern were seen in “Study 26”. The percentage of TEAE for the Winlevi group amounted to 11.4% (42 subjects with 59 TEAE) versus 13.8% (50 subjects with 87 TEAE) for placebo. The percentage of severe, moderate, and mild TEAE for the Winlevi group was 0% (1% placebo), 22% (24% placebo), and 78% (75% placebo), respectively, with only one SAE in the placebo group. Eight subjects on Winlevi had 9 related AEs all of them mild, compared to 13 with 15 for placebo; 7 of them were mild and 2 moderate (acne, peritonsillar abscess): 6 of them with 7 AEs (1 subject with 2 AEs) continued Winlevi treatment (headache, eye irritation, application site hypertrichosis, moderate acne, application site dryness + erythema (same subject), moderate peritonsillar

abscess). Two of them with 2 AEs withdrew from Winlevi treatment (contact dermatitis, hair color change).

Open-label long-term "Study 27" phase III safety trial confirms excellent tolerability
In March 2019, positive results from "Study 27", the long-term open-label phase III trial of Winlevi in acne were announced, which confirmed that the drug is well tolerated with an acceptable safety profile without systemic side effects. The safety data completes the final clinical data set necessary for inclusion in the NDA (new drug application) filing for US approval. In June 2020, coinciding with acne awareness month, the renowned Journal of the American Academy of Dermatology (JAAD) published the results of "Study 27" in its online issue underlining the excellent long-term safety of Winlevi, thereby ensuring a broad range of dermatology healthcare professionals globally have access to these important safety data.

The open-label safety trial enrolled 609 patients who had completed 12 weeks of treatment of Winlevi or placebo in both positive pivotal phase III trials "Study 25" and "Study 26". Patients continued treatment for another 9 months of which 416 (safety population) received Winlevi for an overall period of at least 26 weeks and 123 subjects received Winlevi treatment for a total of 52 weeks.

- Key safety findings include: 18.1% reported TEAEs (treatment-emergent adverse events), where common cold (2.6%) and upper respiratory tract infection (1.3%) were most common, while other TEAEs had an incidence below 1%. No serious drug-related serious events occurred.
- Continued efficacy was reported in the open-label trial with the proportion of patients achieving treatment success defined as IGA (investigator global assessment) with at least a 2-step improvement resulting in 0 (clear) or 1 (almost clear) at week 52 was 56% and 62%, and 40% and 49% at week 40 for face and trunk, respectively.

5) Breezula (hair loss)"

Breezula has completed phase I and phase IIa POC trials in persons with androgenic alopecia in over 180 men and women. In 2017 Cassiopea started a phase IIb dose-ranging trial in up to 400 men with mild to moderate androgenic alopecia treated with Breezula for 12 months with an interim analysis scheduled after 6 months. In July 2018, positive interim analysis (6-months) top-line results were followed by positive topline results in April 2019 after 12 months of treatment with Breezula. Following these positive results, Cassiopea started a phase IIb dose-ranging trial of Breezula in women with alopecia in November 2019. In September 2021, topline results were reported with positive POC results only seen in a subgroup of women (under 30 years). The data will be analyzed in-depth to identify the female subgroups that would potentially benefit from Breezula treatment.

PHASE I – good penetration of the scalp without systemic-related side effects
A phase I trial was conducted on 18 subjects, 16 men and 2 women, with androgenic alopecia. A 50 milligram 5% solution of Breezula was applied twice daily to the scalp for 28 days. The results showed that Breezula: 1) penetrates the scalp and appears in the systemic circulation, with approximately 0.25% of the dosage penetrating beyond the skin to reach the circulatory system with only a diminutive 0.1 to 0.8 nanograms of the metabolite cortexolone detected per milliliter of blood plasma; 2) is well tolerated locally (LSR were mild

and transient); 3) did not cause systemic related side effects; and 4) in men did not cause a decrease in cortisol and testosterone plasma levels.

PHASE II - encouraging phase I/II POC results; positive phase IIb top-line results

A) Phase I/II POC trial: Breezula was also tested in a phase I/IIa POC trial dividing 70 male and female patients with androgenic alopecia in four different treatment groups: 1) Breezula 5% gel; 2) Breezula 1% gel; 3) cyproterone acetate 1%, as active control for men (a steroidal anti-androgen often used in men); and 4) 17α-estradiol 1% as a second active control for women (most frequently used treatment for women).

Breezula was applied to patients' scalps in gel form in five weekly sessions of hydro-electrophoresis, each lasting 20 minutes. Hydro-electrophoresis is an established method of administering drugs for alopecia treatment by dermatologists. Electrodes attached to the scalp create an electrical current that opens local skin pores. This method was chosen to ensure that Breezula and the two active controls would deeply penetrate the subjects' scalp on the same basis. Note that the final application of Breezula will involve a convenient twice-daily topical solution and not hydro-electrophoresis.

BREEZULA PHASE I/IIA POC TRIAL

PARAMETER	BREEZULA 1%			BREEZULA 5%			CYPROTERONE AC. 1%			17α-ESTRADIOL 1%		
	BASAL	T1 *	T2 **	BASAL	T1 *	T2 **	BASAL	T1 *	T2 **	BASAL	T1 *	T2 **
HAIR DIAMETER (MM)	0.41	0.73	0.88	0.66	0.74	0.91	0.51	0.61	0.74	0.53	0.65	0.73
PULL TESTS (SCORE)	3	1	1	3	1	1	3	2	2	3	1	1
WASH TEST (NR. OF HAIRS)	181	123	64	193	117	65	178	132	72	196	136	71
FOLLICULAR DENSITY (NR./CM^2)	71	89	109	73	88	111	70	82	96	74	84	98
SEBOMETRIC EVALUATION (QUALITATIVE)	HIGH	MEDIUM	LOW	HIGH	MEDIUM	LOW	HIGH	MEDIUM	LOW	HIGH	HIGH	HIGH
SUBJECTS IMPROVED (%)	-	76	85	-	79	85	-	59	66	-	61	69

* T1 = ONE WEEK AFTER TREATMENT COMPLETION; ** T2 = FOUR WEEKS AFTER TREATMENT COMPLETION

SOURCE: VALUATIONLAB, CASSIOPEA

As can be seen in the table above, Breezula in either dosage was effective in the four metrics used as endpoints for the trial: 1) hair shaft diameter increased; 2) pull test score declined; 3) follicular density improved; and 4) sebaceous gland evaluation declined to low from high. The difference in activity between the Breezula 1% and 5% dosage was slight, and no local or systemic adverse effects were reported. Generally, Breezula produced better clinical results than the active controls.

B) Phase IIa POC trial: In another phase IIa POC trial Breezula was evaluated in men with androgenic alopecia with a mean age of 40 years (ranging between 20-50 years of age) in three treatment groups: 1) Breezula 5% solution; 2) Rogaine (minoxidil) 5% solution; and 3) vehicle (placebo) solution. Safety and efficacy were evaluated after twice-daily application for up to 26 weeks. 95 men were enrolled of which 78 completed the treatment period, and 73 were included in the PPP (per-protocol population) efficacy analysis (5 men were excluded for compliance or protocol violations). The dropout rate is roughly similar across all arms and in line with other alopecia trials.

The co-primary endpoints included:

1. Changes from baseline in TAHC (target area hair count) in non-vellus hairs (thick terminal hairs) using digital image analysis at month 6
2. Patient satisfaction: the subject's evaluation of treatment benefit via the HGA (hair growth assessment) questionnaire at month 6

CHANGES FROM BASELINE IN NON-VELLUS TARGET AREA HAIR COUNT (TAHC) AT MONTH 6

	BREEZULA 5% (N=23)	MINOXIDIL 5% (N=25)	VEHICLE (N=25)	P-VALUE
PER PROTOCOL				0.0971
MEAN	12.7	18.8	2.9	-
MEDIAN	13.0	19.0	1.0	-
STANDARD DEVIATION	32.94	23.67	18.08	-
MINUMUM, MAXIMUM	-66; 86	-31; 69	-26; 50	-
PAIRED T-TEST P-VALUE	0.078	0.0006	0.4274	-

SOURCE: VALUATIONLAB, CASSIOPEA

The POC trial's topline results indicate Breezula met its two pre-defined co-primary efficacy endpoints. Given the patient sample size (~30 per group), the trial was not powered to show statistical superiority. As shown in the table above, Breezula showed evident clinical efficacy in increasing hair count. At month 6, Breezula's TAHC mean change amounted to 12.7, approaching significance with a p-value of 0.078, compared to vehicle that was not effective (p=0.4274) with a mean change of 2.9. Minoxidil showed significance (p=0.0006) in increasing hair count at month 6 with a TAHC mean change of 18.8 compared to vehicle. The magnitude of efficacy for minoxidil (difference from vehicle ~16 TAHC) was slightly higher than for Breezula (difference ~10 TAHC); however, not likely significant considering the variability of response in the small sample group. Breezula achieved a similar effect on TAHC as Propecia after only 6 months of treatment.

HAIR GROWTH ASSESSMENT (HGA) AT MONTH 6

	BREEZULA 5% (N=23)	MINOXIDIL 5% (N=25)	VEHICLE (N=25)	P-VALUE
PER PROTOCOL				0.2213
+3 = GREATLY INCREASED	1 (4.3%)	0 (0.0%)	0 (0.0%)	-
+2 = MODERATELY INCREASED	3 (13.0%)	2 (8.0%)	2 (8.0%)	-
+1 = SLIGHTLY INCREASED	5 (21.7%)	7 (28.0%)	2 (8.0%)	-
0 = NO CHANGE	8 (34.8%)	12 (48.0%)	11 (44.0%)	-
-1 = SLIGHTLY DECREASED	5 (21.7%)	1 (4.0%)	8 (32.0%)	-
-2 = MODERATELY DECREASED	1 (4.3%)	2 (8.0%)	2 (8.0%)	-
-3 = GREATLY DECREASED	0 (0.0%)	1 (4.0%)	0 (0.0%)	-

SOURCE: VALUATIONLAB, CASSIOPEA

Breezula showed positive patient satisfaction with higher HGA scores (39.1%) compared to placebo (16%), which was slightly higher than minoxidil (36%), as can be seen in the table above. This data correlates with the hair count outcomes in all treatment groups. LSRs (local skin reactions) observed at baseline and during the treatment period for all treatment groups were mostly minimal or mild and decreased over time. Importantly, no significant systemic adverse events were reported. This underlines the excellent safety and tolerability profile of clascoterone, the active pharmaceutical ingredient in Breezula and Winlevi.

Overall, the POC results indicate a favorable efficacy, safety, and tolerability profile for Breezula in alopecia with the potential of showing greater and sustained efficacy over a longer treatment period than 6 months; however, without the systemic side effects seen in oral anti-androgens such as Propecia.

C) Phase IIb dose-ranging trial: In February 2017, approval was received from the German regulator to start a single phase IIb dose-ranging trial of Breezula in men 18-55 years of age

with mild to moderate androgenic alopecia in Germany. In December 2017, enrollment was completed in 404 men who were randomized to 5 treatment arms (~80 subjects each), including Breezula 2.5%, 5%, 7.5%, and vehicle BID (applied twice daily), and Breezula 7.5% QD (once daily). Subjects were treated for a period of 12 months with an interim analysis at 6 months. The co-primary endpoints at month 12 were the same as in the POC trial and included: 1) TAHC (target area hair count); and 2) the subject's evaluation of treatment benefit via the HGA (hair growth assessment) score.

The positive 6-month interim analysis was reported in July 2018…

Positive 6-month interim results were reported for the phase IIb dose-ranging trial of Breezula in alopecia in July 2018. In its two co-primary efficacy endpoints, the interim analysis demonstrated statistically significant improvement in TAHC (Target Area Hair Count) and directional improvement for HGA (Hair Growth Assessment) after 6 months treatment of Breezula in 375 male subjects. The phase IIb 6-month interim efficacy results of Breezula in the high dose (7.5% twice daily) are already comparable to Merck & Co's oral alopecia treatment Propecia (finasteride) after 12 months of treatment. Breezula was well tolerated, and no serious treatment-related side effects were seen. Propecia has a less favorable safety profile being a systemic (oral) anti-androgen compared to the topical application of Breezula, and cannot be used by women.

BREEZULA PHASE IIB DOSE RANGING TRIAL INTERIM TOPLINE RESULTS (6-MONTHS)

PER PROTOCOL POPULATION (N=375)	BREEZULA 2.5% BID*	BREEZULA 5% BID*	BREEZULA 7.5% BID*	BREEZULA 7.5% QD**	VEHICLE
CO-PRIMARY ENDPOINTS:					
1) TAHC (TARGET AREA HAIR COUNT) MEAN CHANGE FROM BASELINE	13.0134	12.2109	20.7879	11.5182	-0.1114
P-VALUE (VS. BASELINE)	<0.0001	<0.0001	<0.0001	<0.0001	0.9660
P-VALUE (VS. VEHICLE)	0.0003	0.0010	<0.0001	0.0017	
2) HGA (HAIR GROWTH ASSESSMENT) FAVORABLE SCORE (+1, +2, +3)	56%	58%	62%	61%	49%

* BID = BIS IN DIE (TWICE DAILY); **QD = QUAQUE DIE (ONCE DAILY)

SOURCE: VALUATIONLAB, CASSIOPEA

…followed by positive 12-month phase IIb dose-ranging trial results in April 2019

Breezula demonstrated positive results across 4 dose ranges (Breezula 2.5%, 5%, and 7.5% twice daily and 7.5% once-daily versus placebo twice daily) in the two co-primary endpoints, including 1) TAHC (target area hair count) of one square centimeter at month 12 from baseline, and 2) HGA (hair growth assessment) score by a patient questionnaire at month 12 from baseline.

BREEZULA PHASE IIB DOSE RANGING TRIAL TOPLINE RESULTS (12-MONTHS)

PER PROTOCOL POPULATION (N=344)	BREEZULA 2.5% BID*	BREEZULA 5% BID*	BREEZULA 7.5% BID*	BREEZULA 7.5% QD**	VEHICLE
CO-PRIMARY ENDPOINTS:					
1) TAHC (TARGET AREA HAIR COUNT) MEAN CHANGES FROM VEHICLE	10.2	13.8	14.3	12.7	
P-VALUE (VS. VEHICLE)	0.0087	0.0006	0.0003	0.0016	
2) HGA (HAIR GROWTH ASSESSMENT) FAVORABLE SCORE (+1, +2, +3)	60.8%	60.0%	61.8%	56.1%	50.0%
SECONDARY ENDPOINT:					
TAHW (TARGET AREA HAIR WIDTH) MEAN CHANGES FROM VEHICLE	521.1	615.0	762.5	658.8	
P-VALUE (VS. VEHICLE)	0.0105	0.0034	0.0003	0.0018	

* BID = BIS IN DIE (TWICE DAILY); **QD = QUAQUE DIE (ONCE DAILY)

SOURCE: VALUATIONLAB, CASSIOPEA

- For the TAHC, statistically highly significant changes versus vehicle (placebo) were observed in all active groups, with the highest change in the Breezula 7.5% twice daily (BID) group, which reached statistical significance at all time points already

starting in the third month (first follow-up visit). In contrast, the vehicle had a decrease in TAHC, representing the progression of hair loss when left untreated.
- More patients in all active groups in the HGA score experienced increased hair growth compared to vehicle. The HGA represents the patient's opinion on hair growth based on a regular questionnaire.
- Statistically significant changes in all active groups versus vehicle were also seen in TAHW (target area hair width), a secondary endpoint, with the highest change observed in the Breezula 7.5% twice-daily group

Positive phase IIb trial results of Breezula only in a subset of women

Hair loss in women is a large untapped market that affects an estimated 50% of women over 40 years, or an estimated 30 mn women suffer from androgenic alopecia (AGA) in the US alone. Breezula's approval for female hair loss would be a key differentiator from Merck & Co's Propecia (finasteride), which cannot be used by women. Breezula is believed to address male and female AGA by directly inhibiting testosterone and DHT binding to local hair follicle androgen receptors.

Based on the positive phase IIb dose-ranging trial in men with androgenic alopecia, a phase IIb dose-ranging trial was started in Germany for Breezula in women suffering from androgenic alopecia to assess the efficacy and safety of Breezula at several doses compared to placebo and minoxidil as an active comparator. In November 2019, 293 women were enrolled aged 18-55 years experiencing androgenic alopecia. Most were Caucasian, with an average age of 40.7 years for the per-protocol population. Approximately 70 eligible women were randomly assigned to four treatment groups, including 1) Breezula 5% twice daily, 2) Breezula 7.5% twice daily, 3) active com paratorminoxidil 2% twice daily, and 4) vehicle (placebo) twice daily, with a treatment duration of 6 months.

The co-primary efficacy endpoints were:

1. Non-vellus Target Area Hair count (TAHC) change from baseline at month 6
2. Hair Growth Assessment (HGA) at month 6.

The target area is defined as one square centimeter. HGA was a trial subject self-administered questionnaire that indicated the favorability of scalp hair growth compared to baseline using a 7-point scale

In September 2021, topline results of the phase II trial were reported. Surprisingly, only a subgroup with women less than 30 years of age receiving Breezula 5% twice daily showed statistically significant differences from baseline in TAHC at month 6 (p-value = 0.0391) although the subgroup was not powered to show statistical significance. The trial was expected to achieve mixed results given the complexities of women's hair loss, which depends on age, hormonal changes, genetics, and other factors. Although the role of androgens, androgen receptors, and androgen synthesis in the skin is less clear in female AGA, some women with AGA respond to oral androgen receptor treatments, but these therapies are associated with side effects. Also, consistently with previous topical hair loss trials in female subjects treated twice-daily with solutions containing propylene glycol, a significant placebo effect was foreseen and effectively observed, and the trial was therefore expected to deliver mixed results. Also, Merck & Co's Propecia 1 mg/day in a double-blind 12-month trial did not increase hair growth or slow the progression of hair thinning in postmenopausal women with AGA.

At 6 months, the incidence of adverse events across active groups was similar. Treatment-emergent adverse events, if they occurred, were mostly minimal or mild, with the majority not deemed related to the trial drug by the investigators. The majority of women did not experience any local skin reactions. The most frequently observed local skin reactions across all treatment groups at 6 months were minimal or mild scaling, minimal erythema, or minimal pruritus. These data are consistent with previous trials of Breezula. No substantive changes in vital signs, weight or laboratory tests at 6 months were seen for any treatment group. Breezula also had encouraging results regarding favorable cosmetic acceptability and ease of use.

6) Aemcolo (travelers' diarrhea / IBS-D):

A) Travelers' diarrhea:
Aemcolo successfully completed its phase III development in 2016 when the results of two pivotal phase III with different trial designs were announced. The antibiotic demonstrated an attractive and competitive profile in travelers' diarrhea. Aemcolo has been administered in more than 600 patients in phase III alone and was well tolerated, with only 5.5% of adverse events possibly drug-related.

The first phase III trial (performed by Santarus) in 264 patients with travelers' diarrhea randomized in two treatment arms (400 mg Aemcolo versus placebo) treated for 3 days demonstrated Aemcolo's superiority compared to placebo.

- Aemcolo achieved the primary endpoint of superiority over placebo with a Clinical Cure rate (percentage of patients showing clinical symptoms remission) for Rifamycin SV of 81.4% versus 56.9% with a statistically significant p-value of 0.0008.
- The main parameter to show efficacy in travelers' diarrhea is TLUS (Time to Last Unformed Stools). TLUS was significantly shorter in Aemcolo compared to placebo.
- Aemcolo had higher microbiological eradication by pathogen than placebo.

The second phase III trial (performed by Dr. Falk) in 835 patients with travelers' diarrhea in two treatment arms (400 mg Relafalk versus 500 mg ciprofloxacin) treated for 3 days; Relafalk demonstrated non-inferiority compared to ciprofloxacin (branded Cipro by Bayer) the current standard of care in travelers' diarrhea.

- Relafalk achieved the primary endpoint of non-inferiority with a Clinical Cure Rate (percentage of patients showing clinical symptoms remission) for Relafalk of 85.0% versus 84.8% for ciprofloxacin, with a hazard ratio of ≤ 0.764 and a statistically significant p-value of 0.0018.
- Relafalk also showed good efficacy in eradicating the whole E. coli bacteria family (65.9% versus 63.7% for ciprofloxacin) and a similar failure rate to ciprofloxacin (14.8 vs. 15.2 for ciprofloxacin).
- Relafalk's TLUS in the Per Protocol Patient population was equivalent to ciprofloxacin at 33.3 hours versus 32.8 hours.
- In terms of Microbiological Cure Rate, in the patients that had a least one isolated microorganism, the efficacy was also equivalent to ciprofloxacin at 49.24% versus 49.60%.

B) IBS-D (irritable bowel syndrome – diarrhea-predominant):
In Q4 2017, Cosmo started the phase II proof-of-concept (POC) trial of Aemcolo/Relafalk in patients with IBS-D. The trial was conducted in 25 sites located in 4 West European

countries, including Belgium, Italy, Spain, and Germany. A total of 279 patients were recruited in the Intention to treat (ITT) population. The patients were randomized equally to three treatment arms, including placebo and two doses of Relafalk: 600 mg Relafalk 2x daily and 600 mg Relafalk 3x daily, for a treatment duration of 2 weeks. The trial investigated the lasting treatment effects during a 3-months follow-up period. The primary endpoint was the proportion of patients who achieved success, defined as an adequate relief of both abdominal pain and diarrhea at the end of the first week of treatment (at least a 30% decrease in pain score and at least a 50% reduction in the number of days per week with diarrhea). Other endpoints included a reduction in bloating, improved stool consistency, decreased sense of urgency, and improvement in quality of life as assessed through the IBS QoL questionnaire.

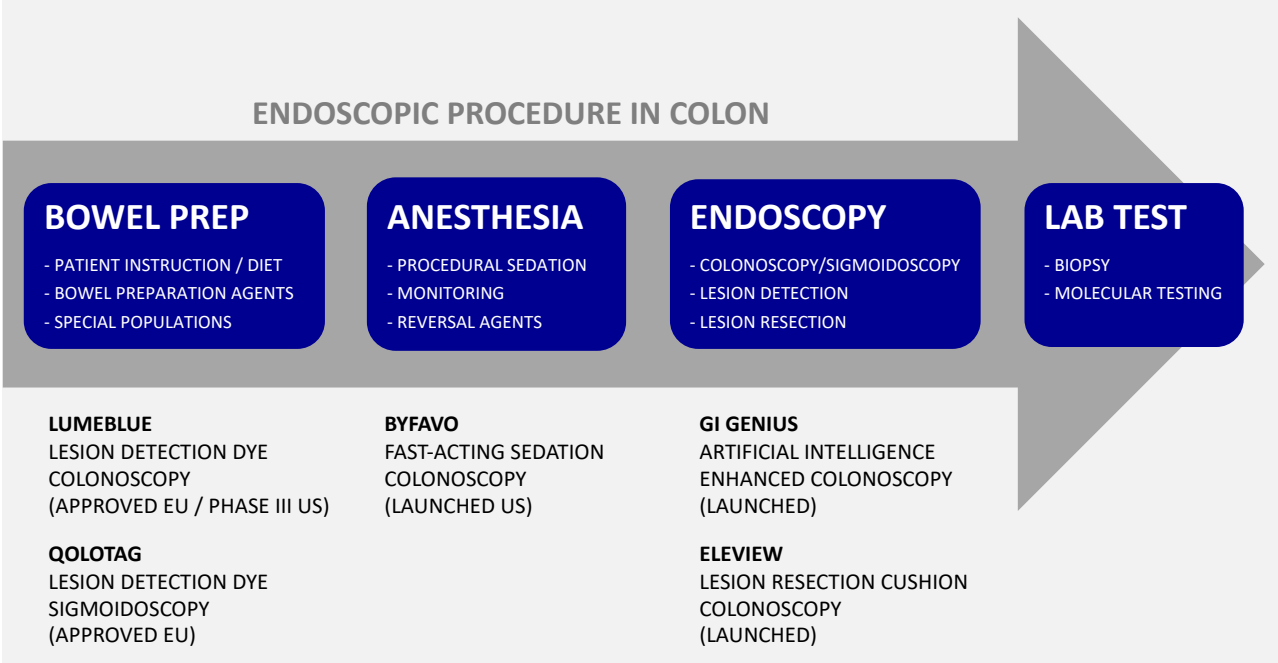
Positive POC results reported in 2021 after a significant delay due to the pandemic

Positive topline results were reported in January 2021. The trial was very successful, notwithstanding the decision by Cosmo to reduce the envisaged patient number by 20% due to COVID-19 restrictions. The results show the achievement of statistical significance in all the trial populations, including ITT, Full Analysis Set (FAS), modified-FAS, and Per Protocol (PP) population for the composite primary endpoint (substantial pain and diarrhea decrease) [OR 3.26 (1.39 – 7.67); p-value 0.0066], and for most secondary endpoints such as adequate relief of IBS-related symptoms [OR 2.18 (1.12 – 4.26); p-value 0.0227], and IBS-related bloating at the end of the treatment period [OR 2.13 (1.11 – 4.07); p-value 0.0223].

III) ENDOSCOPY BUSINESS:

Cosmo's endoscopy/colonoscopy pipeline products are targeted to reduce the risk of colorectal cancer by improving the outcomes of preventive colonoscopy screening with better detection of lesions in the colon such as precancerous adenomas and polyps (**GI Genius, Lumeblue**, **Qolotag**), safer and faster removal of adenomas and polyps (**Eleview**) and faster sedation and recovery times (**Byfavo**).

COMPREHENSIVE PORTFOLIO FOR ENDOSCOPY IN COLON



SOURCE: GASTRO HEALTH; VALUATIONLAB

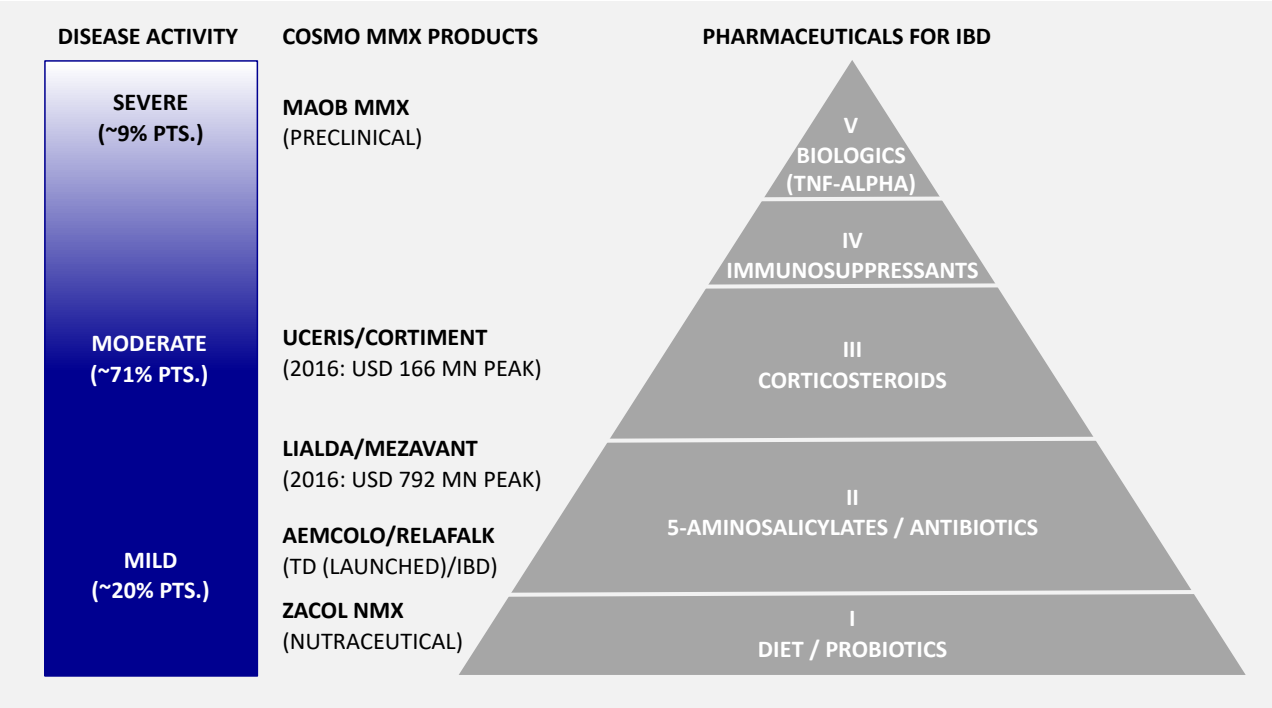
A **colonoscopy** is often used as an effective screening test for colorectal cancer, which reduces the risk of death from colorectal cancer by more than 50% due to the early detection and removal of adenomas and polyps. It is recommended that people of average risk get a colonoscopy or other type of screening every 10 years starting at age 50. According to the American Cancer Society, people at high risk should begin screening earlier and sometimes more often. The patient must have an empty bowel. A restricted diet refraining from solid foods at least 24 hours before the procedure is required. Bowel preparation agents are given to cleanse and empty the bowel. During the colonoscopy procedure, the patient is sedated and monitored by an anesthetist. The physician uses a flexible tube with a camera and light on it – a flexible endoscope - to examine the rectum and the inside of the full length of the colon. If something suspicious is found, such as an adenoma or polyp, these will be removed, often with a wire loop or burning with an electrical current. A sample for biopsy will be taken and sent to the lab to determine the tissue type and to detect any cancer. After the colonoscopy, the patient will be given time to recover from the sedation. A colonoscopy typically takes about 20 minutes to an hour and another hour to recover from the sedative. An alternative to colonoscopy is a so-called **sigmoidoscopy**, which is less invasive than a colonoscopy. A sigmoidoscopy only examines up to the sigmoid, from the rectum to the last part of the colon, while a colonoscopy examines the entire colon. Sedation is not required. Here too, the bowel must be fully emptied through a laxative and an enema (a liquid solution that washes out the intestines) prior to the procedure. The procedure takes 10-20 minutes and is often used to find the cause of diarrhea, abdominal pain, or constipation.

IV) GASTROINTESTINAL BUSINESS:

A) Inflammatory Bowel Disease

Cosmo has built a comprehensive drug portfolio for treating IBD (inflammatory bowel disease), a group of inflammatory conditions of the colon and small intestines. IBD is a complex disease which arises as a result of the interaction of environmental and genetic factors leading to immunological responses and inflammation in the intestine. Crohn's disease and ulcerative colitis are the principal types of IBD. Ulcerative colitis primarily affects the colon and rectum, while Crohn's disease primarily affects the small and large intestine but also the mouth, esophagus, stomach, and anus. Despite Crohn's disease and ulcerative colitis being very different diseases, both may present with any of the following symptoms: abdominal pain, vomiting, diarrhea, rectal bleeding, severe internal cramps/muscle spasms in the region of the pelvis, and weight loss.

COMPREHENSIVE PORTFOLIO FOR INFLAMMATORY BOWEL DISESE



SOURCE: HENDRIKSEN C, KREINER S, BINDER V, GUT 1985; D'HAENS GR, ET AL. LANCET 2008; VALUATIONLAB

Cosmo aims to cover every step in treating IBD

Cosmo aims to cover all disease stages and drug treatment steps in IBD, in particular in ulcerative colitis, through compounds utilizing its proprietary MMX technology platform.

The first step in treating mild ulcerative colitis is with dietary supplements and probiotics. Cosmo offers its dietary supplement **Zacol NMX**, a so-called nutraceutical that uses an amended form of the MMX technology. Zacol NMX is a relatively small product, largely sold in Italy, and is being rolled out in selected Eastern European countries. Zacol NMX sales have not been disclosed, yet.

The second step in treating ulcerative colitis when it progresses to mild-to-moderate disease is with prescription drugs that belong to the aminosalicylates or so-called 5-ASA. **Lialda/Mezavant** (mesalamine MMX), has the highest amount of mesalamine per tablet and was approved for mild-to-moderate ulcerative colitis in 2007, initially for induction, and in

2011 for maintenance of remission, a larger indication area. Sales of Lialda/Mezavant peaked at USD 792 mn in 2016 before cheap generics entered the market.

The third step in mild-to-moderate disease is treatment with (systemic) corticosteroids such as prednisone. These drugs have been used reluctantly due to severe side effects, despite being more effective than 5-ASAs in inflammatory bowel diseases, such as Crohn's disease. Cosmo's locally acting **Uceris/Cortiment** (budesonide MMX) was approved in the US in 2013 and the EU in 2014 for induction of remission. Thanks to the MMX technology, the drug has a clean side effect profile and therefore has the potential to also be used for maintenance of remission. Peak sales forecasts have been severely affected due to the "at-risk" launch of Actavis' generic version of Uceris in the US in July 2018, offsetting increasing sales of Cortiment sales by Ferring outside the US.

The fourth and fifth step in moderate-to-severe ulcerative colitis patients, who do not respond to standard treatments, is treatment with immunosuppressants (e.g., thiopurines) or biologicals (e.g., TNF-alpha inhibitors such as Humira). Cosmo has **CB-01-12/MOAB MMX** (antibody TNF-alpha inhibitor) a biological in preclinical development as an oral "bio-better" in a strategic partnership with AIMM Therapeutics, a therapeutic antibody company based in Amsterdam, the Netherlands. Cosmo acquired a 6.48% stake in AIMM Therapeutics when they started the strategic partnership in 2012.

B) Colon infections – new antibiotics are needed to fend off bacterial resistance

Gastrointestinal infections are viral, bacterial, or parasitic infections that cause gastroenteritis, an inflammation of the gastrointestinal tract involving both the stomach and the small intestine, or cause colon infections where the colon is primarily affected. These infections are quite common. Symptoms include diarrhea, vomiting, and abdominal pain. Dehydration is the main danger of gastrointestinal infections. Most gastrointestinal infections are self-limited and resolve within a few days. However, in a hospital setting and specific populations (newborns/infants, immunocompromised patients, or elderly populations), they are potentially serious. Rapid diagnosis, appropriate treatment, and infection control measures are therefore particularly important. In the case of gastrointestinal infections caused by bacteria, increasing bacterial resistance against current treatments is a major concern, making these antibiotics redundant. Novel antibiotics are needed to supplement or replace current treatments.

Aemcolo/Relafalk has promise in several bacterial infections of the colon

Cosmo's Aemcolo/Relafalk (rifamycin SV MMX) is a reformulation of the generic broad-spectrum antibiotic rifamycin using Cosmo's MMX technology. The MMX technology allows the antibiotic to be delivered directly into the colon, avoiding unwanted effects on beneficial bacterial flora living in the upper gastrointestinal tract. The compound is being developed for travelers' diarrhea and IBS-D (irritable bowel syndrome – diarrhea predominant), two common colon infections affecting millions of people globally. The antibiotic received US and EU approval for travelers' diarrhea in November 2018 with the first launches occurring in 2019. In the US, Aemcolo received QIDP (Qualified Infectious Disease Product) and Fast Track designations for travelers' disease, which underlines the importance of treating colon infections with new chemical entities due to the increasing rise in antibiotic resistance. Aemcolo is eligible for an additional five years of market exclusivity and priority review (6 months instead of 10-12 months) in the US. patients A phase II trial in IBS-D patients started at the end of 2017 and is still enrolling.

V) DERMATOLOGY BUSINESS:

Winlevi (acne) and Breezula (alopecia) originate from Cosmo
Cosmo's two most advanced clinical development projects, Winlevi for treating acne, and Breezula for treating alopecia, contain the same NCE (new chemical entity) and API (active pharmaceutical ingredient) clascoterone a novel anti-androgen that stems from Cosmo. In March 2012, Cosmo granted Medicis exclusive worldwide rights to Winlevi and Breezula. Following the acquisition of Medicis by Valeant Pharmaceuticals (now Bausch Health), Cosmo reacquired global rights from Valeant in July 2014. Bausch Health has a right-to-first refusal if Cosmo (previously Cassiopea) licenses Winlevi or Breezula to a third party in the US or Canada. This right was waived for Winlevi, with Sun Pharma acquiring the exclusive rights in July 2021.

CB-06-01 (acne) and CB-06-02 (genital warts) have been in-licensed by Cosmo
In March 2014, Cosmo acquired the worldwide rights to all dermal applications of CB-06-02 (formerly AS 101), except for alopecia, from the Israeli company BioMAS. Cosmo paid a license fee of USD 1 mn and will pay for all development costs. If CB-06-02 is approved, BioMAS is entitled to a high single-digit royalty on net sales when marketed directly by Cosmo. BioMAS is entitled to a double-digit royalty out of the sub-license revenues if sublicensed. The worldwide rights to CB-06-01 (formerly NAI-acne) were acquired by Cosmo from the Italian company Naicons in February 2015. Cosmo paid a fee of EUR 150,000, agreed to pay milestones in an aggregate amount in the single-digit Euro millions, and will also pay a single-digit royalty on sales. Further R&D is needed before Cosmo decides to go forward with these compounds. The development of CB-06-02 in genital warts might be dropped due to the success of several HPV vaccines.

Ideally positioned to capitalize on new single-product fixed-combinations
Cosmo is ideally positioned to capitalize on next generation single-product fixed-combinations with its attractive product pipeline consisting of three novel NCE's. Almost all the recent market entries have been single-product fixed-combinations, such as Galderma's Epiduo (adapalene and benzoyl peroxide combination) for treating acne with sales of USD ~360 mn in 2014. For instance, Winlevi could be combined with Cosmo's own novel topical antibiotic CB-06-01, or with generic benzoyl peroxide, erythromycin or clindamycin. Such a next generation single-product fixed-combination has possible benefits in terms of efficacy, patient convenience and compliance, and pricing. Moreover, next generation combination products have the potential to extend the life cycle of Cosmo's NCE's substantially beyond our current patent timelines with considerable upside to the company's long-term potential. Additionally, the company could benefit from a line extension of Winlevi at a higher dosage strength formulation given the excellent safety profile and tolerability.

The overall lack of innovation in the research and development of new dermatology products resulted in a limited number of effective treatments in this area. For instance, the three mechanisms of action (MOAs) most used to treat acne have been available for over 30 years. As a result, the few truly innovative therapies launched over the past few decades have resulted in significant sales. With relatively short clinical development timelines, development costs for dermatology drugs are relatively contained. The relatively low number of dermatologists (<14,000) in the US allow for a small and dedicated field force to commercialize and maximize the value of these drugs.

VI) DISEASE MARKETS

Colorectal cancer diagnostic market

We conservatively estimate that globally, at least USD 60 bn is spent annually on colonoscopies alone, of which roughly USD 4.8 bn is spent on endoscopes, catheters, bowel cleansing preparation, et cetera. A sizeable portion can be attributed to colorectal cancer screening. This market is set to grow due to the aging of the population, colorectal cancer screening programs, and new diagnostics entering the market.

COLON CANCER DIAGNOSTIC MARKET - KEY FACTS	
MARKET SIZE	USD ~60 BN (USING AVERAGE COST OF A COLONOSCOPY)
NUMBER OF COLONOSCOPIES	~60 MN GLOBALLY; ~14 MN US, ~25 MN EU/JAP
MAIN GOAL	TO IDENTIFY AND REMOVE ALL POLYPS AND ADENOMAS GROWING IN THE COLON, INCLUDING THOSE IN EARLY STAGE (WITH FLAT MORPHOLOGY AND SMALL SIZE) AS THESE ARE ALL PRECURSORS OF COLON CANCER.
TARGET POPULATION / RISK FACTORS	- OLDER THAN 50 YEARS (ABOUT 90% OF COLON CANCER PATIENTS ARE OLDER THAN 50) AT RISK POPULATION: - PATIENTS WITH ULCERATIVE COLITIS - PATIENTS WITH CROHN'S DISEASE - AFRICAN AMERICAN RACE - A PERSONAL OR FAMILY HISTORY OF COLON CANCER OR POLYPS - OBESITY, PHYSICAL INACTIVITY, SMOKING, HEAVY ALCOHOL USE, DIET HIGH IN RED MEATS
AMERICAN CANCER SOCIETY GUIDELINES EARLY DETECTION OF CANCER	ALL PEOPLE 50 OR OLDER SHOULD FOLLOW ONE OF THE TESTING SCHEDULES: 1) TESTS THAT FIND POLYPS AND CANCER: - FLEXIBLE SIGMOIDSCOPY (EVERY 5 YEARS) - COLONOSCOPY EVERY (10 YEARS) - DOUBLE CONTRAST BARIUM ENEMA (EVERY 5 YEARS) - VIRTUAL COLONOSCOPY - CT SCAN (EVERY 5 YEARS) 2) TESTS THAT PRIMARILY FIND CANCER: - FBOT - FECAL OCCULT BLOOD TEST (EVERY YEAR) - FIT - FECAL IMMUNOCHEMICAL TEST (EVERY YEAR) - SDNA - STOOL DNA TEST (EVERY YEAR - NOT YET APPROVED IN US)
DIAGNOSTICS	INVASIVE DIAGNOSTICS: - COLONOSCOPY (ENDOSCOPE COVERS ENTIRE COLON - STANDARD OF CARE DIAGNOSTIC) - SIGMOIDOSCOPY (SHORTER ENDOSCOPE, COVERS ONLY 1/3 OF COLON) - CHROMOENDOSCOPY (COLONOSCOPY WITH IMAGE ENHANCING CAPABILITIES) - ARTIFICIAL INTELLIGENCE (AI) ENHANCED COLONOSCOPY LESS-INVASIVE DIAGNOSTICS: - DOUBLE-CONTRAST BARIUM ENEMA (X-RAY WITH CONTRAST MEDIA) - FECAL OCCULT BLOOD TEST (MICROSCOPIC TRACES OF BLOOD IN STOOL) - VIRTUAL COLONOSCOPY (MRI OR CT SCAN) - STOOL DNA TEST (IDENTIFY DNA MARKERS IN STOOL) - UNDER REVIEW - SEPTIN-9 TEST (BLOOD-BASED DNA MYELATION TEST) - UNDER REVIEW NOTE: WHEN LESS-INVASIVE TESTS ARE POSITIVE, THE PATIENT NEEDS A COLONOSCOPY TO CONFIRM FINDINGS AND REMOVE POLYPS OR ADENOMAS
DIAGNOSTIC (MAJOR PLAYERS)	- ENDOSCOPES (OLYMPUS, PENTAX, FUJINON, STRYKER, ENDOMED, WELCH ALLYN) - MRI/CT SCANS (PHILIPS, GENERAL ELECTRICS, SIEMENS, 3M, HITACHI, TOSHIBA) - CONTRAST MEDIA (BAYER, BRACCO, COVIDIEN) - CHROMOENDOSCOPY (COSMO WITH METHYLENEBLUE (FILING), VALEANT/PHOTOCURE WITH LUMACAN (PHASE I/II)) - STOOL DNA TEST (EXACT SCIENCES) - BLOOD-BASED MYELATION TEST (EPIGENOMICS WITH EPI PROCOLON) - AI ENHANCED COLONOSCOPY (MEDTRONIC / COSMO WITH AI SMART BOX)

SOURCE: VALUATIONLAB, NIH, WHO, MAYO CLINIC, ACS, COMPANIES

Colorectal cancer is the third most common cancer diagnosed in the US. The American Cancer Society estimates that annually there are >100,000 new cases of colon cancer and >40,000 new cases of rectal cancer. Only 65% of the target population gets screened. The goal is to raise this to 80% by 2018 (National Colorectal Cancer Roundtable). Regular colorectal screening is one of the most powerful and cost-effective weapons for preventing colorectal cancer. Screening is the process of looking for cancer or pre-cancer in people who have no symptoms of the disease. Before cancer develops, a growth of tissue or tumor usually begins as a non-cancerous "polyp" on the inner lining of the colon or rectum. The chance of changing into cancer depends upon the type of polyp:

- **Adenomas** are polyps that can change into cancer. Because of this, adenomas are called a pre-cancerous condition.

- **Hyperplastic and inflammatory polyps**, in general, are not pre-cancerous. But some doctors think this may be a first sign of a greater risk of developing adenomas, particularly when they appear in the ascending colon.

Dysplasia is another kind of pre-cancerous condition. These are cells in the lining of the colon or rectum where the cells appear abnormal (but not like true cancer cells). Dysplasia is usually seen in people with ulcerative colitis or Crohn's disease for many years, which causes chronic inflammation of the colon. From the time the first abnormal cells start to grow into polyps, it usually takes about 10-15 years for them to develop into colorectal cancer, often with no symptoms. Regular screening can, in many cases, prevent colorectal cancer altogether because most polyps can be found and removed before they turn into cancer. Screening can also result in finding colorectal cancer early when it is highly curable. Early-stage (I) CRC has a 74% 5-year survival rate vs. 6% in late-stage (IV) cancer.

Screening can be divided into two broad groups:

1) Tests that find both polyps *and* cancer. The preferred tests look at the structure of the colon itself to find abnormal areas. This is done either with a scope inserted into the rectum or with special imaging tests (X-ray/CT scan). Polyps found before they become cancerous can be removed to prevent colorectal cancer. Tests include flexible sigmoidoscopy, colonoscopy, double-contrast barium enema (X-ray), and CT colonography (virtual colonoscopy).

2) Tests that mainly find cancer. These test the stool (feces) for signs that cancer may be present and include fecal occult blood test (FOBT), fecal immunochemical test (FIT), and stool DNA test (sDNA). These tests are less invasive and easier to do but are less likely to detect polyps. Furthermore, when polyps or cancer is detected, patients are referred to colonoscopy to confirm the diagnosis and to remove the polyps.

New colon diagnostics expected to improve the early detection of colorectal cancer

Several companies are developing new approaches to detecting colorectal cancer or enhancing the detection of polyps and lesions. Epigenomics has developed a new blood-based DNA technology branded **Epi ProColon** (septin 9 test). Exact Sciences has a stool-based DNA technology branded **Cologuard** that detects polyps and cancer in feces. A positive result from both tests will require a follow-up colonoscopy. Cosmo is at the forefront of AI-enhanced colonoscopy with **GI Genius**, which Medtronic commercializes globally. The first launches occurred in the EU in 2019, followed by the US in 2020.

Cosmo and Photocure are developing image-enhancing agents for use in detecting cancerous and pre-cancerous lesions during so-called chromoendoscopy. Cosmo's **Lumeblue** is a novel oral MMX formulation of methylene blue that has proven to enhance the detection of lesions but has not been used frequently in its current liquid form as a "messy" and time-consuming spray. The FDA surprisingly turned down US approval of Lumeblue in 2018, with Cosmo required to perform a second confirmatory trial, delaying US approval to 2026. EU approval occurred in August 2020, with the first EU launch occurring in 2022, significantly delayed by the COVID-19 pandemic. Photocure is developing an oral photodynamic (fluorescence) colorectal diagnostic called **Lumacan**, initially designed to be given by an enema. Lumacan contains hexamiolevulinate and is already on the market in the US and Europe to detect bladder cancer. Lumacan is in phase I/II development.

Acne Prescription Drug Market

Over the past few years, demand for acne treatments and medications surged remarkably. Persistence Market Research estimates that the global acne treatment market amounted to USD 4.9 bn in 2016 and is expected to reach USD 7.4 bn by the end of 2025, reflecting a CAGR of 4.6% over the forecast period (2017 – 2025). The inflammatory acne segment is the largest acne type segment in the global acne treatment market, which is estimated at just over USD 3 bn, or around 60% share of the total market in 2017. It is expected to increase to over USD 4.5 bn by 2025, growing at a CAGR of 5% over the forecast period. Nevertheless, no new chemical entity has been launched since the mid-1990s (e.g., topical retinoids Differin (adapalene) and Tazorac (tazarotene)).

ACNE - KEY FACTS	
MARKET SIZE	USD 4.9 BN IN 2016 AND EXPECTED TO GROW TO USD 7.4 BN BY THE END OF 2025
PREVALENCE	AFFECTS: 9.4% OF POPULATION (~650 MN PEOPLE GLOBALLY); ~85% OF PEOPLE AGED 12-25 YEARS, 8% OF ADULTS AGED 25-34 YEARS, 3% OF ADULTS AGED 35-44 YEARS; MORE PREVALENT IN MEN THAN WOMEN; MORE PREVALENT IN WESTERN COUNTRIES
INCIDENCE	85% OF ADOLESCENTS DEVELOP MILD ACNE; 15-20% HAVE CLINICAL ACNE RANGING FROM MILD TO SEVERE; AFFECTS 40-50 MN PEOPLE ANNUALLY IN THE US
UNDERLYING CAUSE	GENETICS IS THOUGHT TO BE THE PRIMARY CAUSE OF ACNE IN 80% OF CASES. DURING PUBERTY ACNE OFTEN OCCURS BY AN INCREASE IN HORMONES SUCH AS TESTOSTERONE. A FREQUENT FACTOR IS EXCESSIVE GROWTH OF THE BACTERIUM P. ACNES, WHICH IS NORMALLY PRESENT ON THE SKIN. FOUR MAIN PROCESSES THAT LEAD TO THE FORMATION OF ACNE LESIONS: 1) SEBORRHEA: INCREASE OF OILY SEBUM PRODUCTION (INFLUENCED BY ANDROGENS) 2) OBSTRUCTION: EXCESSIVE DEPOSITION OF KERATIN (COMEDO FORMATION) 3) INFECTION: COLONIZATION OF THE FOLLICLE BY BACTERIA (PROPIONIBACTERIUM ACNES) 4) INFLAMMATION: LOCAL RELEASE OF PRO-INFLAMMATORY CHEMICALS IN THE SKIN
SYMPTOMS	- INCREASED SECRETION OF OILY SEBUM BY THE SEBACEOUS GLANDS IN THE SKIN - MICROCOMEDONES, COMEDONES, PAPULES, NODULES (LARGE PAPULES), PUSTULES - ACNE SCARS (LESIONS) CAUSED BY INFLAMMATION WITHIN THE DERMAL LAYER OF THE SKIN - POSTINFLAMMATORY HYPERPIGMENTATION (DARKENED MARK ON SKIN)
DRUG CLASS (KEY BRANDS)	- ORAL RETINOID (E.G. ACCUTANE) - TOPICAL RETINOID (E.G. TAZORAC, DIFFERIN) - ORAL ANTI-ANDROGEN (E.G. SPIRONOLACTONE, CYPROTERONE ACETATE, FLUTAMIDE, BIRTH CONTROL PILLS) - TOPICAL ANTIBIOTIC (E.G. BENZAMYCIN, EMGEL, MINOCYCLINE, DAPSONE) - ORAL ANTIBIOTIC (SOLODYN) - BENZOYL PEROXIDE (EPIDUO, DUAC, BREVOXYL, BENZACLIN, TRIAZ)
MAJOR PLAYERS (KEY BRANDS)	- ROCHE (ACCUTANE) - VALEANT (SOLODYN) - ALLERGAN (TAZORAC, ACZONE) - GALDERMA (EPIDUO) - STIEFEL (DUAC)

SOURCE: VALUATIONLAB, NIH, WHO, AAD, BRITISH J. OF DERM., WEBMD

Acne, also known as acne vulgaris, is a long-term skin disease that occurs when hair follicles are clogged with dead skin cells and oil (sebum) from the skin. Acne is characterized by blackheads or whiteheads (comedones), pimples, oily skin, and possible scarring (acne lesions). It primarily affects areas of the skin with a relatively high number of oil (sebaceous) glands, including the face, upper part of the chest, and back. The resulting appearance can lead to anxiety, reduced self-esteem, and, in extreme cases, depression or thoughts of suicide. Acne is a very common problem, particularly during puberty in teenagers, where 85% develop acne, but it can occur at later stages of life. Approximately 20% of teenagers suffer from moderate-to-severe acne. Acne is more prevalent in men than in women and more prevalent in Western countries. It affects ~650 mn people globally (~9.4% of the population), making it the 8th most common disease worldwide.

Four main processes lead to the formation of acne lesions:

1. **Seborrhea:** increase of oily sebum production (influenced by androgens)
2. **Obstruction:** excessive deposition of keratin (comedo formation)
3. **Infection:** colonization of the hair follicle by the bacteria Propionibacterium acnes
4. **Inflammation:** local release of pro-inflammatory chemicals in the skin

Genetics is thought to be the primary cause of acne in 80% of cases. During puberty, in both sexes, acne is often brought on by an increase in androgens (hormones) such as testosterone and its derivative dihydrotestosterone (DHT) which increase the production of oily sebum. This leads to the formation of a plug (microcomedone), which is driven primarily by excessive growth, reproduction, and accumulation of skin cells in the hair follicle. The oily sebum causes the dead skin cells to stick together and block the hair follicle. A frequent factor is an excessive growth of the bacterium Propionibacterium acnes (P. acnes), which is normally present on the skin, and also provokes skin inflammation by altering the fatty composition of oily sebum. The inflammatory cascade typically leads to the formation of inflammatory acne lesions, including papules, infected pustules, or nodules. If the inflammatory reaction is severe, the follicle can break into deeper layers of the skin and cause the formation of deep nodules.

The severity of acne can be classified as:

- **Mild:** the presence of comedones limited to the face with occasional inflammatory lesions (papular/pustular)
- **Moderate:** a higher number of inflammatory papules and pustules occur on the face than in mild acne and are found on the trunk of the body
- **Severe:** when nodules (painful bumps lying under the skin) are the characteristic facial acne lesions and involvement of the trunk is extensive

Current acne treatments are limited to reformulations of existing chemical entities

Many treatment options for acne are available, including lifestyle changes, medications, and medical procedures. Most treatments are based on reformulations or combinations of existing chemical entities with little innovation. Prescription treatments for acne include drugs that target the four main processes that lead to the formation of acne: 1) Seborrhea: drugs that target the blocking of the sebaceous gland (e.g. oral anti-androgens such as spironolactone, low dose oral corticosteroids, estrogens such a birth control pills, or isotretinoin; 2) Obstruction: drugs that normalize pattern of follicular keratinization (e.g. adapalene, isotretinoin, tazarotene, tretinoin); 3) Infection: topical and oral antibiotics (e.g. benzoyl peroxide, minocycline); and 4) Inflammation: anti-inflammatory drugs (e.g. intra-lesional and oral corticosteroids, NSAIDS).

The American Academy of Dermatology guidelines recommends treatment should target as many pathogenic factors as possible. Treatment is dependent on the severity of acne and whether inflammation is involved. In mild acne, the first treatment choice is a topical retinoid when no inflammation is involved or combined with a topical antimicrobial when there is inflammation. In moderate acne, an oral antibiotic is often added on top of the topical retinoid, sometimes combined with benzoyl peroxide. In the case of nodules, oral isotretinoin can be given. In severe acne oral isotretinoin is the first choice. Maintenance therapy consists of a topical retinoid in mild acne and a topical retinoid +/- benzoyl peroxide.

New market entrants expected to boost growth

Promising late-stage drugs in development for moderate to severe acne include Paratek/Allergan's **Seysara** (sarecycline), an oral, narrow-spectrum tetracycline-derived antibiotic (approved 2018); Foamix Pharmaceuticals' **AMZEEQ**, a topical foam reformulation of minocycline, an existing oral antibiotic (approved 2019), and Cassiopea's **Winlevi**, a novel anti-androgen called clascoterone (launched in the US by Sun Dermatology in early November 2021), and **CB-06-01**, a novel topical antibiotic (phase II).

Androgenic Alopecia Market

Androgenic alopecia is the most common type of hair loss. In the US alone, an estimated 35 mn men and 21 mn women experience hair loss. Statista estimates that the value of the non-surgical alopecia treatment market worldwide amounted to USD 2 bn in 2010 and is expected to increase to around USD 2.8 bn by 2017. Hair restoration surgery is a more invasive but relatively common treatment for alopecia with an estimated value of USD 1.9 bn. Global sales for alopecia treatments amounted to approximately USD 600 mn in 2013 according to EvaluatePharma. Despite the very high incidence of alopecia, Merck & Co's Propecia (finasteride) and Pfizer's Rogaine (minoxidil) are the only two approved prescription drugs for hair loss in the US. GlaxoSmithKline's Avodart (dutasteride), which belongs to the same class as Propecia, was only approved for alopecia in a few such as South Korea and Japan. The current size of the prescription market is of limited relevance as Propecia and Rogaine are widely available as generics, while Rogaine is also available over the counter (OTC). Moreover, both drugs have limited effectiveness (Rogaine) with use often hampered by (systemic) side effects or cannot be used by women (Propecia).

ALOPECIA - KEY FACTS	
MARKET SIZE	USD ~2 BN (NON-SURGICAL TREATMENTS); USD 1.9 BN (SURGICAL HAIR RESTORATION)
PREVALENCE	MN GLOBALLY, >50 MN US, >90 MN EU/ROW
INCIDENCE	AFFECTS ~16% OF POPULATION; INCREASES WITH AGE E.G. ~40% OF MEN HAVE HAIR LOSS BY AGE 35, 65% BY AGE 60, AND 80% BY AGE 80; AFFECTING UP TO 40% OF WOMEN
UNDERLYING CAUSE	HAIR LOSS IS MULTIFACTORIAL WITH EVIDENCE SUGGESTING IT MOST LIKELY FUNCTIONS BY A GENETIC PREDISPOSITION. THE PATHOPHYSIOLOGY IS PRIMARILY HORMONE-DRIVEN. ANDROGENS AND ANDROGEN RECEPTORS ARE THE INITIATING CAUSE OF ANDROGENIC ALOPECIA. ANDROGENS REGULATE SEBACEOUS GLANDS (OVERPRODUCTION LEADS TO ACNE), APOCRINE HAIR GROWTH AND LIBIDO. WITH AGE THEY STIMULATE FACIAL HAIR GROWTH BUT SUPPRESS IT AT THE TEMPLES AND SCALP VERTEX (REFERRED TO AS THE "ANDROGEN PARADOX")
SYMPTOMS	- CLASSIC MALE-PATTERN HAIR LOSS: BEGINS ABOVE THE TEMPLES AND VERTEX OF THE SCALP, AS IT PROGRESSES A RIM OF HAIR AT THE SIDES AND REAR OF THE HEAD REMAINS - FEMALE-PATTERN HAIR LOSS: TYPICALLY CAUSES THINNING WITHOUT HAIRLINE RECESSION, FEMALE ANDROGENIC ALOPECIA RARELY LEADS TO TOTAL HAIR LOSS
DRUG CLASS (KEY BRANDS)	- 5-ALPHA REDUCTASE INHIBITORS: 1) FINASTERIDE (PROPECIA); 2) DUTASTERIDE (AVODART) - TOPICAL VASODILATOR: MINOXIDIL (ROGAINE)
MAJOR PLAYERS (KEY BRANDS)	- MERCK & CO (PROPECIA) - GLAXOSMITHKLINE (AVODART) - PFIZER (ROGAINE)
	SOURCE: VALUATIONLAB, NIH, WHO, MEDSCAPE, AM. ACAD. DERMATOLOGY, EJD, MEDLINE

Classic male-pattern hair loss (MPHL) also known as androgenic alopecia (AGA) is the most common type of hair loss. It is characterized by progressive thinning of the scalp hair and a reduction in hair density and diameter. Classic MPHL presents with a typical pattern of bi-temporal and frontal recession of the hairline or scalp vertex thinning, which gradually extends to the back. As it progresses typically a rim of hair at the sides and rear of the head remains. The prevalence increases with age, from 30% for men in their 30s to 50% for men in their 50s. Similarly, female-pattern hair loss (FPHL) is the most common type of hair loss in women. It usually causes thinning without hairline recession and rarely leads to total hair loss. The incidence and prevalence of MPHL are dependent on age and race. Chinese, Japanese, and African American people are affected less than Caucasians. Its incidence increases by age. Prevalence values have variable ranges from 16–96%, depending on the age group and whether or not mild forms of MPHL are included. Prevalence values for female-pattern hair loss are comparable to male-pattern hair loss.

Norwood Hamilton Classification for men, Ludwig scale for women

The severity of MPHL is based on the Norwood Hamilton Classification, which considers bi-temporal and scalp vertex hair loss. FPHL is evaluated based on the Ludwig scale, which ranges from I-III. These classification systems differ because hair loss and thinning in men most commonly occur in an orderly fashion and involve the temporal and vertex region;

diffuse thinning and loss of density with a normal distribution and maintenance of the frontal hairline are often seen in women.

Androgens such as testosterone and dihydrotestosterone play a role in hair loss

MPHL is multifactorial and is caused by a combination of genetics and the effects of androgens such as the male hormone testosterone and its derivative dihydrotestosterone (DHT). The cause of FPHL remains unclear. Androgens are important in male sexual development around birth and at puberty. They regulate e.g., sebaceous glands (overproduction of sebum leads to acne), pubic hair growth, and libido. With increasing age, androgens stimulate hair growth on the face, but can suppress it at the temples and scalp vertex, a condition that has been referred to as the "androgen paradox". Men typically have higher 5-alpha-reductase, lower total testosterone, higher unbound/free testosterone, and higher free androgens, including DHT. 5-alpha-reductase, converts free testosterone into DHT and is highest in the scalp and prostate gland. DHT is most commonly formed at the tissue level by 5α-reduction of testosterone.

Current treatment limited to two drugs with limited efficacy and side effects

Prescription treatment of alopecia in the US and EU is limited to only two approved drugs:

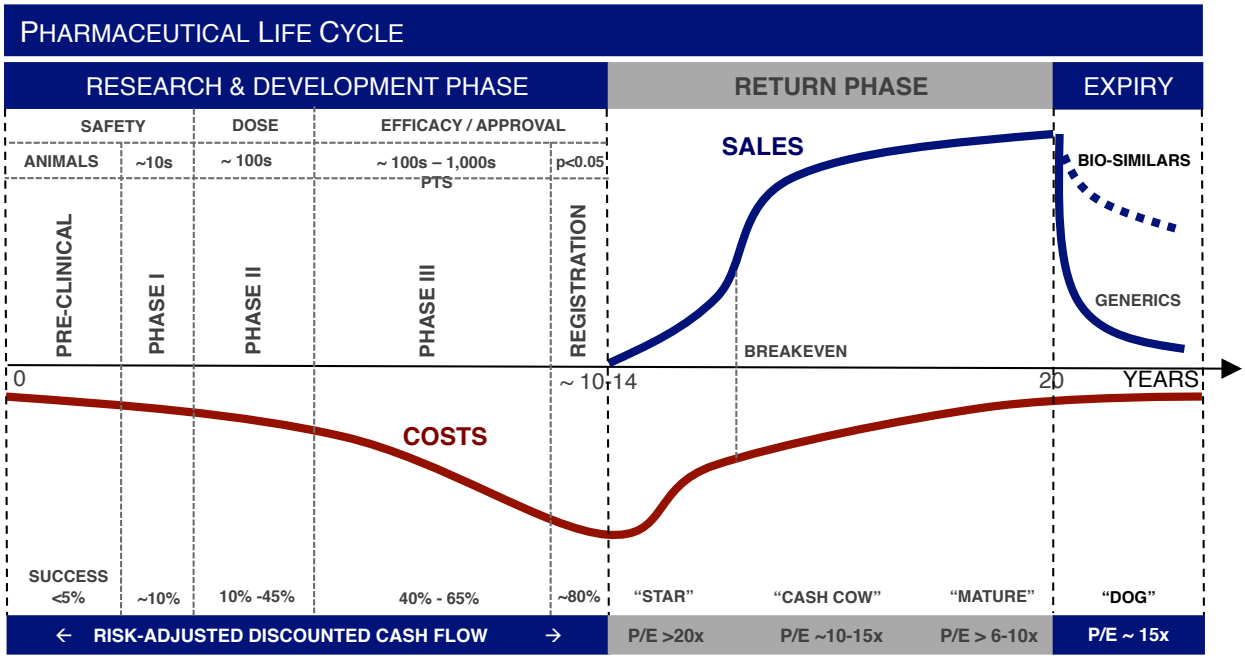
1. **Propecia** was originally used in higher doses for the treatment of enlarged prostate (benign prostate hyperplasia) in adult men and was subsequently approved for treating alopecia. Propecia works by blocking the formation of 5-alpha-reductase and thereby DHT in hair follicles at the top of the scalp. Propecia is a once-daily prescription-only tablet. Full effects of daily use of Propecia can take three months or more to appear; stopping treatment leads to reversal of effect within 12 months. An FDA analysis of side effects revealed a wide range of sexual side effects (e.g. erectile dysfunction, libido disorders). These problems persisted for an average of 40 months after the men ceased treatment. Propecia is not approved in women because it can cause birth defects. GlaxoSmithKline's Avodart (dutasteride) belongs to the same drug class. Global sales peaked at USD 450 mn before patent expiry in 2013.
2. **Rogaine** is a topical vasodilator that stimulates already-damaged hair follicles to produce normal hair. Rogaine works on hair follicles to reverse their shrinking process to stimulate new hair growth. The effects are most promising in younger people who are just beginning to show signs of balding or who have small bald patches. Rogaine is a solution that is applied to balding spots twice daily and must be continued indefinitely; hair loss will recur if treatment is stopped. More than 50% of users claim that it can thicken hair and slow hair loss, but it is not considered effective in men who already have extensive alopecia. Side effects appear to be minimal, but in some users, the medication may cause skin irritation. The drug is approved for use in men and women and is also available over the counter (OTC) at a pharmacy or drug store. Global sales peaked at USD 190 mn in 1996.

Lack of new market entrants despite a high incidence of alopecia

Despite the high incidence of alopecia, there are limited treatments expected to enter the market due to the lack of research in this area. Cosmo's **Breezula** (clascoterone) is the most advanced completing phase IIb development (positive 6-months interim and 12-months results announced). JAK (Janus kinase) inhibitors such as Novartis' **Jakafi** (ruxolitinib) and Pfizer's **Xeljanz** (tofacitinib) have shown promising effects in small open-label trials in treating alopecia areata (spot baldness), a less common autoimmune hair loss disorder.

Pharmaceutical life cycle

To determine the value of a prescription (bio)pharmaceutical compound, it is critical to understand its life cycle. Fortunately, all compounds follow the same life cycle. The clock starts ticking after the compound is patented, providing 20 years of protection from generic competition. Market exclusivities can extend this protection period. The average Research & Development Phase takes 10-14 years, leading to an effective Return Phase of 6-10 years. The Development Phase has 3 distinct Phases, focused on safety (Phase I), dose (Phase II), and efficacy/clinical benefit (Phase III). The compound is filed for registration/approval at the FDA (US) or EMA (EU). The Return Phase is characterized by a star, cash cow, and mature phase. After patent expiry (or loss of market exclusivity) generic manufacturers may copycat the branded prescription drug, at significantly lower costs, leading to a sales and earnings implosion of the branded drug.



SOURCE: VALUATIONLAB

Success probabilities & royalties

Our risk-adjusted NPV calculations use standardized success probabilities based on historical clinical success rates—the success rate increases as the project progress through development. Sales and earnings forecasts are based on the clinical and competitive profile of the compound. The more advanced the compound is, the more accurate the forecasts become as the target market can be defined. We conservatively exclude projects that lack Phase IIa proof-of-concept data in our valuations.

SUCCESS PROBABILITIES & ROYALTIES

DEVELOPMENT STAGE	AIM	WHAT / WHO	SUCCESS PROBABILITY (%)	COSTS (USD MN)	ROYALTIES (%)
PRE-CLINICAL	SAFETY & PHARMACOLOGY DATA	LAB TESTS / ANIMALS - NO HUMANS!	< 5	3	
PHASE I	SCREENING FOR SAFETY	HEALTHY VOLUNTEERS (10'S)	5-15	3	< 5
PHASE IIA	PROOF-OF-CONCEPT	PATIENTS WITH DISEASE (10'S)	10-20		
PHASE II	ESTABLISH THE TESTING PROTOCOL	PATIENTS WITH DISEASE (100'S)	15-35	5	5-15
PHASE IIB	OPTIMAL DOSAGE	PATIENTS WITH DISEASE (100'S)	20-45	5-10	
PHASE III	EVALUATE OVERALL BENEFIT/RISK	PATIENTS WITH DISEASE (1,000'S)	40-65	> 20-1,000	10-25
REGULATORY FILING	DETERMINE PHYSICIAN LABELING	CLINICAL BENEFIT ASSESSMENT	80-90		
APPROVAL	MARKETING AUTHORIZATION	PHYSICIANS FREE TO PRESCRIBE	100		15-30

SOURCE: VALUATIONLAB, TUFTS, FDA, EMA, CLINICALTRIALS.GOV

Important Research Disclosures

valuationLAB AG is an independent healthcare research boutique with no securities or banking services. The company does not hold any positions in the securities mentioned in this report.

Our financial analyses are based on the "Directives on the Independence of Financial Research" issued by the Swiss Bankers Association in January 2008.

Purpose of the Research

This research report has been commissioned by Cosmo Pharmaceuticals NV and prepared and issued by valuationLAB AG for general circulation and is circulated for general information only. This document has been furnished to you solely for your information and may not be reproduced or redistributed to any other person. Information has been obtained from publicly available sources believed to be reliable but no representation or warranty, either expressed or implied, is provided in relation to the accuracy, completeness, or reliability of the information contained herein. Views and estimates constitute our judgment as of the date of this report and are subject to change without notice. Past performance is not indicative of future results. This research report is not intended as an offer or solicitation for the purchase or sale of any financial instrument. Securities, financial instruments, or strategies mentioned herein may not be suitable for all investors. The views and recommendations herein do not consider individual client circumstances, objectives, or needs and are not intended as recommendations of particular securities, financial instruments, or strategies to particular clients. The recipient of this research report must make his or her own independent decisions regarding any securities or financial instruments mentioned herein.

The information contained herein is directed exclusively at market professionals and institutional investors and does not apply to, and should not be relied upon by, private clients. valuationLAB AG accepts no liability for any loss or damage of any kind arising out of the use of this research report or its contents. This research report is not directed to or intended for distribution to or use by any person or entity in any jurisdiction where such distribution, publication, or use would be unlawful. By accepting this document, you agree to be bound by the foregoing limitations.

Achievement of the (risk-adjusted) Fair Value

Recipients of this research report should seek financial advice regarding the appropriateness of investing in any security; financial instrument or strategy discussed in this report and should understand that future (risk-adjusted) fair values may not be realized. The (risk-adjusted) fair value estimate is based on a number of factors and assumptions. It should be noted that if any of these are inaccurate or are not achieved, it might be necessary to adjust the fair value. Investors should note that income from such securities or financial instruments or strategies, if any, may fluctuate and that each security's price or value may rise or fall. Accordingly, investors may receive back less than originally invested. Foreign currency rates of exchange may adversely affect the value, price, or income of any security or related investment mentioned in this research report. In addition, investors in securities such as ADRs, whose values are influenced by the currency of the underlying security, effectively assume currency risk. Fair values for stocks under coverage are calculated by submitting the analyst(s)' financial projections to one or more of a variety of valuation approaches. These include "absolute" methodologies such as DCF and NPV modeling, as well as relative methodologies such as peer group and market valuation multiple comparisons.

Risk Analysis

Speculative	less than 1 year cash and breakeven beyond 1 year
High Risk	profitable within 2 years and 1 approved product/key indication (patent expiry > 5 years)
Medium Risk	profitable and/or sales from at least 2 marketed products/key indications (patent expiry > 5 years)
Low Risk	profitable and sales from >2 marketed products/key indications (patent expiry > 5 years)

Analyst Certification

The research analyst(s) identified on the first page of this research report hereby attest that all of the views expressed in this report accurately reflect their personal views about any and all of the subject securities or issuers. To ensure the independence of our research analysts, and their immediate households, are expressly prohibited from owning any securities in the valuationLAB AG research universe, which belong to their sector(s). Neither the research analyst nor his/her immediate household serves as an Officer, Director, or Advisory Board Member of Cosmo Pharmaceuticals NV.

FELSENRAINSTRASSE 17 I 8832 WOLLERAU I SWITZERLAND I WWW.VALUATIONLAB.COM I T: +41 79 652 67 68