UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 OR 15(d) of The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): **April 13, 2022**

COLLEGIUM PHARMACEUTICAL, INC.
(Exact Name of Registrant as Specified in its Charter)

Virginia	**001-37372**	**03-0416362**
(State or Other Jurisdiction of Incorporation or Organization)	(Commission File Number)	(IRS Employer Identification No.)

100 Technology Center Drive
Suite 300
Stoughton, MA 02072
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code: **(781) 713-3699**

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common stock, par value $0.001 per share	COLL	The NASDAQ Global Select Market

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Other Information.

On April 13, 2022, Collegium Pharmaceutical, Inc. posted a corporate presentation to its website that representatives of the Company may use from time to time in presentations or discussions with investors, analysts or other parties. A copy of the presentation is attached hereto as Exhibit 99.1 and is being furnished, not filed, under Item 7.01 of this Current Report on Form 8-K.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

99.1	Corporate presentation, dated April 13, 2022.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: April 13, 2022

Collegium Pharmaceutical, Inc.

By: /s/ Colleen Tupper
Name: Colleen Tupper
Title: Executive Vice President and Chief Financial Officer


Collegium
PHARMACEUTICAL
Corporate Presentation
April 2022 | Nasdaq: COLL
Investor Presentation

Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. We may, in some cases, use terms such as "predicts," "forecasts," "believes," "potential," "proposed," "continue," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "should" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Examples of forward-looking statements contained in this presentation include, among others, statements related to our full-year 2022 financial guidance, including total projected product revenue, adjusted operating expenses and adjusted EBITDA, current and future market opportunities for our products and our assumptions related thereto, expectations (financial or otherwise) and intentions, and other statements that are not historical facts. Such statements are subject to numerous important factors, risks and uncertainties that may cause actual events or results, performance, or achievements to differ materially from the company's current expectations. Actual results may differ materially from management's expectations and such forward-looking statements in this presentation could be affected as a result of various important factors, including risks relating to, among others: risks related to the ability to realize the anticipated benefits of our acquisition of BDSI, including the possibility that the expected benefits from the BDSI acquisition will not be realized or will not be realized within the expected time period; the risk that BDSI's business will not be integrated successfully; negative effects of the consummation of the BDSI acquisition on the market price of our common stock and/or operating results; unknown liabilities; risks related to future opportunities and plans for the products acquired with BDSI, including uncertainty of the expected financial performance of such products; the impact of the COVID-19 pandemic on our ability to conduct our business, reach our customers, and supply the market with our products; our ability to commercialize and grow sales of our products; our ability to manage our relationships with licensors; the success of competing products that are or become available; our ability to obtain and maintain regulatory approval of our products and any product candidates, and any related restrictions, limitations, and/or warnings in the label of an approved product; the size of the markets for our products and product candidates, and our ability to service those markets; our ability to obtain reimbursement and third-party payor contracts for our products; the rate and degree of market acceptance of our products and product candidates; the costs of commercialization activities, including marketing, sales and distribution; changing market conditions for our products; the outcome of any patent infringement, opioid-related or other litigation that may be brought by or against us, including litigation with Purdue Pharma, L.P.; the outcome of any governmental investigation related to our business; our ability to secure adequate supplies of active pharmaceutical ingredient for each of our products and manufacture adequate supplies of commercially saleable inventory; our ability to obtain funding for our operations and business development; regulatory developments in the U.S.; our expectations regarding our ability to obtain and maintain sufficient intellectual property protection for our products; our ability to comply with stringent U.S. and foreign government regulation in the manufacture of pharmaceutical products, including U.S. Drug Enforcement Agency, or DEA, compliance; our customer concentration; and the accuracy of our estimates regarding expenses, revenue, capital requirements and need for additional financing. These and other risks are described under the heading "Risk Factors" in our Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q and other filings with the SEC. Any forward-looking statements that we make in this presentation speak only as of the date of this presentation. We assume no obligation to update our forward-looking statements whether as a result of new information, future events or otherwise, after the date of this presentation.

Non-GAAP Financial Measures

To supplement our financial results presented on a GAAP basis, we have included information about certain non-GAAP financial measures such as adjusted EBITDA and adjusted operating expenses. We use these non-GAAP financial measures to understand, manage and evaluate our business as we believe they provide additional information on the performance of our business. We believe that the presentation of these non-GAAP financial measures, taken in conjunction with our results under GAAP, provide analysts, investors, lenders and other third parties insight into our view and assessment of our ongoing operating performance. In addition, we believe that the presentation of these non-GAAP financial measures, when viewed with our results under GAAP , provide supplementary information that may be useful to analysts, investors, lenders, and other third parties in assessing our performance and results from period to period. We report these non-GAAP financial measures to portray the results of our operations prior to considering certain income statement elements. These non-GAAP financial measures should be considered in addition to, and not as a substitute for, or superior to, net income or other financial measures calculated in accordance with GAAP.

Adjusted EBITDA is a non-GAAP financial measure that represents GAAP net income adjusted to exclude interest expense, interest income, the benefit from or provision for income taxes, depreciation, amortization, stock-based compensation, restructuring expenses, acquisition costs and litigation settlements. Adjusted EBITDA, as used by us, may be calculated differently from, and therefore may not be comparable to, similarly titled measures used by other companies.

There are several limitations related to the use of adjusted EBITDA rather than net income, which is the nearest GAAP equivalent, such as:

- adjusted EBITDA excludes depreciation and amortization, and, although these are non-cash expenses, the assets being depreciated or amortized may have to be replaced in the future, the cash requirements for which are not reflected in adjusted EBITDA;
- we exclude stock-based compensation expense from adjusted EBITDA although (a) it has been, and will continue to be for the foreseeable future, a significant recurring expense for our business and an important part of our compensation strategy and (b) if we did not pay out a portion of our compensation in the form of stock-based compensation, the cash salary expense included in operating expenses would be higher, which would affect our cash position;
- adjusted EBITDA does not reflect changes in, or cash requirements for, working capital needs;
- adjusted EBITDA does not reflect the benefit from or provision for income taxes or the cash requirements to pay taxes;
- adjusted EBITDA does not reflect historical cash expenditures or future requirements for capital expenditures or contractual commitments;
- we exclude restructuring expenses from adjusted EBITDA. Restructuring expenses primarily include employee severance and contract termination costs. The amount and/or frequency of these restructuring expenses are not part of our underlying business;
- we exclude acquisition costs related to the acquisition of BDSI from adjusted EBITDA; and
- we exclude litigation settlements from adjusted EBITDA, as well as any applicable income items or credit adjustments due to subsequent changes in estimates. This does not include our legal fees to defend claims, which are expensed as incurred.

Adjusted operating expenses is a non-GAAP financial measure that represents GAAP operating expenses adjusted to exclude stock-based compensation expense, restructuring, acquisition costs, and litigation settlements.

The Company has not provided a reconciliation of its full-year 2022 guidance for adjusted EBITDA or adjusted operating expenses to the most directly comparable forward-looking GAAP measures because it is unable to predict, without unreasonable efforts, the timing and amount of items that would be included in such a reconciliation, including, but not limited to, stock-based compensation expense. These items are uncertain and depend on various factors that could have a material impact on GAAP net income and operating expenses for the guidance period.

Mission Driven

Building a leading, diversified specialty pharmaceutical company committed to improving the lives of people living with serious medical conditions

GUIDED BY OUR CORE VALUES

Collegium PHARMACEUTICAL

- **I** — Uphold **Integrity**
- **D** — Embrace **Differences**
- **E** — Encourage **Expression**
- **A** — Be **Accountable**

Focused on Sustainability and Social Impact

ENVIRONMENTAL

Be a responsible steward of the environment

- Transitioning Xtampza® ER to 2x scale manufacturing
- Product packaging with recyclable materials
- Hybrid work week
- Single stream recycling and light automation at Headquarters
- Offering hybrid vehicles through Fleet Program

SOCIAL

Do the right thing for our employees, patients, providers, and communities

- External awards recognizing our culture
- Volunteerism and charitable giving to community partners
- Diversity, equity, and inclusion council leading our initiatives
- Pain Points of View website supporting patients and communities
- Innovative health and well-being programs
- Training and professional development of all employees

GOVERNANCE

Act in the best interests of our stakeholders

- Board oversight of risk management, including ESG
- ESG strategy set by ESG Executive Steering Committee
- Diverse senior leadership team and Board of Directors
- Adopted governance changes to increase and enhance shareholder access and transparency
- Strong Code of Ethics and related training
- Commitment to core values

Experienced Management Team and Board of Directors

Collegium Board of Directors

Joseph Ciaffoni
President & CEO, Collegium Pharmaceutical

Michael Heffernan
Chairman of the Board & Collegium Founder

Rita Balice-Gordon
Chief Executive Officer, Muna Therapeutics

Garen Bohlin
Former COO, Sirtris, Former CEO, Syntonix

John Fallon, M.D.
Former SVP & CMO, Blue Cross Blue Shield of MA

Neil McFarlane
Former CEO, Adamas Pharmaceuticals

John Freund, M.D.
Co-Founder & Partner, Skyline Ventures

Gwen Melincoff
Former Senior BD roles, BTG International, Shire, Adolor

Gino Santini
Former SVP, Corp. Strategy & BD, President, Eli Lilly

2022 is a Pivotal Year

Grow Top and Bottom Lines

Grow Xtampza ER and Belbuca®

Maximize Nucynta® Franchise and Symproic®

Launch Elyxyb™

Renegotiate Xtampza ER contracts

Integrate BDSI

Seamless transition of core operations

Achieve annual run rate **synergies of at least $75 million**

Deploy Capital

Business development focused on commercial-stage neurology assets

Rapidly pay down debt

Opportunistically return capital to shareholders

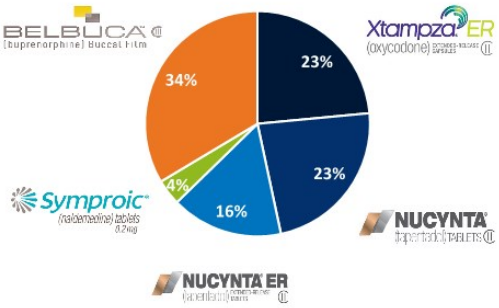
Collegium PHARMACEUTICAL

BDSI Acquisition is Strategically and Financially Transformative

Scales and Diversifies Revenue

$441.5m

pro forma 2021 net revenue[1]



Immediately and Highly Accretive[2]

EXPECT TO DELIVER

>$75 MILLION

IN ANNUAL RUN RATE SYNERGIES[2]

EXPECT TO GENERATE

2x ADJ. EBITDA[3]

2022 vs. 2021

Foothold in Neurology

Business Development Priority

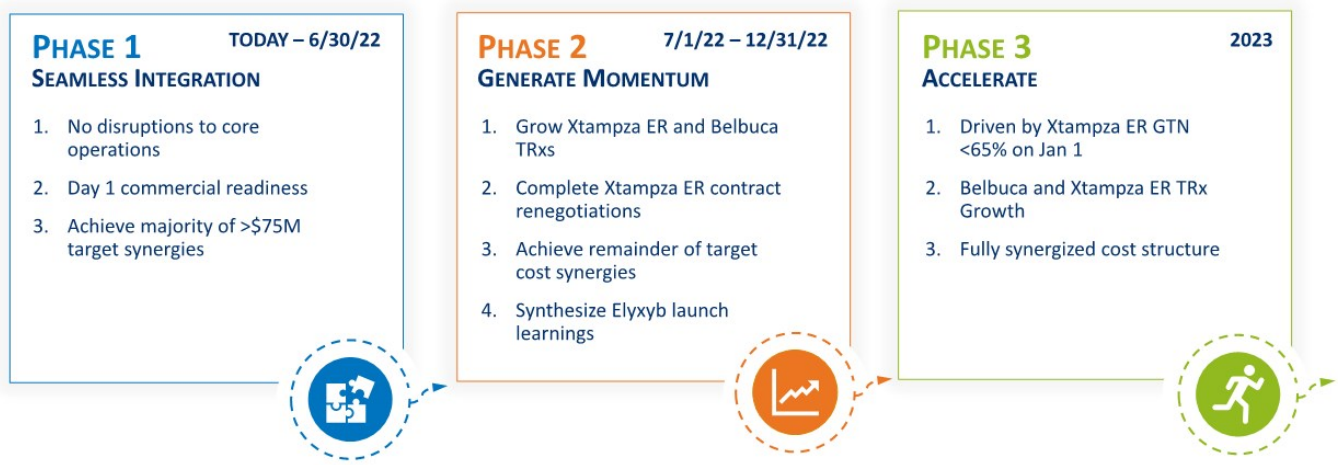
Elyxyb™ (celecoxib) Oral Solution

Launch Opportunity

Collegium PHARMACEUTICAL

1. Pro forma 2021 net revenue is: a) FY 2021 Collegium reported net product revenue of $103.7M for Xtampza ER, $102.2 for Nucynta IR and $70.9M for Nucynta ER inclusive of a $13.8M and $24.5M for product revenue adjustments related to returns of Xtampza ER and Nucynta products respectively and b) FY 2021 BDSI reported net product revenue of $148.2M for Belbuca and $16.4M for Symproic as reported on BDSI form 10-K.
2. Estimated cost synergies expected to be achieved within first 12 months post-close.
3. Adjusted EBITDA is a non-GAAP financial measure that represents GAAP net income adjusted to exclude interest expense, interest income, the benefit from or provision for income taxes, depreciation, amortization, stock-based compensation, restructuring expenses, litigation settlements, and acquisition-related expenses. Increase in Adj. EBITDA year-over-year is calculated based on financial data provided by Collegium on form 10-k filed with the SEC on February 24, 2022, compared to the mid-point of the guidance ranges provided by Collegium in its press release filed with the SEC on April 5, 2022.

Collegium 3-Phase Action Agenda



Strong Financial Position[1,2]

Revenue Growth & Scale

Est. 2022 **revenue** of **$450-465M**
~+65% y/y at mid-point

Robust Cash Flows[4]

Est. 2022 **Adj. EBITDA** of **$235-250M**
~+105% y/y at mid-point

Significant Cost Leverage[3]

Est. 2022 **Adj. Op Ex** of **$130-140M**
~+33% y/y at mid-point

Expect to grow revenue approximately 2x the rate of operating expenses

Rapid Deleveraging of Balance Sheet[5]

First year deleveraging of term loan of **$100.0M,** full paydown over 4 years

Est. 2022 YE **Debt/EBITDA ratio <3.0x**

1. This financial data was provided by Collegium in its press release filed with the SEC on April 5, 2022.
2. Percent change year-over-year is calculated based on financial data provided by Collegium on form 10-k filed with the SEC on February 24, 2022, compared to the mid-point of the guidance ranges provided by Collegium in its press release filed with the SEC on April 5, 2022.
3. Adjusted operating expenses is a non-GAAP financial measure that represents GAAP operating expenses adjusted to exclude stock-based compensation expense, restructuring, litigation settlements, and acquisition-related expenses
4. Adjusted EBITDA is a non-GAAP financial measure that represents GAAP net income adjusted to exclude interest expense, interest income, the benefit from or provision for income taxes, depreciation, amortization, stock-based compensation, restructuring expenses, litigation settlements, and acquisition-related expenses.
5. Details regarding the Pharmakon term-loan debt amortization schedule provided by Collegium on form SC TO-C filed with the SEC on February 14, 2022.

Diverse and Durable Commercial Portfolio

The Leader in Responsible Pain Management

Portfolio Spans the Continuum of Care

~48% Market Share of the Branded ER market[1]

Highly differentiated products that are viewed favorably by physicians, with a high future intent to prescribe[2]

Pain Portfolio distinctly positioned and sources differently

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Sources:
1. IQVIA NPA, February 2022
2. ATU (Attitudes, Trial & Awareness) Market Research Study fielded Q1 2021

Xtampza ER and Belbuca: Durable Growth Drivers

	Xtampza ER (oxycodone) Extended-Release Capsules	BELBUCA (buprenorphine) Buccal Film
Durable Assets	Exclusivity through at least September 2033	Exclusivity through at least January 2027
Strong Market Position	~34% share of OER market[1]	~42% share of growing buprenorphine market[1]
Growing Prescriber Base	~19,200 unique prescribers in Q4 2021, up 30% year-over-year[2]	~8,700 unique prescribers in Q4 2021, up ~9% year-over-year[3]
GtN Impacts	<65% GtN beginning in 2023 driven by contract optimization	Expect stable mid-50% GtNs
Broad Market Access	Strong coverage across all payor types	

Collegium Pharmaceutical

Sources:
1. IQVIA Monthly NPA through Feb 2022
2. IQVIA Exponent through Q4 2021
3. Symphony Metas data through Q4 2021

A Strategic Foothold in Neurology

Neurology is a Target Adjacency

- Business Development Priority
- Aligned to organizational capabilities
- Complimentary to Pain

Elyxyb Launch Opportunity

- Focused and Phased Approach
- Where we choose to play, we will play to win
- Success gated expansion

Migraine Market Opportunity

Large & Growing US Market

- **39 million** people suffer from migraines in the US[1]

Patients Cycling Through Many Standard Therapies

- **>70% of patients** report inadequate treatment response with acute migraine[2]
- **Acute migraine market** dominated by Triptan Rxs (70% of prescriptions)[3]
- CGRPs showing **discontinuation at a high rate** (~50% therapy abandonment 90-day post start)[4]
- **NSAIDs** are the most used class of drugs for the acute treatment of headache in general, and migraine in particular[5]

ELYXYB: The 1st & only Cox-2 inhibitor formulated as a ready to use oral solution for the acute treatment of migraine[6]

- **Beneficial data for patients:** Achieved 1-hour T_{max}.[6]
- **Patented SMEDDs Technology:** Differentiated delivery and improved solubility suggest the possibility of better absorption[7]
- **Safety Profile:** Low incidence of GI side effects and no drowsiness[6]
- **Indication:** a nonsteroidal anti-inflammatory drug (NSAID) indicated for the acute treatment of migraine with or without aura in adults. Elyxyb is not indicated for the prevention of migraine.[6]

A Focused & Phased Launch

- **25** Territories, **3,500** Targets
- **15%** of acute migraine market

Boxed Warning: Elyxyb™ carries serious risk of cardiovascular and gastrointestinal events. NSAIDs cause an increased risk of serious and potentially fatal cardiovascular thrombotic events, such as myocardial infarction and stroke, and serious and potentially fatal gastrointestinal (GI) adverse events, including bleeding, ulceration, and perforation of the stomach or intestines. This risk of serious thrombotic events may occur early in the treatment and may increase with duration and use. Elyxyb is contraindicated in the setting of coronary artery bypass graft (CABG) surgery. The risk of serious GI adverse events can occur at any time during use and without any warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events.

Please see Important Safety Information at the end of this presentation, and Full Prescribing Information, Including Boxed Warning and Medication Guide at elyxyb.com.

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1. Migraine Research Foundation, 2021
2. Lipton RB et al. Headache. 2017
3. IQVIA NPA Monthly YTD 2022
4. Symphony Health Patient Claims
5. Pardutz, NSAIDs in the Acute Treatment of Migraine: A review of Clinical Experiment and Data, 2010
6. Elyxyb Full Prescribing Information, 2022
7. Arindam Pal, Srinivas Shenoy, Anirudh Gautam, Sagar Munjal, Jing Niu, Mathangi Gopalakrishnan & Joga Gobburru, Clinical Drug Investigation volume 37, pages 937–946(2017)

Maximizing the Value of Nucynta and Symproic as Key Contributors

NUCYNTA® (tapentadol) TABLETS CII

NUCYNTA® ER (tapentadol) EXTENDED-RELEASE TABLETS CII

- Differentiated opioid with proposed dual mechanism of action[1,2]
- Nucynta ER is the only ER product indicated for pain associated with Diabetic Peripheral Neuropathy[2]
- ~70% of Nucynta Franchise prescriptions are covered by the pain salesforce[3]
- Maximize profitability through contracting strategy

Symproic® (naldemedine) tablets 0.2mg

- The only OIC therapy with a strong recommendation and high quality of evidence from the American Gastroenterological Association[4]
- Complementary to pain portfolio

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Sources:
1. Nucynta Full Prescribing Information, 2022
2. Nucynta ER Full Prescribing Information, 2022
3. IQVIA Exponent through Jan 2022
4. Crockett SD, et al. Gastroenterology. 2019;156(1): 218-226

Capital Allocation Priorities

1 FOCUSED BUSINESS DEVELOPMENT

- Commercial-stage neurology assets

2 RAPIDLY PAYDOWN DEBT

- New $650M Pharmakon loan issued on 3/22/22[2]
- $100M to be repaid in first 12 months[1]
- >$450M to be repaid in first 36 months[1]

3 OPPORTUNISTICALLY RETURN CAPITAL TO SHAREHOLDERS

- ~$50M remaining on $100M share repurchase program[2]

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1. This financial data was provided by Collegium in its press release issued February 14, 2022.
2. This financial data was provided by Collegium in its from 10-k filed with the SEC on February 24, 2022.

Building A Leading, Diversified Specialty Pharmaceutical Company Through Financially Transformative Acquisitions

STRONG TRACK RECORD

- ✓ Nucynta Franchise (February 2020)
- ✓ BDSI (March 2022)

BUSINESS DEVELOPMENT FOCUS

- Commercial-stage neurology assets

2022 Financial Guidance[1]

	TARGET
Total Revenues	$450.0 million - $465.0 million
Adjusted Operating Expenses[2]	$130.0 million - $140.0 million
Adjusted EBITDA[3]	$235.0 million - $250.0 million

1. This financial data was provided by Collegium in its press release filed with the SEC on April 5, 2022.
2. Adjusted EBITDA is a non-Adjusted operating expenses is a non-GAAP financial measure that represents GAAP operating expenses adjusted to exclude stock-based compensation expense, restructuring, litigation settlements, and acquisition-related expenses.
3. GAAP financial measure that represents GAAP net income adjusted to exclude interest expense, interest income, the benefit from or provision for income taxes, depreciation, amortization, stock-based compensation, restructuring expenses, litigation settlements, and acquisition-related expenses.

Building a Leading, Diversified Specialty Pharmaceutical Company

DIVERSE AND DURABLE PORTFOLIO

- ✓ Leadership in pain
- ✓ Foothold in neurology
- ✓ Xtampza ER exclusive to Sept. 2033, Belbuca exclusive to Jan. 2027

STRONG FINANCIAL POSITION

- ✓ Revenue expected to grow ~65% YoY[1]
- ✓ Significant cost leverage: revenue expected to grow ~2x rate of OPEX[1]
- ✓ Est. 2022 YE debt/EBITDA ratio <3.0x[1]

LONG-TERM VALUE CREATION

- ✓ Focused business development
- ✓ Rapidly pay down debt
- ✓ Opportunistically return capital to shareholders

Collegium PHARMACEUTICAL

1. Percent change year-over-year, growth rates and financial ratios are calculated based on financial data provided by Collegium on form 10-k filed with the SEC on February 24, 2022, compared to the mid-point of the guidance ranges provided by Collegium in its press release filed with the SEC on April 5, 2022.

Important Safety Information

Important Safety Information about XTAMPZA ER (oxycodone) extended-release capsules

XTAMPZA ER
(Oxycodone) extended-release capsules

WARNING: ADDICTION, ABUSE, AND MISUSE; RISK EVALUATION AND MITIGATION STRATEGY (REMS); LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; CYTOCHROME P450 3A4 INTERACTION; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

Addiction, Abuse, and Misuse
Xtampza ER exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk prior to prescribing Xtampza ER and monitor all patients regularly for the development of these behaviors or conditions.

Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)
To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the Food and Drug Administration (FDA) has required a REMS for these products. Under the requirements of the REMS, drug companies with approved opioid analgesic products must make REMS-compliant education programs available to healthcare providers. Healthcare providers are strongly encouraged to:

- **Complete a REMS-compliant education program**
- **Counsel patients and/or their caregivers, with every prescription, on safe use, serious risks, storage, and disposal of these products**
- **Emphasize to patients and their caregivers the importance of reading the Medication Guide every time it is provided by their pharmacist, and**
- **Consider other tools to improve patient, household, and community safety**

Life-Threatening Respiratory Depression
Serious, life-threatening, or fatal respiratory depression may occur with use of Xtampza ER. Monitor for respiratory depression, especially during initiation of Xtampza ER or following a dose increase.

Collegium PHARMACEUTICAL

See full prescribing information, including Boxed Warning on Addiction, Abuse and Misuse, and other serious risks at XtampzaER.com/PI

Important Safety Information about XTAMPZA ER (oxycodone) extended-release capsules

XTAMPZA ER
(Oxycodone) extended-release capsules

Accidental Ingestion
Accidental ingestion of even one dose of Xtampza ER, especially by children, can result in a fatal overdose of Oxycodone.

Neonatal Opioid Withdrawal Syndrome
Prolonged use of Xtampza ER during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

Cytochrome P450 3A4 Interaction
The concomitant use of Xtampza ER with all cytochrome P450 3A4 inhibitors may result in an increase in Oxycodone plasma concentrations, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression. In addition, discontinuation of a concomitantly used cytochrome P450 3A4 inducer may result in an increase in Oxycodone plasma concentration. Monitor patients receiving Xtampza ER and any CYP3A4 inhibitor or inducer.

Risks From Concomitant Use With Benzodiazepines or Other CNS Depressants
Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death.

- **Reserve concomitant prescribing of Xtampza ER and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate**
- **Limit dosages and durations to the minimum required**
- **Follow patients for signs and symptoms of respiratory depression and sedation**

Collegium PHARMACEUTICAL

See full prescribing information, including Boxed Warning on Addiction, Abuse and Misuse, and other serious risks at XtampzaER.com/PI

Important Safety Information about BELBUCA (buprenorphine buccal film)

BELBUCA
(buprenorphine buccal film)

WARNING: ADDICTION, ABUSE, AND MISUSE; RISK EVALUATION AND MITIGATION STRATEGY (REMS); LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL EXPOSURE; NEONATAL OPIOID WITHDRAWAL SYNDROME; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES AND OTHER CNS DEPRESSANTS

Addiction, Abuse, and Misuse

BELBUCA exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk prior to prescribing BELBUCA and monitor regularly for these behaviors and conditions.

Risk Evaluation and Mitigation Strategy (REMS)

To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the FDA has required a REMS for these products. Under the requirements of the REMS, drug companies with approved opioid analgesic products must make REMS-compliant education programs available to healthcare providers. Healthcare providers are strongly encouraged to

- **Complete a REMS-compliant education program,**
- **Counsel patients and/or their caregivers, with every prescription, on safe use, serious risks, storage, and disposal of these products,**
- **Emphasize to patients and their caregivers the importance of reading the Medication Guide every time it is provided by their pharmacist, and**
- **Consider other tools to improve patient, household, and community safety**

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of BELBUCA. Monitor for respiratory depression, especially during initiation of BELBUCA or following a dose increase. Misuse or abuse of BELBUCA by chewing, swallowing, snorting, or injecting Buprenorphine extracted from the buccal film will result in the uncontrolled delivery of Buprenorphine and poses a significant risk of overdose and death.

Accidental Exposure

Accidental exposure to even one dose of BELBUCA, especially in children, can result in a fatal overdose of Buprenorphine.

Collegium PHARMACEUTICAL

See full prescribing information, including Boxed Warning on Addiction, Abuse and Misuse, and Other Serious Risks at Belbuca.com/#isi-block.

Important Safety Information about BELBUCA (buprenorphine buccal film)

BELBUCA
(buprenorphine buccal film)

Neonatal Opioid Withdrawal Syndrome
Prolonged use of BELBUCA during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated. If prolonged opioid use is required in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

Risks from Concomitant Use with Benzodiazepines Or Other CNS Depressants
Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing for use in patients for whom alternative treatment options are inadequate; limit dosages and durations to the minimum required; and follow patients for signs and symptoms of respiratory depression and sedation.

Collegium PHARMACEUTICAL

See full prescribing information, including Boxed Warning on Addiction, Abuse and Misuse, and Other Serious Risks at Belbuca.com/#isi-block.

Important Safety Information about NUCYNTA ER (tapentadol) extended-release tablets

NUCYNTA ER
(tapentadol) extended-release tablets

WARNING: ADDICTION, ABUSE, AND MISUSE; RISK EVALUATION AND MITIGATION STRATEGY (REMS); LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; INTERACTION WITH ALCOHOL and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

Addiction, Abuse, and Misuse
NUCYNTA ER exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk prior to prescribing NUCYNTA ER and monitor all patients regularly for the development of these behaviors and conditions.

Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)
To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the Food and Drug Administration (FDA) has required a REMS for these products. Under the requirements of the REMS, drug companies with approved opioid analgesic products must make REMS-compliant education programs available to healthcare providers. Healthcare providers are strongly encouraged to:

- **Complete a REMS-compliant education program**
- **Counsel patients and/or their caregivers, with every prescription, on safe use, serious risks, storage, and disposal of these products**
- **Emphasize to patients and their caregivers the importance of reading the Medication Guide every time it is provided by their pharmacist, and**
- **Consider other tools to improve patient, household, and community safety**

Life-Threatening Respiratory Depression
Serious, life-threatening, or fatal respiratory depression may occur with use of NUCYNTA ER. Monitor for respiratory depression, especially during initiation of NUCYNTA ER or following a dose increase. Instruct patients to swallow NUCYNTA ER tablets whole; crushing, chewing, or dissolving NUCYNTA ER tablets can cause rapid release and absorption of a potentially fatal dose of Tapentadol.

Accidental Ingestion
Accidental ingestion of even one dose of NUCYNTA ER, especially by children, can result in a fatal overdose of Tapentadol.

Collegium PHARMACEUTICAL

See full prescribing information, including Boxed Warning on Addiction, Abuse and Misuse, and other serious risks at Nucynta.com/erPI

Important Safety Information about NUCYNTA ER (tapentadol) extended-release tablets

NUCYNTA ER
(tapentadol) extended-release tablets

Neonatal Opioid Withdrawal Syndrome
Prolonged use of NUCYNTA ER during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

Interaction with Alcohol
Instruct patients not to consume alcoholic beverages or use prescription or non-prescription products that contain alcohol while taking NUCYNTA ER. The co-ingestion of alcohol with NUCYNTA ER may result in increased plasma Tapentadol levels and a potentially fatal overdose of Tapentadol.

Risks From Concomitant Use With Benzodiazepines Or Other CNS Depressants
Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death

- **Reserve concomitant prescribing of NUCYNTA ER and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate**
- **Limit dosages and durations to the minimum required**
- **Follow patients for signs and symptoms of respiratory depression and sedation**

Collegium PHARMACEUTICAL

See full prescribing information, including Boxed Warning on Addiction, Abuse and Misuse, and other serious risks at Nucynta.com/erPI

Important Safety Information about NUCYNTA (Tapentadol) tablets

WARNING: ADDICTION, ABUSE, AND MISUSE; RISK EVALUATION AND MITIGATION STRATEGY (REMS); LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

Addiction, Abuse, and Misuse

NUCYNTA tablets expose patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk prior to prescribing NUCYNTA tablets and monitor all patients regularly for the development of these behaviors and conditions.

Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)

To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the Food and Drug Administration (FDA) has required a REMS for these products. Under the requirements of the REMS, drug companies with approved opioid analgesic products must make REMS-compliant education programs available to healthcare providers. Healthcare providers are strongly encouraged to:

- **Complete a REMS-compliant education program**
- **Counsel patients and/or their caregivers, with every prescription, on safe use, serious risks, storage, and disposal of these products**
- **Emphasize to patients and their caregivers the importance of reading the Medication Guide every time it is provided by their pharmacist, and**
- **Consider other tools to improve patient, household, and community safety**

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of NUCYNTA tablets. Monitor for respiratory depression, especially during initiation of NUCYNTA tablets or following a dose increase.

Accidental Ingestion

Accidental ingestion of even one dose of NUCYNTA tablets, especially by children, can result in a fatal overdose of Tapentadol.

Collegium PHARMACEUTICAL

See full prescribing information, including Boxed Warning on Addiction, Abuse and Misuse and other serious risks at Nucynta.com/irPI

Important Safety Information about NUCYNTA (Tapentadol) tablets

Neonatal Opioid Withdrawal Syndrome

Prolonged use of NUCYNTA tablets during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

Risks From Concomitant Use With Benzodiazepines Or Other CNS Depressants

Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death.

- **Reserve concomitant prescribing of NUCYNTA tablets and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate**
- **Limit dosages and durations to the minimum required**
- **Follow patients for signs and symptoms of respiratory depression and sedation**

Important Safety Information about ELYXYB (celecoxib) oral solution

WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS

Cardiovascular Thrombotic Events

- **Nonsteroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in the treatment and may increase with duration of use.**
- **ELYXYB is contraindicated in the setting of coronary artery bypass graft (CABG) surgery.**

Gastrointestinal Bleeding, Ulceration, and Perforation

- **NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious (GI) events.**

Important Safety Information about ELYXYB (celecoxib) oral solution

ELYXYB
(celecoxib) oral solution

CONTRAINDICATIONS

ELYXYB is contraindicated in the following patients:

- Known hypersensitivity to celecoxib or any components of the drug product or sulfonamides
- History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs
- In the setting of coronary artery bypass graft (CABG) surgery

WARNINGS AND PRECAUTIONS

- Post-MI Patients: Avoid the use of ELYXYB in patients with a recent MI unless the benefits are expected to outweigh the risk of recurrent CV thrombotic events. If ELYXYB is used in patients with a recent MI, monitor patients for signs of cardiac ischemia.

- Hepatotoxicity: Elevations of ALT or AST have been reported in patients with NSAIDs. In addition, rare, sometimes fatal, cases of severe hepatic injury, including fulminant hepatitis, liver necrosis, and hepatic failure, have been reported. Inform patients of warning signs and symptoms of hepatotoxicity. Discontinue if abnormal liver tests persist or worsen or if clinical signs and symptoms of liver disease develop.

- Hypertension: NSAIDs, including ELYXYB, can lead to new onset of hypertension or worsening of preexisting hypertension, either of which may contribute to the increased incidence of CV events. Patients taking some antihypertension medications may have impaired response to these therapies when taking NSAIDs. Monitor blood pressure.

- Heart Failure and Edema: Avoid the use of ELYXYB in patients with severe heart failure unless the benefits are expected to outweigh the risk of worsening heart failure. If ELYXYB is used in patients with severe heart failure, monitor patients for signs of worsening heart failure.

- Renal Toxicity: Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury and may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decompensation. Monitor renal function in patients with renal or hepatic impairment, heart failure, dehydration, or hypovolemia. Avoid use of ELYXYB in patients with severe renal impairment unless benefits are expected to outweigh the risk of worsening renal function. If ELYXYB is used in patients with advanced renal disease, monitor patients for signs of worsening renal function.

- Hyperkalemia: Increases in serum potassium concentration, including hyperkalemia, have been reported with use of NSAIDs, even in some patients without renal impairment. In patients with normal renal function, these effects have been attributed to a hyporeninemic-hypoaldosteronism state.

Collegium PHARMACEUTICAL

See full prescribing information, including boxed warning and other serious risks at Elyxyb.com/#isi.

Important Safety Information about ELYXYB (celecoxib) oral solution

ELYXYB
(celecoxib) oral solution

- Anaphylactic Reactions: Celecoxib has been associated with anaphylactic reactions in patients with and without known hypersensitivity to celecoxib and in patients with aspirin-sensitive asthma. Celecoxib is a sulfonamide and both NSAIDs and sulfonamides may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people.

- Exacerbation of Asthma Related to Aspirin Sensitivity: ELYXYB™ is contraindicated in patients with aspirin-sensitive asthma. Monitor patients with preexisting asthma (without known aspirin sensitivity).

- Serious Skin Reactions: Serious skin reactions have occurred following treatment with celecoxib, including erythema multiforme, exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalized exanthematous pustulosis (AGEP). These serious events may occur without warning and can be fatal. Discontinue ELYXYB at the first appearance of skin rash or any other sign of hypersensitivity.

- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS): DRESS has been reported in patients taking NSAIDs. Some of these events have been fatal or life-threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Eosinophilia is often present. If such signs or symptoms are present, discontinue ELYXYB and evaluate the patient immediately.

- Medication Overuse Headache: Overuse of acute migraine drugs (e.g., ergotamine, triptans, opioids, NSAIDs, or combination of these drugs for 10 or more days per month), including ELYXYB, may lead to exacerbation of headache (medication overuse headache). Detoxification of patients, including withdrawal of the overused drugs and treatment of withdrawal symptoms may be necessary.

- Premature Closure of Fetal Ductus Arteriosus: ELYXYB may cause premature closure of the fetal ductus arteriosus. Avoid use of NSAIDs, including ELYXYB, in pregnant women starting at about 30 weeks gestation and later.

- Oligohydramnios/Neonatal Renal Impairment: Use of NSAIDs, including ELYXYB, at about 20 weeks gestation or later in pregnancy may cause fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. If NSAID treatment is necessary between about 20 weeks and 30 weeks gestation, limit ELYXYB use to the lowest effective dose and shortest duration possible. Discontinue ELYXYB if oligohydramnios occurs.

- Hematological Toxicity: Anemia has occurred in NSAID-treated patients. Monitor hemoglobin or hematocrit in patients with any signs or symptoms of anemia or blood loss. NSAIDs, including ELYXYB™, may increase the risk of bleeding events. Monitor patients for signs of bleeding.

Collegium PHARMACEUTICAL

See full prescribing information, including boxed warning and other serious risks at Elyxyb.com/#isi.

Important Safety Information about ELYXYB (celecoxib) oral solution

ELYXYB
(celecoxib) oral solution

- Masking of Inflammation and Fever: The pharmacological activity of celecoxib in reducing inflammation, and possibly fever, may diminish the utility of diagnostic signs in detecting infections.

- Laboratory Monitoring: Because serious GI bleeding, hepatotoxicity, and renal injury can occur without warning symptoms or signs, consider monitoring patients on long-term NSAID, including ELYXYB, treatment with a CBC and a chemistry profile periodically.

- Disseminated Intravascular Coagulation (DIC): ELYXYB is not indicated in pediatric patients or for the treatment of juvenile rheumatoid arthritis (JRA). Disseminated intravascular coagulation has occurred with use of celecoxib capsules in pediatric patients with systemic-onset JRA, which required monitoring for signs and symptoms of abnormal clotting or bleeding.

ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the labeling:

- Cardiovascular Thrombotic Events
- GI Bleeding, Ulceration, and Perforation
- Hepatotoxicity
- Hypertension
- Heart Failure and Edema
- Renal Toxicity and Hyperkalemia
- Anaphylactic Reactions
- Exacerbation of Asthma Related to Aspirin Sensitivity
- Serious Skin Reactions
- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
- Medication Overuse Headache
- Fetal Toxicity
- Hematologic Toxicity

To report SUSPECTED ADVERSE REACTIONS, contact FDA at 1-800-FDA-1088 or www.fda.gov/safety/medwatch.

Intended for healthcare professionals of the United States of America only.

Collegium PHARMACEUTICAL

See full prescribing information, including boxed warning and other serious risks at Elyxyb.com/#isi.

Important Safety Information about ELYXYB (celecoxib) oral solution

ELYXYB
(celecoxib) oral solution

USE IN SPECIFIC POPULATIONS

Infertility: NSAIDs are associated with reversible infertility. Consider withdrawal of ELYXYB™ in women who have difficulties conceiving.

Pregnancy and Fetal/Neonatal Adverse Reactions

Use of NSAIDs, including ELYXYB, can cause premature closure of the fetal ductus arteriosus and fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Because of these risks, limit dose and duration of Elyxyb use between about 20 and 30 weeks of gestation and avoid ELYXYB use at about 30 weeks of gestation and later in pregnancy

Premature Closure of Fetal Ductus Arteriosus

Use of NSAIDs, including ELYXYB, at about 30 weeks gestation or later in pregnancy increases the risk of premature closure of the fetal ductus arteriosus.

Oligohydramnios/Neonatal Renal Impairment

Use of NSAIDs at about 20 weeks gestation or later in pregnancy has been associated with cases of fetal renal dysfunction leading to oligohydramnios, and in some cases, neonatal renal impairment.

Labor and Delivery

There are no studies on the effects of celecoxib during labor or delivery. In animal studies, NSAIDs, including celecoxib, inhibit prostaglandin synthesis, cause delayed parturition, and increase the incidence of stillbirth.

Lactation

There is no information available regarding the effects of celecoxib on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ELYXYB and any potential adverse effects on the breastfed infant from the celecoxib or from the underlying maternal condition.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established. Disseminated intravascular coagulation has occurred in pediatric patients.

Geriatric Use

Elderly patients, compared to younger patients, are at greater risk for NSAID-associated serious cardiovascular, gastrointestinal, and/or renal adverse reactions. If the anticipated benefit for the elderly patient outweighs these potential risks, treat for the fewest number of days per month, as needed, and monitor patients for adverse effects.

Hepatic and Renal Impairment

No dosage adjustment is needed for patients with mild hepatic impairment (Child-Pugh Class A). Reduce the dose of ELYXYB in patients with moderate hepatic impairment (Child-Pugh Class B). The use of ELYXYB in patients with severe hepatic impairment (Child-Pugh Class C) is not recommended.

No dosage adjustment is needed for patients with mild or moderate renal impairment. ELYXYB is not recommended in patients with severe renal impairment.

Collegium PHARMACEUTICAL

See full prescribing information, including boxed warning and other serious risks at Elyxyb.com/#isi.

Important Safety Information about SYMPROIC (naldemedine) tablets

SYMPROIC
(naldemedine) tablets

SYMPROIC may cause serious side effects, including:

- **Tear in your stomach or intestinal wall (perforation). Stomach pain that is severe can be a sign of a serious medical condition. If you get stomach pain that does not go away, stop taking SYMPROIC and get emergency medical help right away**
- **Opioid withdrawal. You may have symptoms of opioid withdrawal during treatment with SYMPROIC including sweating, chills, tearing, warm or hot feeling to your face (flush), sneezing, fever, feeling cold, abdominal pain, diarrhea, nausea, and vomiting. Tell your healthcare provider if you have any of these symptoms**

Do not take SYMPROIC if you:

- **Have a bowel blockage (intestinal obstruction) or have a history of bowel blockage**
- **Are allergic to SYMPROIC or any of the ingredients in SYMPROIC. See the Medication Guide for a complete list of ingredients in SYMPROIC. Tell your healthcare provider or pharmacist before you start or stop any medicines during treatment with SYMPROIC**

Before you take SYMPROIC, tell your healthcare provider about all of your medical conditions, including if you:

- **Have any stomach or bowel (intestines) problems, including stomach ulcer, Crohn's disease, diverticulitis, cancer of the stomach or bowel, or Ogilvie's syndrome**
- **Have liver problems**
- **Are pregnant or plan to become pregnant. Taking SYMPROIC during pregnancy may cause opioid withdrawal symptoms in your unborn baby. Tell your healthcare provider right away if you become pregnant during treatment with SYMPROIC**
- **Are breastfeeding or plan to breastfeed. It is not known if SYMPROIC passes into your breast milk. You should not breastfeed during treatment with SYMPROIC and for 3 days after your last dose. Taking SYMPROIC while you are breastfeeding may cause opioid withdrawal symptoms in your baby. You and your healthcare provider should decide if you will take SYMPROIC or breastfeed. You should not do both**
- **The most common side effects of SYMPROIC include stomach (abdomen) pain, diarrhea, nausea and vomiting (gastroenteritis)**
- **Tell your healthcare provider if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of SYMPROIC. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088**

Collegium PHARMACEUTICAL

See full prescribing Information and other serious risks at Symproic.com/#isi.

Important Safety Information about SYMPROIC (naldemedine) tablets

SYMPROIC
(naldemedine) tablets

INDICATIONS AND USAGE

SYMPROIC is indicated for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation.

CONTRAINDICATIONS

SYMPROIC is contraindicated in:

- Patients with known or suspected gastrointestinal obstruction and patients at increased risk of recurrent obstruction, due to the potential for gastrointestinal perforation
- Patients with a history of a hypersensitivity reaction to Naldemedine. Reactions have included bronchospasm and rash

WARNINGS AND PRECAUTIONS

Gastrointestinal Perforation: Cases of gastrointestinal perforation have been reported with use of another peripherally acting opioid antagonist in patients with conditions that may be associated with localized or diffuse reduction of structural integrity in the wall of the gastrointestinal tract (e.g., peptic ulcer disease, Ogilvie's syndrome, diverticular disease, infiltrative gastrointestinal tract malignancies, or peritoneal metastases). Take into account the overall risk-benefit profile when using SYMPROIC in patients with these conditions or other conditions which might result in impaired integrity of the gastrointestinal tract wall (e.g., Crohn's disease). Monitor for the development of severe, persistent, or worsening abdominal pain; discontinue SYMPROIC in patients who develop this symptom.

Opioid Withdrawal: Clusters of symptoms consistent with opioid withdrawal, including hyperhidrosis, chills, increased lacrimation, hot flush/flushing, pyrexia, sneezing, feeling cold, abdominal pain, diarrhea, nausea, and vomiting have occurred in patients treated with SYMPROIC. Patients having disruptions to the blood-brain barrier may be at increased risk for opioid withdrawal or reduced analgesia. Take into account the overall risk-benefit profile and monitor for symptoms of opioid withdrawal when using SYMPROIC in such patients.

ADVERSE REACTIONS

- The most common adverse reactions with SYMPROIC compared to placebo in two pooled 12-week studies were: abdominal pain (8% vs 2%), diarrhea (7% vs 2%), nausea (4% vs 2%), and gastroenteritis (2% vs 1%).
- The incidence of adverse reactions of opioid withdrawal in two pooled 12-week studies was 1% (8/542) for SYMPROIC and 1% (3/546) for placebo. In a 52-week study, the incidence was 3% (20/621) for SYMPROIC and 1% (9/619) for placebo.

OVERDOSAGE

Single doses of Naldemedine up to 100 mg (500 times the recommended dose) and multiple doses of up to 30 mg (150 times the recommended dose) for 10 days have been administered to healthy subjects in clinical studies. Dose-dependent increases in gastrointestinal-related adverse reactions, including abdominal pain, diarrhea, and nausea, were observed. Single doses of Naldemedine up to 3 mg (15 times the recommended dose) and multiple doses of 0.4 mg (twice the recommended dose) for 28 days have been administered to patients with OIC in clinical studies. Dose dependent increases in gastrointestinal-related adverse reactions, including abdominal pain, diarrhea, nausea, and vomiting, were observed. Also, chills, hyperhidrosis, and dizziness were reported more frequently at 1 and 3 mg doses and hyperhidrosis at the 0.4 mg dose. No antidote for Naldemedine is known. Hemodialysis is not an effective means to remove Naldemedine from the blood.

Collegium PHARMACEUTICAL

See full prescribing Information and other serious risks at Symproic.com/#isi.

Important Safety Information about SYMPROIC (naldemedine) tablets

USE IN SPECIFIC POPULATIONS

Pregnancy

There are no available data with Naldemedine in pregnant women to inform a drug-associated risk of major birth defects and miscarriage. There is a potential for opioid withdrawal in a fetus when SYMPROIC is used in pregnant women. SYMPROIC should be used during pregnancy only if the potential benefit justifies the potential risk.

Fetal/Neonatal Adverse Reactions

Naldemedine crosses the placenta and may precipitate opioid withdrawal in a fetus due to the immature fetal blood-brain barrier.

Lactation

There is no information regarding the presence of Naldemedine in human milk, the effects on the breastfed infant, or the effects on milk production. Because of the potential for serious adverse reactions, including opioid withdrawal in breastfed infants, a decision should be made to discontinue breastfeeding or discontinue the drug, taking into account the importance of the drug to the mother. If drug is discontinued in order to minimize drug exposure to a breastfed infant, advise women that breastfeeding may be resumed 3 days after the final dose of SYMPROIC.

Pediatric Use

The safety and effectiveness of SYMPROIC have not been established in pediatric patients.

Geriatric Use

Of the 1163 patients exposed to SYMPROIC in clinical studies, 183 (16%) were 65 years of age and over, while 37 (3%) were 75 years and over. No overall differences in safety or effectiveness between these and younger patients were observed, but greater sensitivity of some older individuals cannot be ruled out. In a population pharmacokinetic analysis, no age-related alterations in the pharmacokinetics of Naldemedine were observed.

Hepatic Impairment

The effect of severe hepatic impairment (Child-Pugh Class C) on the pharmacokinetics of Naldemedine has not been evaluated. Avoid use of SYMPROIC in patients with severe hepatic impairment. No dose adjustment of SYMPROIC is required in patients with mild or moderate hepatic impairment.

Non-GAAP Reconciliations

Non-GAAP Reconciliations

Collegium Pharmaceutical, Inc.
Reconciliation of GAAP Net Income to Adjusted EBITDA
(in thousands)
(unaudited)

	Three months ended December 31,		Years ended December, 31	
	2021	**2020**	**2021**	**2020**
GAAP net (loss) income	$ (25,034)	$ 6,958	$ 71,517	$ 26,752
Adjustments:				
Interest expense	4,757	7,737	21,014	28,882
Interest income	(3)	(3)	(12)	(232)
Provision for (benefit from) income taxes	(13,842)	304	(74,891)	830
Depreciation	424	281	1,736	870
Amortization	16,795	16,795	67,181	60,680
Stock-based compensation expense	4,912	6,210	24,255	21,910
Restructuring	4,578	-	4,578	-
Litigation settlements	2,935	-	2,935	-
Total adjustments	$ 20,556	$ 31,324	$ 46,796	$ 112,940
Adjusted EBITDA	$ (4,478)	$ 38,282	$ 118,313	$ 139,692

Non-GAAP Reconciliations

Collegium Pharmaceutical, Inc.
Reconciliation of GAAP Operating Expenses to Adjusted Operating Expenses
(in thousands)
(unaudited)

	Three months ended December 31,		Years ended December 31,	
	2021	2020	2021	2020
GAAP Operating expenses	$ 32,789	29,296	132,989	123,604
Adjustments:				
Stock-based compensation	4,912	6,210	24,255	21,910
Restructuring	4,578	-	4,578	-
Litigation settlements	2,935	-	2,935	-
Total adjustments	12,425	6,210	31,768	21,910
Adjusted operating expenses	$ 20,364	$ 23,086	$ 101,221	$ 101,694