Collegium®
PHARMACEUTICAL

Investor Presentation

February 2023

Nasdaq: COLL

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 2023 financial guidance, including 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, including risks relating to, among others: risks related to the ability to realize the anticipated benefits of our acquisitions at all or within the expected time period; unknown liabilities; risks related to future opportunities and plans for our products, 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 or other litigation that may be brought by or against us; 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. 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 and the accompanying reconciliations, 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.

In this presentation, we discuss the following financial measures that are not calculated in accordance with GAAP, to supplement our consolidated financial statements presented on a GAAP basis.

Adjusted EBITDA

Adjusted EBITDA is a non-GAAP financial measure that represents GAAP net income (loss) adjusted to exclude interest expense, interest income, the benefit from or provision for income taxes, depreciation, amortization, stock-based compensation, and other adjustments to reflect changes that occur in our business but do not represent ongoing operations. 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 (loss), 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 impairment expenses from adjusted EBITDA and, although these are non-cash expenses, the asset being impaired may have to be replaced in the future, the cash requirements for which are not reflected in adjusted EBITDA;
- we exclude restructuring expenses from adjusted EBITDA. Restructuring expenses primarily include employee severance and contract termination costs that are not related to acquisitions. The amount and/or frequency of these restructuring expenses are not part of our underlying business;
- 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;
- we exclude acquisition related expenses as the amount and/or frequency of these expenses are not part of our underlying business. Acquisition related expenses include transaction costs, which primarily consisted of financial advisory, banking, legal, and regulatory fees, and other consulting fees, incurred to complete the acquisition, employee-related expenses (severance cost and benefits) for terminated employees after the acquisition, and miscellaneous other acquisition related expenses incurred; and
- we exclude recognition of the step-up basis in inventory from acquisitions (i.e., the adjustment to record inventory from historic cost to fair value at acquisition) as the adjustment does not reflect the ongoing expense associated with sale of our products as part of our underlying business.

Adjusted Operating Expenses

Adjusted operating expenses is a non-GAAP financial measure that represents GAAP operating expenses adjusted to exclude stock-based compensation expense, and other adjustments to reflect changes that occur in our business but do not represent ongoing operations.

Reconciliations of adjusted EBITDA and adjusted operating expenses to the most directly comparable GAAP financial measures are included in this presentation.

The Company has not provided a reconciliation of its full-year 2023 guidance for adjusted EBITDA or adjusted operating expenses to the most directly comparable forward-looking GAAP measures, in reliance on the unreasonable efforts exception provided under Item 10(e)(1)(i)(B) of Regulation S-K, because the Company 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, acquisition related expense and litigation settlements. These items are uncertain and depend on various factors that are outside of the Company's control or cannot be reasonably predicted. While the Company is unable to address the probable significance of these items, they could have a material impact on GAAP net income and operating expenses for the guidance period. A reconciliation of adjusted EBITDA or adjusted operating expenses would imply a degree of precision and certainty as to these future items that does not exist and could be confusing to investors.

Healthier people.
Stronger communities.

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

Uphold Integrity	Embrace Differences	Encourage Expression	Be Accountable
I	D	E	A
We maintain uncompromising **integrity** in everything we say and do.	We **embrace** differences as they make our ideas richer and serve our patients better.	We **encourage** everyone to think big, push ourselves and make our voices heard.	We are **accountable** to each other, our customers and our community.

Committed to Sustainability, Social Impact and Ethical Governance

Environmental

Be a responsible steward of the environment

- Implementing process improvements to mitigate manufacturing inefficiencies
- Improving waste management systems and evaluating other improvements
- Considering greenhouse gas emissions reduction opportunities

Social

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

- Strengthening customer relationships by leading with science
- Fostering Diversity, Equity and Inclusion (DEI) through Collegium DEI Council initiatives
- Increasing corporate social responsibility with charitable giving and volunteering
- Deepening employee engagement through career development and well-being programming

Governance

Act in the best interests of our stakeholders

- Operating with the highest ethical standards
- Implementing governance that promotes transparency
- Protecting shareholder value with risk management and Board oversight
- Aligning management and shareholder interests with compensation and policies

Inaugural ESG Report for 2022 Now Published: Read Here

Building a Leading, Diversified Specialty Pharmaceutical Company

Investment Highlights — Our Path to Long-term Value Creation

Leading Commercial Portfolio

- **Leader** in responsible pain management
- **Differentiated** and **distinctly positioned** pain portfolio spanning the continuum of care
- Anchored by **two growth drivers**, Belbuca® and Xtampza® ER, with Nucynta Franchise and Symproic® as significant contributors

Strong Financial Position

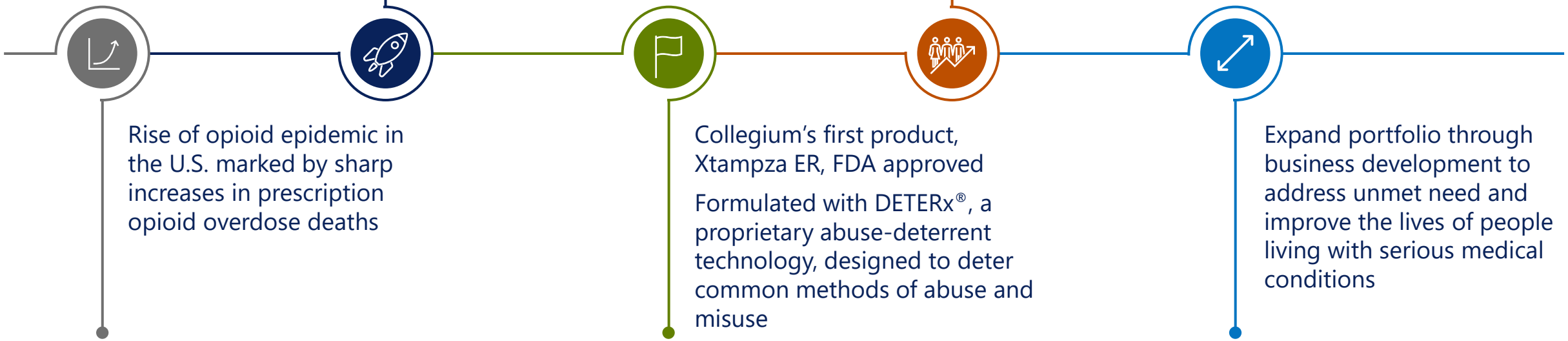
- **Durable revenue** with targeted growth opportunities
- Positioned to **grow adjusted EBITDA** at ~1.5x revenue and ~2.5x adjusted operating expenses in 2023[1]
- Strong, **growing cash generation**
- **Healthy balance sheet**

Disciplined Capital Deployment

- Focused **business development strategy**
- **Rapid debt pay-down**
- **Share repurchase plan available** to opportunistically return capital to shareholders

1. Adjusted EBITDA and adjusted operating expenses are non-GAAP financial measures. See Non-GAAP Financial Measures on Slide 2. Adjusted EBITDA to revenue and adjusted EBITDA to adjusted operating expenses are calculated based on financial data provided by Collegium in its Form 10-K filed with the SEC on February 23, 2023, compared to the mid-point of the 2023 guidance ranges provided by Collegium in its press release filed with the SEC on February 23, 2023.

The Collegium Story



Collegium's Operational Excellence in 2022

Delivered Strong Financial Performance[1]

- ✓ **Record product revenues, net:** $463.9M, up 68% YoY
- ✓ **Adjusted operating expenses:** $122.0, up 21% YoY[2]
- ✓ **Record adjusted EBITDA:** $266.0, up 125% YoY[2]

Achieved Operational Objectives

- ✓ **Achieved** annual run-rate BDSI synergies of ~$85 million
- ✓ **Renegotiated** Xtampza® ER contracts to improve GTNs to <65% in 2023
- ✓ **Achieved** Phases 1 and 2 of Three Phase Action Agenda
- ✓ **Resolved** all 27 opioid industry-related lawsuits

Deployed Capital

- ✓ **Acquired BDSI,** expanding leadership position in responsible pain management and building durable revenue
- ✓ **Rapidly** paid down debt, with year-end 2022 net debt/adjusted EBITDA of 2.0x[2,3]
- ✓ **Opportunistically** returned $19.1M of capital to shareholders through share repurchases in 2022[1]

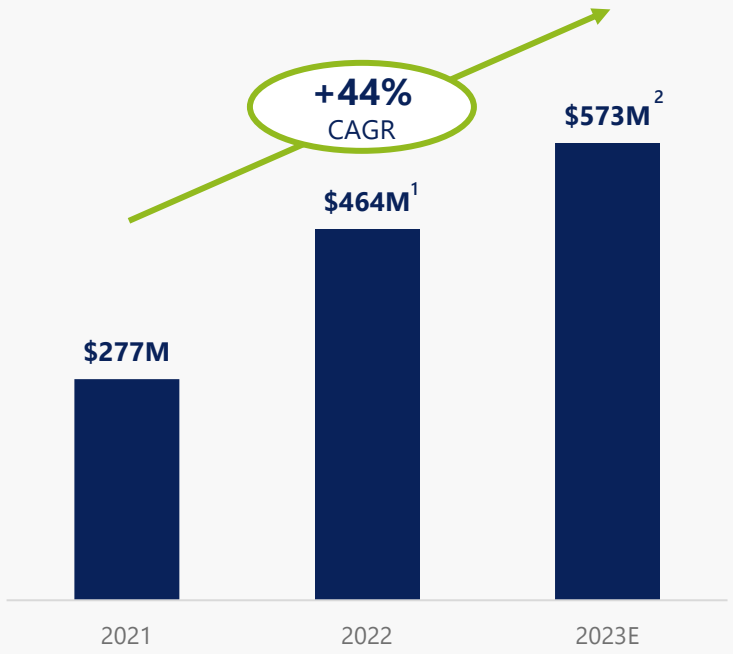
1. This financial data was provided by Collegium in its press release filed with the SEC on February 23, 2023.
2. Adjusted EBITDA and adjusted operating expenses are non-GAAP financial measures. See Non-GAAP Financial Measures on Slide 3.
3. The net debt/adjusted EBITDA ratio is calculated based on financial data provided by Collegium in its Annual Report on Form 10-K filed with the SEC on February 23, 2023. 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.

Collegium PHARMACEUTICAL

2023 To Be A Banner Year

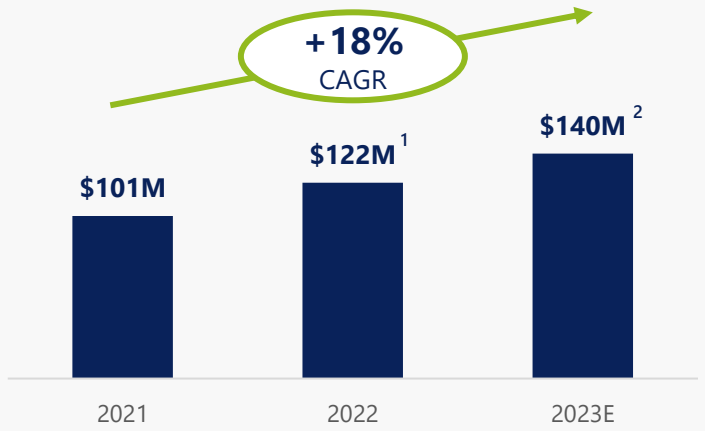
ACCELERATE

Product Revenues, Net



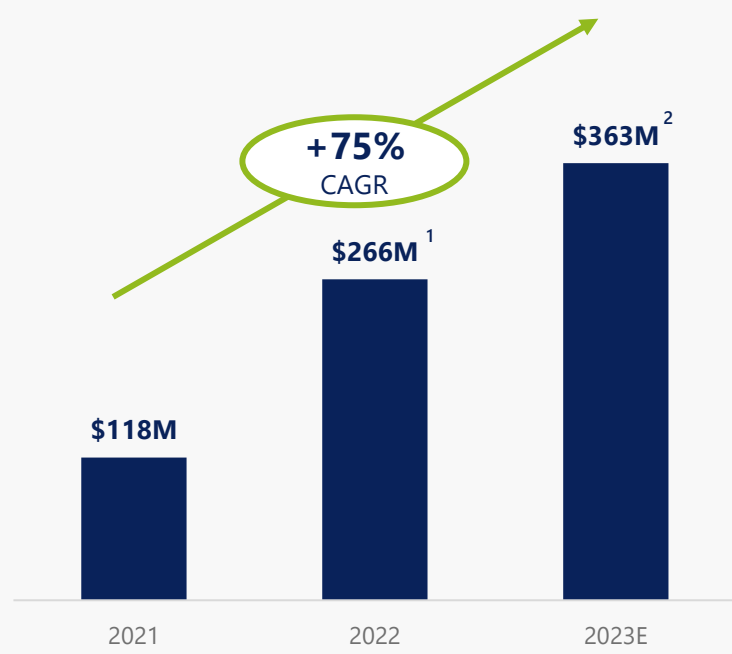
MANAGE

Adjusted Operating Expenses[3]



LEVERAGE

Adjusted EBITDA[3]



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2. This financial data was provided by Collegium in its press release filed with the SEC on February 23, 2023, and represents the mid-point of 2023 financial guidance ranges.
3. Adjusted operating expenses and adjusted EBITDA are non-GAAP financial measures. See Non-GAAP Financial Measures on Slide 3.

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Strategy for a Banner 2023

Maximize Portfolio

- **Generate** strong cash flow from pain portfolio and leveraging cost structure
- **Grow** Belbuca and Xtampza ER prescriptions
- **Maximize** Nucynta Franchise and Symproic®

Deploy Capital

- **Conduct** business development focused on commercial-stage, durable assets
- **Rapidly** pay down debt
- **Opportunistically** return capital to shareholders

Action Agenda Phase 3: Accelerate Top- and Bottom-Line Growth

COMPLETED

Phase 1 (03/22/22–06/30/22)
Seamless Integration

1. Executed with no disruptions to core operations
2. Achieved day one field force readiness
3. Realized majority of targeted run rate synergies

Phase 2 (07/01/22–12/31/22)
Generate Momentum

1. Grew Belbuca® and Xtampza ER
2. Completed Xtampza ER contract renegotiations
3. Achieved remainder of target synergies
4. Synthesized Elyxyb™ launch learnings

2023

Phase 3 (2023)
Accelerate Top- and Bottom-Line Growth

1. Propelled by Xtampza ER gross-to-net of 61% to 63% starting in January 2023
2. Driven by Belbuca and Xtampza ER full year TRx growth
3. Bolstered by fully synergized cost structure

Leading Pain Portfolio Spans the Continuum of Care

Acute

Chronic

Collegium's portfolio holds 50% market share of the branded ER market[1]

NUCYNTA® (tapentadol) TABLETS CII

- Immediate-release formulation of tapentadol

BELBUCA™ CIII (buprenorphine) Buccal Film

- Extended-release buprenorphine
- Classified as schedule III controlled substance

NUCYNTA® ER (tapentadol) EXTENDED-RELEASE TABLETS CII

- Extended-release formulation of tapentadol
- Only extended-release drug approved for neuropathic pain associated with diabetic peripheral neuropathy

Xtampza® ER (oxycodone) EXTENDED-RELEASE CAPSULES CII

- Extended-release oxycodone
- Formulated with DETERx, an abuse-deterrent technology
- Labeling includes human abuse potential studies

Pain Portfolio Distinctly Positioned to Treat Acute and Chronic Pain Responsibly

Sources:
1. IQVIA NPA, December 2022 (Belbuca, Xtampza ER, and Nucynta® ER).

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The Leader in Responsible Pain Management

Collegium is rated #1 in responsible pain management by HCPs

BELBUCA™ (buprenorphine) Buccal Film C III

#1 highest rated branded ER opioid in terms of product differentiation and favorability

74% of surveyed target HCPs plan to increase prescribing

Xtampza® ER (oxycodone) EXTENDED-RELEASE CAPSULES C II

#1 highest rated ER oxycodone in terms of product differentiation and favorability

48% of surveyed target HCPs plan to increase prescribing, while **60%** plan to decrease prescribing of OxyContin®

NUCYNTA® ER (tapentadol) EXTENDED-RELEASE TABLETS C II

#2 highest rated branded ER opioid in terms of product differentiation (only after buprenorphine products)

34% of surveyed target HCPs plan to increase prescribing

Source: ATU (Awareness, Trial, & Usage) Market Research Study, fielded Q4 2022

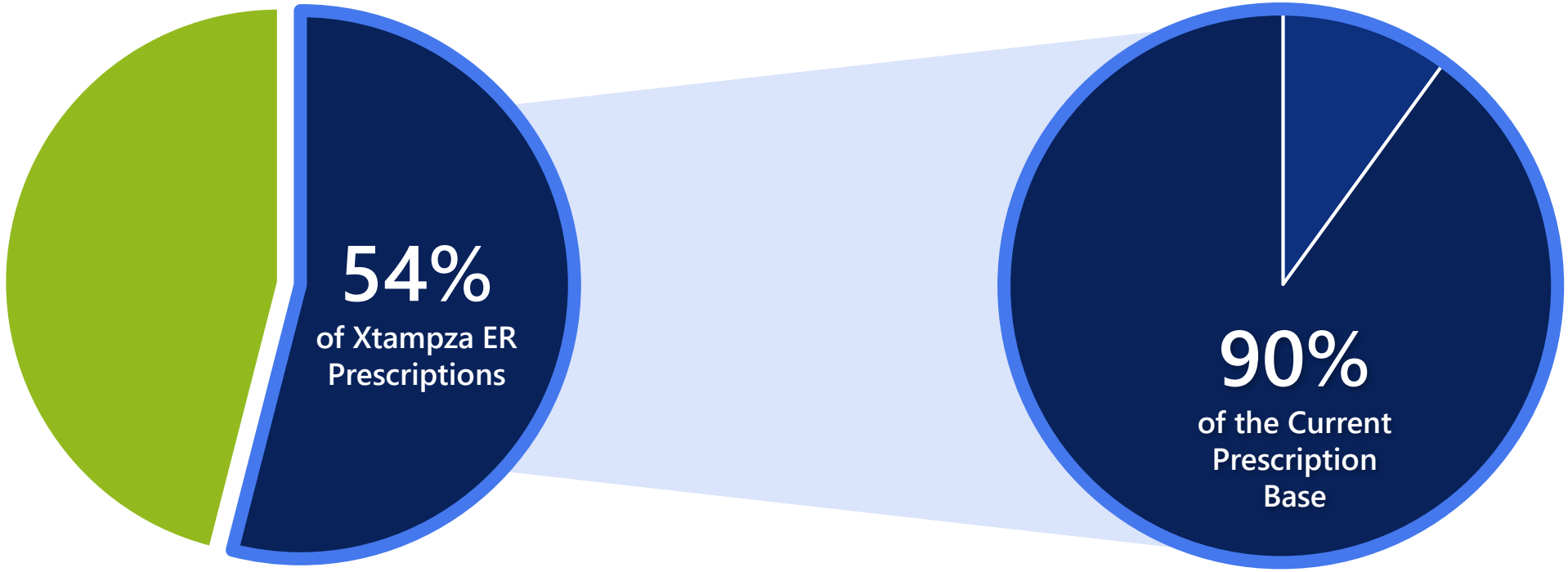
Growth Drivers: Strong Fundamentals, Positioned to Grow

	Strong Market Position	Growing Prescriber Base	GtN Impacts	Market Access
Xtampza ER (oxycodone) Extended-Release Capsules (II)	**35.5% share** of OER market[1]	**~19,000 unique prescribers** in Q4 2022, up 0.5% Q4'22 vs. Q4'21[2]	Expect **61-63% GtN**	Strong coverage across **all payor types**
BELBUCA (buprenorphine) Buccal Film (III)	**38.2% share** of growing buprenorphine market[1]	**~9,100 unique prescribers** in Q4 2022, up 1.7% Q4'22 vs. Q4'21[2]	Expect **stable GtN**	Strong **commercial** coverage

Sources:
1. IQVIA NPA through December 2022.
2. IQVIA Xponent through December 2022.

Collegium Pharmaceutical

Committed to Managing Xtampza ER Gross to Net to <65% Going Forward



Plans representing 54% of Xtampza ER prescriptions successfully renegotiated in 2022 to support **GtN of 61-63% in 2023**

~90% of the renegotiated contracts will maintain Xtampza ER as its exclusive ER oxycodone position or parity position with OxyContin

Additional ~30% of the Xtampza ER contracts are up for renegotiation in 2023

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Maximizing the Value of Nucynta Franchise and Symproic

NUCYNTA® (tapentadol) TABLETS CII

NUCYNTA® ER (tapentadol) EXTENDED-RELEASE TABLETS CII

- Maximize profitability through contracting strategy

Symproic® (naldemedine) tablets 0.2 mg

- Complementary to pain portfolio

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Patent Protected Commercial Portfolio

Growth Drivers

Contributors

Teva currently is the **only** generic manufacturer that has resolved legal challenges to its Xtampza ER and Belbuca ANDAs. Teva does not have tentative or final approval for **either** ANDA and has **waived** its first filer exclusivity with respect to Belbuca.

Projected Exclusivity

Latest Patent Expiry

Reflects (i) for Xtampza ER, the September 2033 entry date set forth in Collegium's settlement agreement with Teva; (ii) for Belbuca, the January 2027 entry date set forth in BDSI's settlement agreement with Teva; (iii) for the Nucynta franchise, and based on the judgment upholding its Orange-Book listed patents, the July 2025 expiry of such patents; and (iv) for Symproic, which does not have any ANDA filers yet, the November 2031 expiry of its Orange Book-listed patents.

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Capital Deployment Priorities Focused on Long-Term Value Creation

Focused Business Development

- Targeting commercial-stage assets to diversify specialty pharmaceutical portfolio
- Peak sales potential of >$150M
- Differentiated product with a leading market position
- Durable with exclusivity into 2030s

Rapidly Paydown Debt

- Net debt/adjusted EBITDA of 2.0x at year-end 2022; expect <1.5x by year-end 2023[1,2]
- Tracking to repay >$160M of Pharmakon loan ($650M issued 3/22/2022) in 2023[2]

Return Capital to Shareholders

- Strong track record of opportunistic share repurchases
- Returned $42.9M and $19.1M to shareholders in 2021 and 2022, respectively[3]
- 2023 share repurchase plan authorizes up to $100M

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2. 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.
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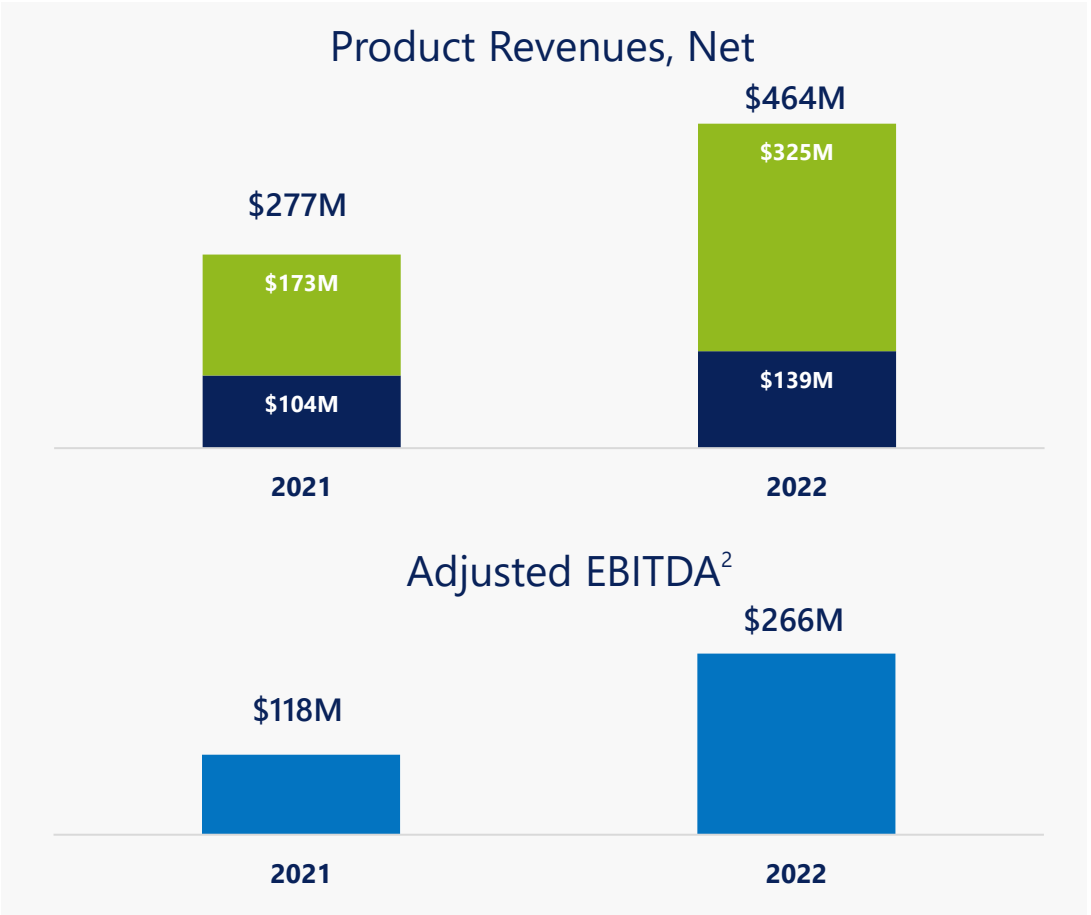
Strong Track Record of Successful Business Development

Expanded top- and bottom-line with Nucynta Franchise (February 2020) and BDSI (March 2022) acquisitions

Impact of Accretive Acquisitions[1]



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3. Represents Xtampza ER product revenues.
4. Represents Nucynta IR, Nucynta ER, Belbuca, Symproic, Elyxyb, and Other product revenues.

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2023 Financial Guidance[1]

Product Revenues, Net	Adjusted Operating Expenses[2] (Excluding Stock-Based Compensation)	Adjusted EBITDA[3] (Excluding Stock-Based Compensation)
$565 – 580M	$135 – 145M	$355 – 370M

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Experienced Management Team and Board of Directors

Joseph Ciaffoni
President, CEO &
Board Member

endo · Biogen · SHIONOGI · Schering-Plough · NOVARTIS · sanofi~synthelabo

Colleen Tupper
EVP & Chief Financial Officer

Takeda · agenus · Gurnet Point Capital · Shire

Scott Dreyer
EVP & Chief
Commercial Officer

The Medicines Company · Biogen · MERCK

Bart Dunn
EVP, Strategy &
Corporate Development

Pfizer · patheon by Thermo Fisher Scientific · INSPIRE Pharmaceuticals · NuPathe · Vivelix · pepsi

Shirley Kuhlmann
EVP, General Counsel &
Chief Administrative Officer

Pepper Hamilton LLP Attorneys at Law · EMORY UNIVERSITY · COLUMBIA COLLEGE

Thomas Smith, M.D., FAAFP
EVP & Chief Medical Officer

biodelivery · teva · Ameritox Medication Monitoring Solutions · Abbott · Charleston Laboratories

Scott Sudduth
EVP & Head of
Technical Operations

moderna · SANOFI GENZYME

Kelly Clements
VP, Chief People Officer

ZEALAND PHARMA · FOUNDATION MEDICINE · Sage Therapeutics · Alkermes · Biogen

Collegium Board of Directors

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President & CEO,
Collegium Pharmaceutical

Neil McFarlane
Former CEO,
Adamas Pharmaceuticals

Michael Heffernan
Chairman of the Board &
Collegium Founder

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

Rita Balice-Gordon
Chief Executive Officer,
Muna Therapeutics

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

Garen Bohlin
Former COO, Sirtris,
Former CEO, Syntonix

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

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

Building a Leading, Diversified Specialty Pharmaceutical Company

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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.

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.

- Complete a REReserve 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

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.

Important Safety Information about 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.

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.

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

Important Safety Information about NUCYNTA (Tapentadol) tablets

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.

Important Safety Information about NUCYNTA (Tapentadol) tablets

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 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

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.

Important Safety Information about SYMPROIC (naldemedine) tablets

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

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

	Years Ended December 31,	
	2022	2021
GAAP net (loss) income	$ (25,002)	$ 71,517
Adjustments:		
Interest expense	63,213	21,014
Interest income	(1,047)	(12)
Benefit from income taxes	(3,845)	(74,891)
Depreciation	2,684	1,736
Amortization	131,469	67,181
Impairment expense	4,786	—
Stock-based compensation expense	22,874	24,255
Restructuring	—	4,578
Litigation settlements	—	2,935
Acquisition related expenses	31,297	—
Recognition of step-up basis in inventory	39,584	—
Total adjustments	$ 291,015	$ 46,796
Adjusted EBITDA	$ 266,013	$ 118,313

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

	Years Ended December 31,	
	2022	2021
GAAP operating expenses	$ 176,169	$ 132,989
Adjustments:		
Stock-based compensation	22,874	24,255
Restructuring	—	4,578
Litigation settlements	—	2,935
Acquisition related expenses	31,297	—
Total adjustments	$ 54,171	$ 31,768
Adjusted operating expenses	$ 121,998	$ 101,221