Investor Presentation

Collegium® PHARMACEUTICAL

February 2024 | 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 2024 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: unknown liabilities; risks related to future opportunities and plans for our products, including uncertainty of the expected financial performance of such 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 maintain regulatory approval of our products, and any related restrictions, limitations, and/or warnings in the label of our products; the size of the markets for our products, 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; 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 believe the presentation of these non-GAAP financial measures, when viewed with our results under GAAP and the accompanying reconciliations, provide analysts, investors, lenders, and other third parties with insights into how we evaluate normal operational activities, including our ability to generate cash from operations, on a comparable year-over-year basis and manage our budgeting and forecasting. In addition, certain non-GAAP financial measures, primarily Adjusted EBITDA, are used to measure performance when determining components of annual compensation for substantially all non-sales force employees, including senior management.

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 or 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 or 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: (i) 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 (ii) 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(s) 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;
- 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; and
- we exclude losses on extinguishments of debt as these expenses are episodic in nature and do not directly correlate to the cost of operating our business on an ongoing basis.

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.

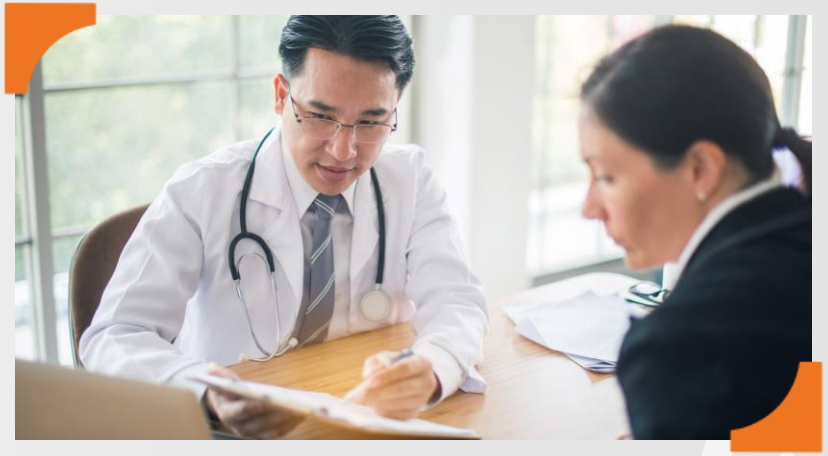
Adjusted Net Income and Adjusted Earnings Per Share

Adjusted net income is a non-GAAP financial measure that represents GAAP net income or loss adjusted to exclude significant income and expense items that are non-cash or not indicative of ongoing operations, including consideration of the tax effect of the adjustments. Adjusted earnings per share is a non-GAAP financial measure that represents adjusted net income per share. Adjusted weighted-average shares - diluted is calculated in accordance with the treasury stock, if-converted, or contingently issuable accounting methods, depending on the nature of the security.

Reconciliations of adjusted EBITDA, adjusted operating expenses, adjusted net income, and adjusted earnings per share to the most directly comparable GAAP financial measures are included in this presentation.

The Company has not provided a reconciliation of its full-year 2024 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.

Doing Good As We Do Well

Partnering with organizations driving equitable access to STEM education in underserved communities to support the next generation of scientists.

Committed To Environmental, Social And Governance (ESG) Initiatives

Operating with integrity, accountability and responsibility and investing in the long-term sustainability of our business and the health of our broader communities.

Read our ESG report collegiumpharma.com.

2024 Focus:
Operational Execution

2024 Priorities: Operational Execution

DELIVER ON

Financial Commitments

- **ACHIEVE** record revenue, adjusted EBITDA and net income
- **GENERATE** record free cash flow

STRATEGICALLY

Deploy Capital

- **RAPIDLY** pay down debt, de-levering on a quarterly basis
- **OPPORTUNISTICALLY** leverage $150M share repurchase program

2024 Financial Guidance[1]

Product Revenues, Net

$580–595M

*Up **3.7%** YoY[2]*

Adjusted Operating Expenses[3]

(Excluding Stock-Based Compensation)

$120–125M

*Down **(0.9)%** YoY[2]*

Adjusted EBITDA[3]

(Excluding Stock-Based Compensation)

$380–395M

*Up **5.6%** YoY[2]*

1. This financial data was provided by Collegium in its press release filed with the SEC on February 22, 2024.
2. This financial data is calculated based on data provided by Collegium in its press release filed with the SEC on February 22, 2024, and represents the percent change of the mid-point of 2024 financial guidance ranges compared to 2023 results.
3. Represents a non-GAAP financial measure. Refer to "Non-GAAP Financial Measures" on slide 2.

Collegium PHARMACEUTICAL

Disciplined Capital Deployment

Rapidly Pay Down Debt

- Ended 2023 with net debt/adjusted EBITDA of **~1.0x;** expect **de minimis by year-end 2024**[1,2]
- **Repaid $162.5M** of Pharmakon loan in 2023 ($650M issued 3/22/2022) and will repay $183.3M in 2024[2]
- Pharmakon loan expected to be **paid in full in Q1'26**[2]

Leverage Share Repurchase Program

- To date, **returned $137M** to shareholders by repurchasing 6.3M shares at average price of $21.65[3]
- Board authorized **new $150M share repurchase program through Q2'25**

1. Adjusted EBITDA is a non-GAAP financial measure. Refer to "Non-GAAP Financial Measures" on slide 2. 2023 net debt/adjusted EBITDA is calculated based on financial data provided by Collegium in its Form 8-K and Form 10-K filed with the SEC on February 22, 2024. 2024 net debt/adjusted EBITDA is calculated based on Collegium's forecast of net debt at year-end 2024, compared to the mid-point of the 2024 guidance ranges provided by Collegium in its press release filed with the SEC on February 22, 2024. This financial data assumes no additional debt is incurred.
2. Details regarding the Pharmakon term-loan debt amortization schedule were provided by Collegium on form SC TO-C filed with the SEC on February 14, 2022.
3. This financial data is calculated from data provided by Collegium in its Annual Report on Form 10-K filed with the SEC on February 22, 2024.

Collegium: The Leader in Responsible Pain Management

Path to Building a Leading Pain Portfolio

Rated #1 in responsible pain management by HCPs[1]; portfolio holds over 50% market share of branded ER market[2]

1990s – 2000s

Rise of opioid epidemic in the U.S., marked by sharp increases in prescription opioid overdose deaths

2002

Collegium formed to address opioid epidemic through development of prescription pain treatments with abuse-deterrent properties

2015

Initial Public Offering

2016

FDA approved Collegium's first product, Xtampza® ER

Formulated with DETERx®, a proprietary abuse-deterrent technology, designed to deter common methods of abuse and misuse

2018 – 2022

Collegium in-licenses and acquires the Nucynta Franchise and acquires BioDelivery Sciences International (BDSI) adding Belbuca® to the pain portfolio

Present

Collegium is the leader in responsible pain management with a differentiated pain portfolio of four products distinctly positioned to treat acute and chronic pain responsibly

1. ATU (Awareness, Trial, & Usage) Market Research Study, fielded Q4 2022.
2. IQVIA NPA through December 2023 (Belbuca, Xtampza ER, and Nucynta® ER).

Pain Portfolio Growth Drivers

	BELBUCA™ (buprenorphine) Buccal Film	Xtampza® ER (oxycodone) EXTENDED-RELEASE CAPSULES
	Expect prescription and revenue growth in 2024	**Expect revenue growth in 2024**
Strong Market Position	**36.6% share** of growing buprenorphine market[1]	**37.1% share** of OER market[1]
Large Prescriber Base	**~9.9K unique prescribers** in Q4'23[2]	**~17.0K unique prescribers** in Q4'23[2]
GtN Impacts	Expect **stable GtN**	Expect **GtN improvement to 56-58%**
Market Access	Strong **commercial** coverage	Strong coverage across **all payor types**

1. IQVIA NPA through December 2023.
2. IQVIA Xponent through December 2023; approximate quarterly prescriber counts.

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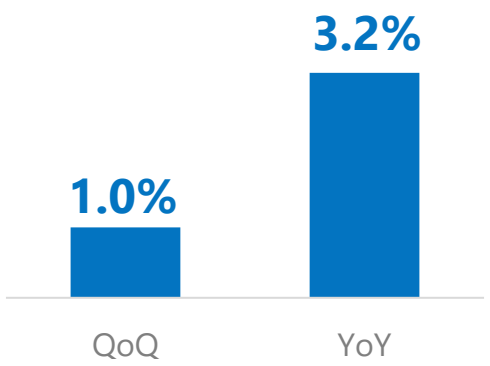
Well Positioned to Grow Belbuca Prescriptions and Revenue in 2024

Positive Momentum for Belbuca Coming Out of 2023

GROWING BELBUCA PRESCRIPTIONS

Growth in Q4'23 Belbuca prescriptions[1]



EXPANDING BUPRENORPHINE MARKET

+6.4%

growth in total buprenorphine prescriptions in 2023[1]

STRONG BRAND FUNDAMENTALS & PAYOR PROGRESS

#1 highest rated branded ER opioid in terms of product differentiation and favorability[2]

74% of surveyed target HCPs plan to increase prescribing[2]

In 2023, successfully renegotiated major Medicare Part D plan representing **12%** of Belbuca prescriptions; maintained formulary position at significantly lower rebate

Achieved new payor win for Belbuca in Medicare Part D plan representing **~1M** covered lives

1. IQVIA NPA through December 2023.
2. ATU (Awareness, Trial, & Usage) Market Research Study, fielded Q4 2022.

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Xtampza ER Poised to Grow Revenue in 2024

SUCCESSFUL CONTRACT RENEGOTIATION STRATEGY

Plans representing **84%** of Xtampza ER prescriptions renegotiated in 2022 and 2023

77% *of renegotiation opportunity maintained position at equal or better rebate*

23% *of renegotiation opportunity removed from formulary to parity position with Oxycontin® with no rebate*

Xtampza ER GtN expected to improve to 56%–58% in 2024

STRONG BRAND FUNDAMENTALS & MARKET ACCESS POSITION

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

48% of surveyed target HCPs plan to increase prescribing, while 60% plan to decrease prescribing of OxyContin[1]

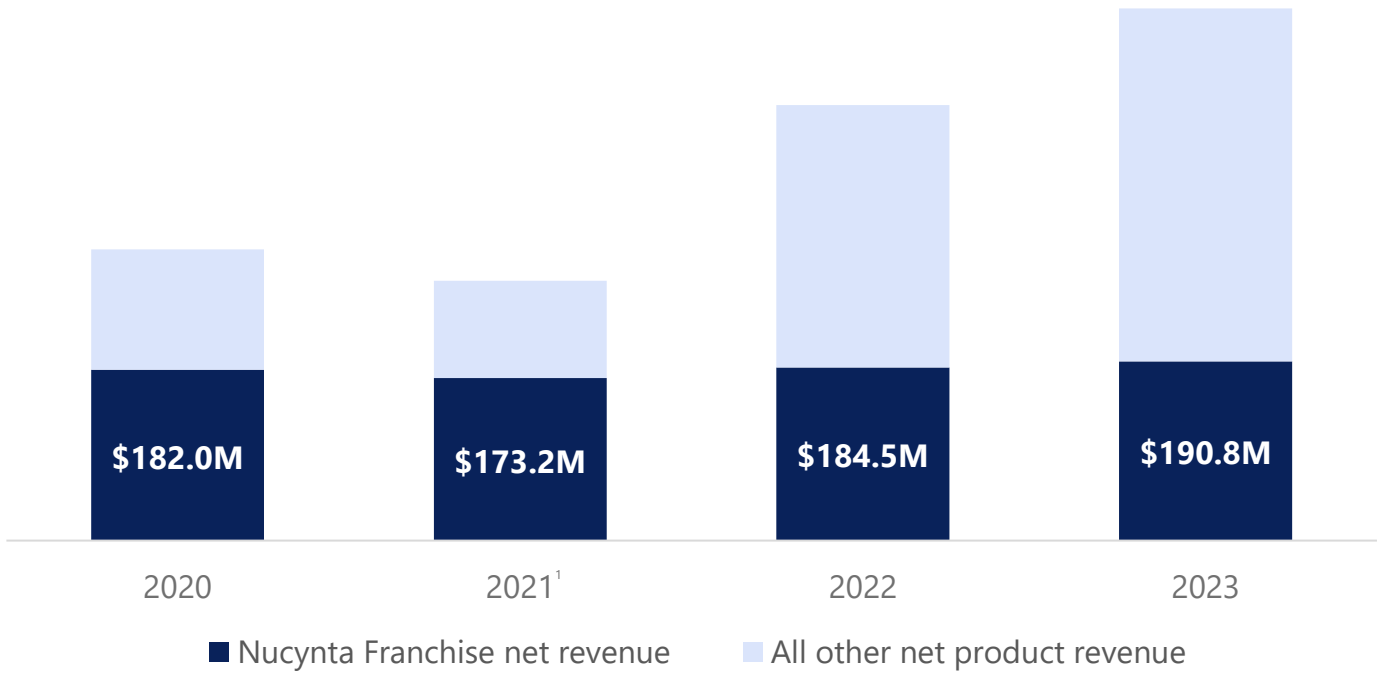
Strong market access coverage across all payor types, commercial and Medicare Part D

1. ATU (Awareness, Trial, & Usage) Market Research Study, fielded Q4 2022.

Nucynta Franchise: Stable Contributor with Mid-Term Outlook Bolstered by Regulatory Exclusivity Extension

Stable Contributor to the Pain Portfolio

Product Revenues, Net



Improved Outlook for 2025 and 2026

- Nucynta® granted New Patient Population exclusivity in pediatrics; U.S. regulatory exclusivity extended from June 27, 2025, to July 3, 2026
- Potential for 6-month pediatric exclusivity (Dec. 2025 for Nucynta® ER, Jan. 2027 for Nucynta)
- Royalty declines from 14% to 7% in 2025

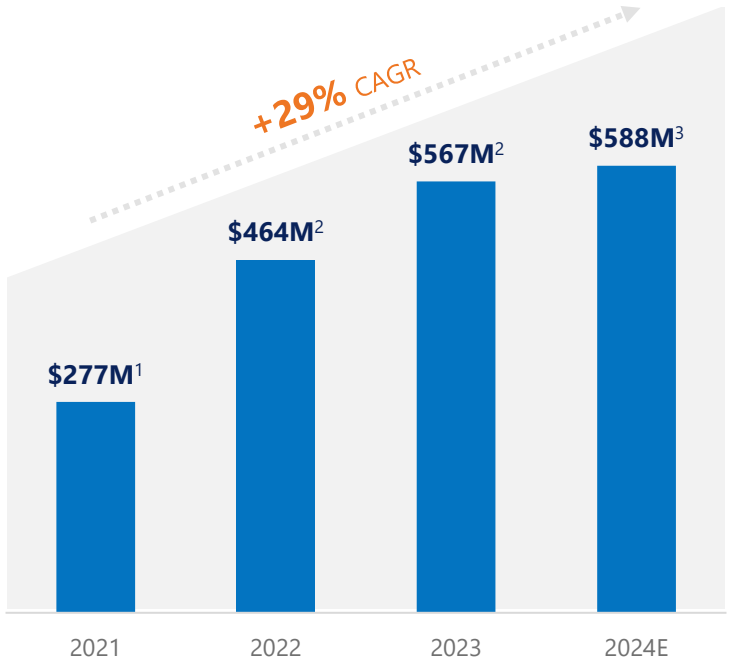
1. 2021 product revenues, net were impacted by a negative $38.3M returns adjustment, including a negative $24.5M returns adjustment related to Nucynta.

Strong Track Record of Execution and Achieving Financial Commitments

Track Record of Strong Top- and Bottom-Line Growth

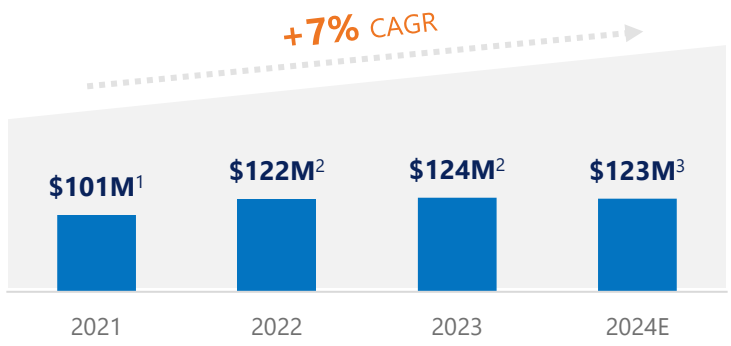
GROW

Product Revenues, Net



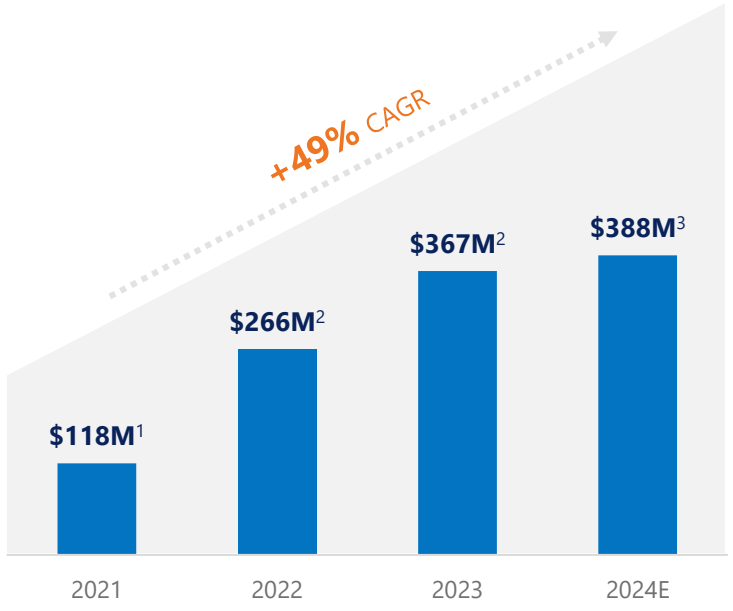
LEVERAGE

Adjusted Operating Expenses[4]



EXPAND

Adjusted EBITDA[4]



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4. Represents a non-GAAP financial measure. Refer to "Non-GAAP Financial Measures" on slide 2.

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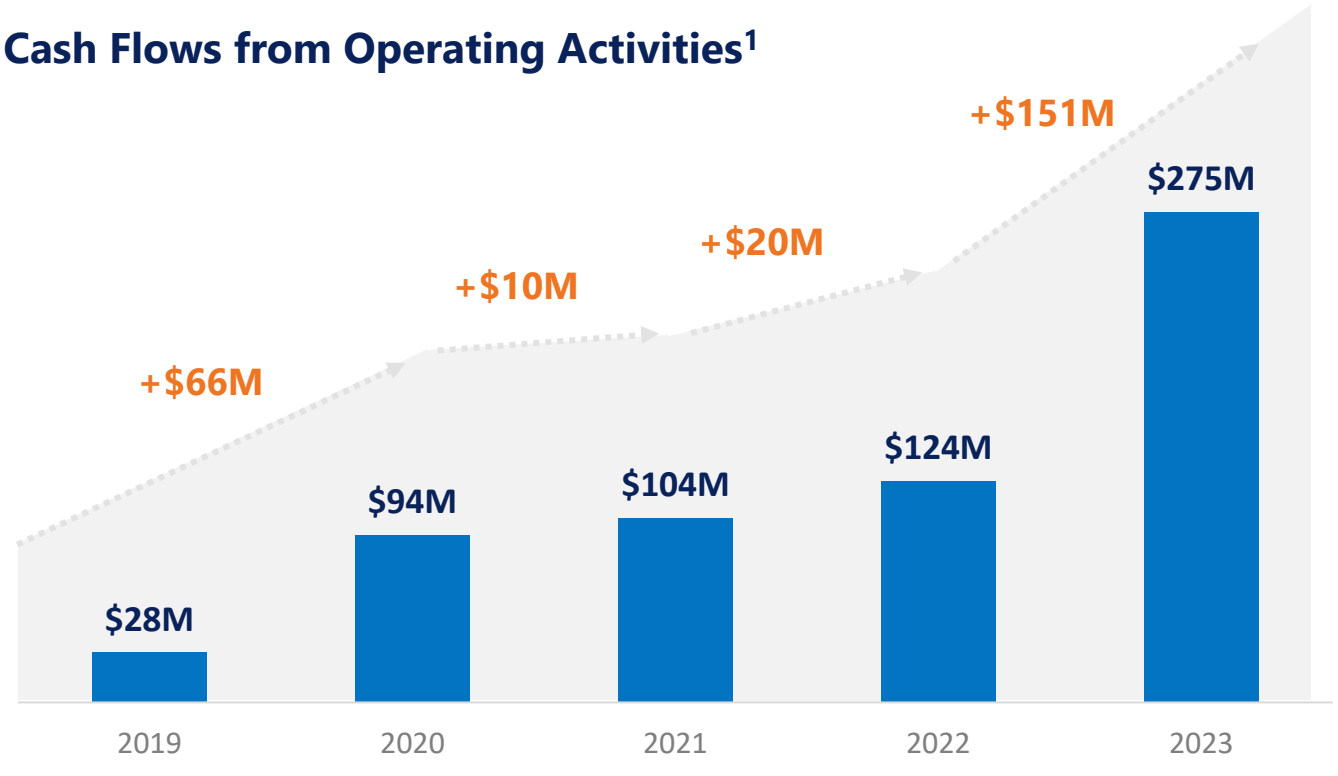
Robust Operating Cash Flow Generation from Pain Portfolio

Cash Flows from Operating Activities[1]



	2019	2020	2021	2022	2023
Period End Cash and Marketable Securities[2]	$170M	$174M	$186M	$174M	$311M

- Strong cash generation enables disciplined capital deployment strategy
- Executed $137M in share repurchases to date[1]
- Invested ~$1B in business development 2019–2023[3]

1. This financial data was provided by Collegium in its Annual Reports on Form 10-K filed with the SEC on February 25, 2021; February 24, 2022; February 23, 2023; and February 22, 2024.
2. Period end cash and marketable securities excludes restricted cash.
3. Represents the sum of the purchase price consideration paid for the Nucynta Acquisition in 2020 and the BDSI Acquisition in 2022 as disclosed on Annual Reports on Form 10-K filed with the SEC on February 25, 2021 and February 23, 2023, respectively.

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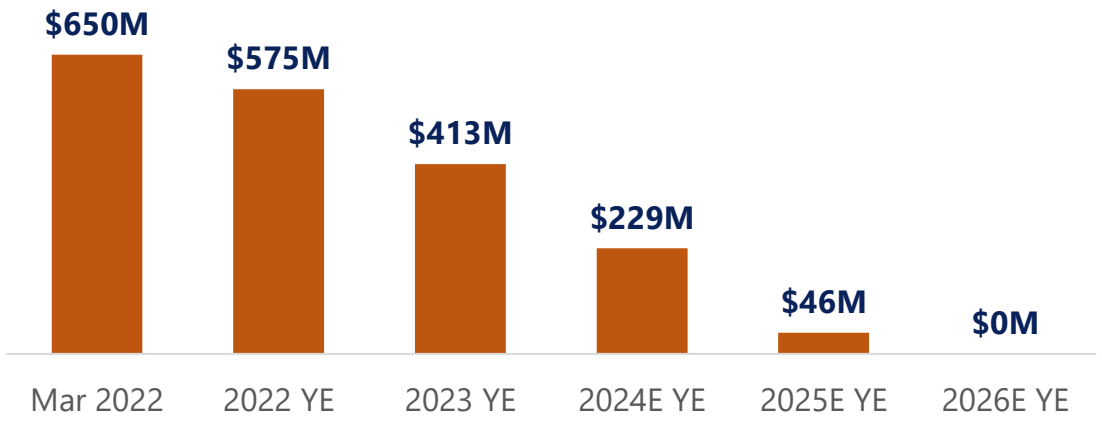
Disciplined Capital Deployment

Rapid Paydown of Debt

Pharmakon Loan Principal Balance



- Ended 2023 with net debt/adjusted EBITDA of ~1.0x; expected to be de minimis by year-end 2024[1,2]
- Repaid $162.5M of Pharmakon loan in 2023 ($650M issued 3/22/2022) and will repay $183.3M in 2024[2]
- Pharmakon loan expected to be paid in full in Q1'26[2]

Convertible Debt

- $267.9M in convertible debt principal as of 12/31/2023
- In February 2023, completed a $241.5M convertible note financing:
  - Due in February 2029
  - Interest rate of 2.875%
  - Conversion premium: ~30% (conversion price of $36.56 per share)
  - Used portion of proceeds to repurchase $117.4M of principal related to previously issued convertible notes due 2026
  - Later maturity provides more financial flexibility in the management of debt
  - Net increase in principal balance of convertible debt was $124.1M from 12/31/2022

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2. Details regarding the Pharmakon term-loan debt amortization schedule were provided by Collegium on form SC TO-C filed with the SEC on February 14, 2022.

Opportunistic Share Repurchases[1]

Returned $137M of Capital to Shareholders from 2021 to 2023

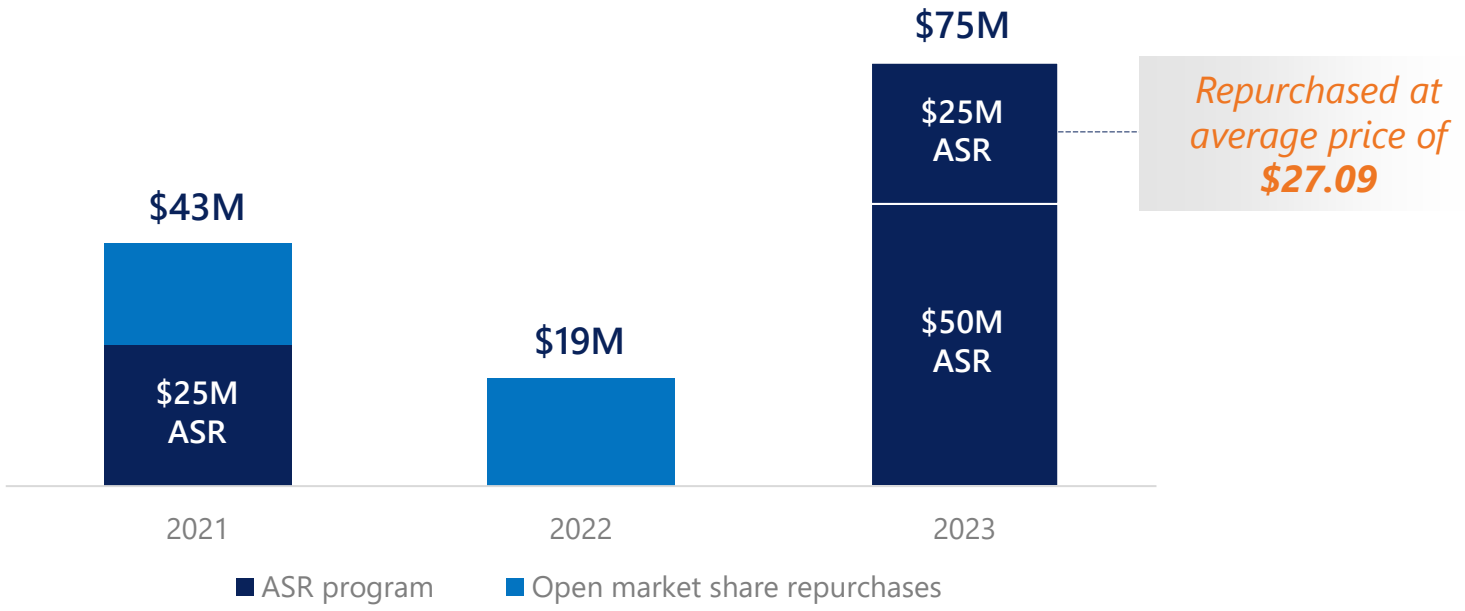
Repurchased 6.3M shares at average price of $21.65

Average Repurchase Price

2021 - **$19.93**

2022 - **$17.57**

2023 - **$24.29**



Board Authorized New $150M Share Repurchase Program Through Q2'25

1. This financial data is calculated from data provided by Collegium in its Annual Reports on Form 10-K filed with the SEC on February 22, 2024.

Track Record of Successful Business Development

Strategically Compelling Acquisitions

NUCYNTA® (tapentadol) TABLETS CII

NUCYNTA® ER (tapentadol) EXTENDED-RELEASE TABLETS CII

Nucynta Franchise (February 2020)

biodelivery SCIENCES

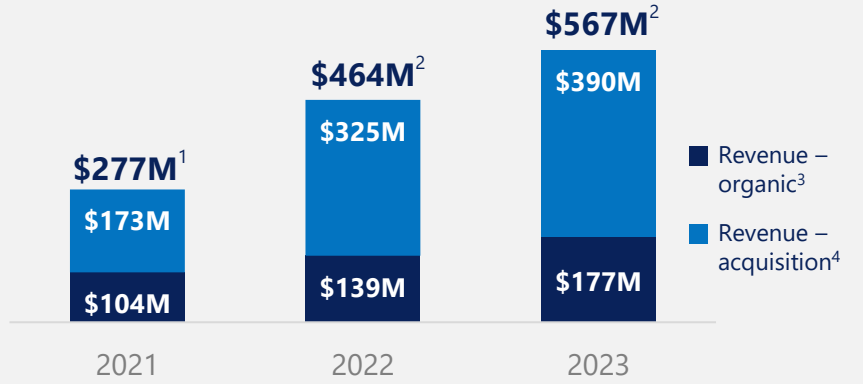
BELBUCA™ CIII (buprenorphine) Buccal Film

BDSI (March 2022)

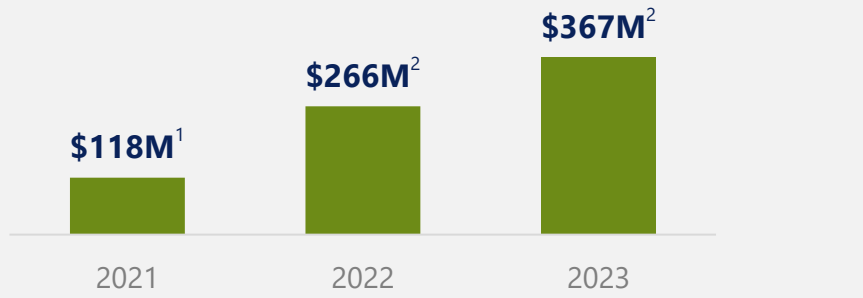
Successful business development established Collegium as the leader in responsible pain management and added diversified revenue streams and growth opportunities to the business

Impact of Accretive Acquisitions

Product Revenues, Net



Adjusted EBITDA[5]



1. This financial data was provided by Collegium on Form 10-K filed with the SEC on February 23, 2023.
2. This financial data was provided by Collegium on Form 10-K filed with the SEC on February 22, 2024.
3. Represents Xtampza ER product revenues.
4. Represents Nucynta IR, Nucynta ER, Belbuca, Symproic, and Other product revenues.
5. Represents a non-GAAP financial measure. Refer to "Non-GAAP Financial Measures" on slide 2.

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Strong IP Management

Patent Protected Commercial Portfolio

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.

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, the New Patient Population exclusivity granted to Nucynta, and based on the judgment upholding its Orange-Book listed patents, the July 2025 and 2028 expiries of such patents for Nucynta ER; 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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Summary

Creating Long-Term Value Through Operational Execution

DELIVER ON

Financial commitments of top- and bottom-line growth:

- Achieve record revenue, adjusted EBITDA and net income
- Generate record free cash flow

STRATEGICALLY

Deploy capital in a disciplined manner:

- Rapidly pay down $183.3M in debt in 2024
- Return capital to shareholders by leveraging $150M share repurchase program

Creating value for shareholders by:

✓ **Growing** revenue

✓ **Increasing** profitability

✓ **Generating** strong cash flows

✓ **Strategically deploying** capital

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Important Safety Information

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

XTAMPZA ER (Oxycodone) extended-release capsules

WARNING: SERIOUS AND LIFE-THREATENING RISKS FROM USE OF XTAMPZA ER

Addiction, Abuse, and Misuse

Because the use of 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 and reassess all patients regularly for the development of these behaviors and conditions.

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of XTAMPZA ER, especially during initiation or following a dosage increase. To reduce the risk of respiratory depression, proper dosing and titration of XTAMPZA ER are essential.

Accidental Ingestion

Accidental ingestion of even one dose of XTAMPZA ER, especially by children, can result in a fatal overdose of oxycodone.

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.

Neonatal Opioid Withdrawal Syndrome (NOWS)

If opioid use is required for an extended period of time in a pregnant woman, advise the patient of the risk of NOWS, which may be life-threatening if not recognized and treated. Ensure that management by neonatology experts will be available at delivery.

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

Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)

Healthcare providers are strongly encouraged to complete a REMS-compliant education program and to counsel patients and caregivers on serious risks, safe use, and the importance of reading the Medication Guide with each prescription.

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. Regularly evaluate patients receiving XTAMPZA ER and any CYP3A4 inhibitor or inducer.

Important Safety Information about BELBUCA (buprenorphine buccal film)

WARNING: SERIOUS AND LIFE-THREATENING RISKS FROM USE OF BELBUCA

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 and reassess all patients regularly for the development of these behaviors and conditions.

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of BELBUCA, especially during initiation or following a dosage increase. To reduce the risk of respiratory depression, proper dosing and titration of BELBUCA are essential. 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 of even one dose of BELBUCA, especially in children, can result in a fatal overdose of buprenorphine.

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 BELBUCA and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate.

Neonatal Opioid Withdrawal Syndrome (NOWS)

If opioid use is required for an extended period of time in a pregnant woman, advise the patient of the risk of NOWS, which may be life-threatening if not recognized and treated. Ensure that management by neonatology experts will be available at delivery.

Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)

Healthcare providers are strongly encouraged to complete a REMS-compliant education program and to counsel patients and caregivers on serious risks, safe use, and the importance of reading the Medication Guide with each prescription.

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

NUCYNTA ER (tapentadol) extended-release tablets

WARNING: SERIOUS AND LIFE-THREATENING RISKS FROM USE OF NUCYNTA ER

Addiction, Abuse, and Misuse

Because the use of 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 and reassess all patients regularly for the development of these behaviors and conditions.

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of NUCYNTA ER, especially during initiation or following a dosage increase. To reduce the risk of respiratory depression, proper dosing and titration of NUCYNTA ER are essential. 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.

Interaction with Alcohol

Instruct patients not to consume alcoholic beverages or use prescription or nonprescription 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.

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

Neonatal Opioid Withdrawal Syndrome

If opioid use is required for an extended period of time in a pregnant woman, advise the patient of the risk of NOWS, which may be life-threatening if not recognized and treated. Ensure that management by neonatology experts will be available at delivery.

Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)

Healthcare providers are strongly encouraged to complete a REMS-compliant education program and to counsel patients and caregivers on serious risks, safe use, and the importance of reading the Medication Guide with each prescription.

Important Safety Information about NUCYNTA (Tapentadol) tablets

NUCYNTA
(tapentadol) tablets

WARNING: SERIOUS AND LIFE-THREATENING RISKS FROM USE OF NUCYNTA TABLETS

Addiction, Abuse, and Misuse

Because the use of NUCYNTA tablets 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 and reassess all patients regularly for the development of these behaviors and conditions.

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of NUCYNTA tablets, especially during initiation or following a dosage increase. To reduce the risk of respiratory depression, proper dosing and titration of NUCYNTA tablets are essential.

Accidental Ingestion

Accidental ingestion of even one dose of NUCYNTA tablets, especially by children, can result in a 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 tablets and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate.

Neonatal Opioid Withdrawal Syndrome (NOWS)

If opioid use is required for an extended period of time in a pregnant woman, advise the patient of the risk of NOWS, which may be life-threatening if not recognized and treated. Ensure that management by neonatology experts will be available at delivery.

Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)

Healthcare providers are strongly encouraged to complete a REMS-compliant education program and to counsel patients and caregivers on serious risks, safe use, and the importance of reading the Medication Guide with each prescription.

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 (Loss) to Adjusted EBITDA
(in thousands)
(unaudited)

	Years Ended December 31,		
	2023	2022	2021
GAAP net income (loss)	$ 48,155	$ (25,002)	$ 71,517
Adjustments:			
Interest expense	83,339	63,213	21,014
Interest income	(15,615)	(1,047)	(12)
Loss on extinguishment of debt	23,504	—	—
Provision for (benefit from) income taxes	27,578	(3,845)	(74,891)
Depreciation	3,496	2,684	1,736
Amortization	145,760	131,469	67,181
Impairment expense	—	4,786	—
Stock-based compensation	27,136	22,874	24,255
Restructuring	—	—	4,578
Litigation settlements	8,500	—	2,935
Acquisition related expenses	—	31,297	—
Recognition of step-up basis in inventory	15,116	39,584	—
Total adjustments	$ 318,814	$ 291,015	$ 46,796
Adjusted EBITDA	$ 366,969	$ 266,013	$ 118,313

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

	Years Ended December 31,		
	2023	2022	2021
GAAP operating expenses	$ 159,208	$ 176,169	$ 132,989
Adjustments:			
Stock-based compensation	27,136	22,874	24,255
Restructuring	—	—	4,578
Litigation settlements	8,500	—	2,935
Acquisition related expenses	—	31,297	—
Total adjustments	$ 35,636	$ 54,171	$ 31,768
Adjusted operating expenses	$ 123,572	$ 121,998	$ 101,221