Aptinyx Reports Fourth Quarter and Full Year 2020 Financial Results and Provides Corporate Update

Phase 2 studies in fibromyalgia and painful DPN enrolling as planned – data readouts expected in 1H 2022

Phase 2 study in cognitive impairment expected to recommence imminently – data readout expected in 2H 2022

Reported data from Phase 2 exploratory study of NYX-783 in PTSD, supporting further clinical development – meeting with FDA to discuss future development path April 29, 2021

Strong cash position expected to support operations through multiple clinical data readouts and into 2023

Conference call today at 5:00 p.m. EST

EVANSTON, Ill., March 24, 2021 -- Aptinyx Inc. (Nasdaq: APTX), a clinical-stage biopharmaceutical company developing transformative therapies for the treatment of brain and nervous system disorders, today reported financial results for the fourth quarter and full year 2020 and provided updates across the company's pipeline of novel NMDA receptor modulators.

"Despite the COVID-19 pandemic, we are excited to be advancing clinical development across all four of our pipeline programs," said Norbert Riedel, Ph.D., chief executive officer of Aptinyx. "The recent and upcoming recommencements of key clinical studies are a testament to the dedication of our team at Aptinyx, and I am grateful to all of my colleagues who have been instrumental in these efforts."

Dr. Riedel continued, "2020 was a very important year in further validating the novel mechanism through which our NMDA receptor modulators act. The results from our completed PTSD study enhance our understanding of the neurobiology of PTSD and the potential for NYX-783 to be a significant advancement in the field. We have observed the therapeutically relevant activity of our compounds across numerous studies, both in patients and in healthy volunteers. We believe the foundational data we have collected across our pipeline thus far have informed and de-risked the multiple Phase 2 studies that we expect to readout in the next 12-24 months. All of this progress sets us up nicely to bring much needed therapeutic innovation to multiple challenging CNS disorders in the years to come. And, with these important clinical milestones ahead, we are pleased to be in a strong financial position, with a cash balance that we anticipate will support our planned operations into 2023."

Pipeline Updates

Chronic Pain Pipeline – NYX-2925

Aptinyx is developing NYX-2925 for the treatment of chronic centralized pain conditions. To date, NYX-2925 has been studied in more than 400 human subjects, including in three Phase 1 studies in healthy volunteers and two completed Phase 2 studies in patients with chronic pain. Across all studies, NYX-2925 has been well tolerated with no drug-related serious adverse events reported.

- **Development in fibromyalgia:** Following the completion of a successful Phase 2a neuroimaging biomarker study in 2019, Aptinyx initiated a Phase 2b study to evaluate NYX-2925 in patients with fibromyalgia. In March 2020, Aptinyx temporarily suspended enrollment of new patients in the Phase 2b study due to the COVID-19 pandemic.

    - In September 2020, Aptinyx recommenced enrollment in the Phase 2b study with targeted protocol amendments designed to streamline enrollment and ensure safety of patients and study personnel amidst the ongoing COVID-19 pandemic.

    - Study design:
        - The study is a randomized, double-blind, parallel-design, placebo-controlled study to evaluate once-daily oral dosing of two dose levels of NYX-2925 (50 mg and 100 mg) compared to placebo in approximately 300 patients with fibromyalgia.
        - The primary endpoint is the change in average daily pain score over a 12-week treatment period as reported on the 10-point numeric rating scale (NRS).
        - Multiple secondary endpoints will be evaluated to characterize the effects of NYX-2925 across the broad array of symptoms experienced by patients with fibromyalgia.

    - Enrollment to date has been consistent with the company's plan and Aptinyx anticipates reporting top-line data from the study in the first half of 2022.

- **Development in painful diabetic peripheral neuropathy (DPN):** Following the completion of a Phase 2 study in 2019, in which NYX-2925 exhibited the strongest activity in patients with advanced DPN, Aptinyx initiated a Phase 2b study to support findings from the prior study. In March 2020, Aptinyx temporarily suspended enrollment of new patients in the Phase 2b study due to the COVID-19 pandemic.

    - In December 2020, Aptinyx recommenced the Phase 2b study with targeted protocol amendments designed to streamline enrollment and ensure safety of patients and study personnel amidst the ongoing COVID-19 pandemic.

    - Study design:
        - The study is a randomized, double-blind, parallel-design, placebo-controlled study to evaluate once-daily oral dosing of 50 mg of NYX-2925 compared to placebo in approximately 200 patients with advanced DPN.
        - The primary endpoint is the change in average daily pain score over a 12-week treatment period as reported on the 10-point NRS.
        - Multiple secondary endpoints will be evaluated to characterize the effects of NYX-2925 across symptoms experienced by patients with painful DPN.

    - Enrollment to date has been consistent with the company's plan and Aptinyx anticipates reporting top-line data from the study in the first half of 2022.

- **Publication of review article in *Medicine in Drug Discovery* highlighting preclinical data supporting the potential of NYX-2925 to treat chronic, centralized pain conditions:** In January 2021, Aptinyx announced the publication of a recent review article in *Medicine in Drug Discovery* featuring data on its investigational novel NMDA receptor modulator, NYX-2925. The data span across numerous preclinical models and highlight the potential therapeutic benefits of NYX-2925 in treating chronic, centralized pain conditions.

Psychiatry Pipeline – NYX-783
Aptinyx is developing NYX-783 for the treatment of PTSD. Across the completed Phase 1 and Phase 2 studies, including more than 200 human subjects combined, NYX-783 was well tolerated with no drug-related serious adverse events reported.

- **Development in PTSD:** In October 2020, Aptinyx reported results from a Phase 2a exploratory study of NYX-783 in patients with PTSD.
    - The study was a double-blind, placebo-controlled, sequential parallel comparison design (SPCD) study in approximately 160 patients with PTSD. The study consisted of two four-week treatment stages, in which patients were randomly assigned to receive once-daily oral doses of either placebo, 10 mg NYX-783, or 50 mg NYX-783.
    - This was an initial exploratory study and thus was powered based on clinical, and not statistical, considerations to detect signals of efficacy. Nonetheless, statistically significant separation from placebo was observed on some measures.
    - Results:
        - Clinically meaningful improvements from baseline were observed on the CAPS-5 Total score within four weeks in the 50 mg dose arm.
            - Compared to placebo, a significantly greater proportion of patients on NYX-783 50 mg achieved a clinically meaningful improvement in CAPS-5 Total score in Stage 1 of treatment.
        - Statistically significant improvement was observed on CAPS-5 Arousal and Reactivity score.
        - Consistent improvements were observed across three of the four CAPS-5 symptom cluster scores, with statistically significant improvements compared to placebo observed on two of the four symptom clusters in Stage 1.
    - Next steps:
        - Aptinyx is scheduled to hold a Type C meeting with the U.S. Food and Drug Administration (FDA) on April 29, 2021 to discuss the future development path for NYX-783 in PTSD.
        - Aptinyx expects to initiate a Phase 2b study in the second half of 2021, with a design consistent with that of a registration-supportive study and focused on evaluating effects on the CAPS-5 Total score.
    - Data from the Phase 2a exploratory study will be presented at the 2021 Society of Biological Psychiatry (SOBP) Annual Meeting to be held virtually on April 29 – May 1, 2021.

Neurology Pipeline – NYX-458
Aptinyx is developing NYX-458 for the treatment of cognitive impairment. In a Phase 1 study conducted in 62 healthy volunteers, NYX-458 exhibited a favorable pharmacokinetic profile and was well tolerated with no drug-related serious adverse events reported.

- **Development in cognitive impairment associated with Parkinson's disease and dementia with Lewy bodies:** In December 2019, based on positive preclinical data, including those from a highly translatable model in non-human primates, Aptinyx initiated a Phase 2a exploratory study of NYX-458 in patients with mild cognitive

impairment associated with Parkinson's disease. In March 2020, Aptinyx temporarily suspended enrollment of new patients in the Phase 2 study due to the COVID-19 pandemic.

- Following the suspension of enrollment, Aptinyx incorporated certain study design changes to improve study feasibility amidst the COVID-19 pandemic, simplify study execution, and optimize the potential for the study to detect signals of efficacy.

- Phase 2a exploratory study design:
  - The Phase 2 study is a randomized, double-blind, parallel-design, placebo-controlled study to evaluate the safety and potential cognitive benefits of NYX-458 in patients with cognitive impairment associated with Parkinson's disease or dementia with Lewy bodies.
  - Patients with dementia with Lewy bodies have been included in consideration of the pathophysiology in common with Parkinson's cognitive impairment – believed to be caused by increased levels of alpha synuclein, which, in turn, decreases NMDA receptor expression and activity.
  - The study will evaluate daily oral dosing of NYX-458 30 mg compared to placebo over a 12-week period.
  - The study is expected to enroll approximately 100 patients.
  - The primary endpoint in the study is safety and tolerability.
  - Secondary endpoints include multiple computerized neurocognitive assessments to evaluate the effects of NYX-458 on attention, memory, and executive functions.
  - Exploratory endpoints include various clinical assessments to broadly evaluate the signals of efficacy of NYX-458 in patients with cognitive impairment.

- Next steps:
  - Aptinyx expects to re-initiate patient screening and enrollment in the coming weeks and anticipates reporting top-line data from this study in the second half of 2022.

Corporate Updates

- **Harald Murck, M.D, Ph.D., joined Aptinyx as vice president, medical and pharmacovigilance:** In January 2021, Harald Murck, an experienced drug development executive trained at the Max Planck Institute of Psychiatry, Germany, and a leader in NMDA receptor research since the late 1990s, began working with Aptinyx in the role of vice president, medical and pharmacovigilance.

- **Andy Kidd, M.D., appointed president and COO:** In December, Aptinyx announced the appointment of Andy Kidd, the company's then-incumbent chief operating officer, to the role of president and chief operating officer.

- **Strengthened the company's financial position through a $48 million common stock offering:** In early October 2020, Aptinyx announced the closing of a public offering of common stock with gross proceeds totaling $48 million, inclusive of the full exercise of the underwriters' option to purchase additional shares and before deducting underwriting discounts and commissions and offering expenses. The offering included participation from new and existing investors. The company's current cash balance, inclusive of the proceeds from the offering, is expected to provide financial support into 2023.

Upcoming Milestones

- Recommencement of patient screening in Phase 2a study of NYX-458 in patients with cognitive impairment associated with Parkinson's disease or dementia with Lewy bodies – First week of April 2021
- Meeting with FDA to discuss development path for NYX-783 in PTSD – April 29, 2021
- Presentation of detailed data from Phase 2a exploratory study of NYX-783 in PTSD at SOBP – April 29 – May 01, 2021
- Initiation of Phase 2b study, with registration-supportive design, of NYX-783 in patients with PTSD – 2H 2021
- Data readout from Phase 2b study of NYX-2925 in patients with fibromyalgia – 1H 2022
- Data readout from Phase 2b study of NYX-2925 in patients with painful DPN – 1H 2022
- Data readout from Phase 2a study of NYX-458 in cognitive impairment – 2H 2022

Fourth Quarter and Full Year 2020 Financial Results

Cash Position: Cash and cash equivalents were $141.0 million at December 31, 2020, compared to $98.8 million at December 31, 2019.

Collaboration Revenue: Revenue was $0.0 million and $1.6 million for the fourth quarter and full year 2020, respectively, as compared to $1.0 million and $3.7 million for same periods in 2019. Aptinyx's revenue was derived from its research collaboration agreement with Allergan, now a wholly owned subsidiary of AbbVie, which came to its contractual conclusion during the third quarter of 2020.

Research and Development (R&D) Expenses: R&D expenses were $6.8 million and $32.8 million for the fourth quarter and full year 2020, respectively, as compared to $10.6 million and $44.3 million for same periods in 2019. The decrease in R&D expenses during 2020 was primarily driven by reduced costs associated with the temporary suspension of enrollment across three Phase 2 clinical studies.

General and Administrative (G&A) Expenses: G&A expenses were $4.8 million and $19.5 million for the fourth quarter and full year 2020, respectively, as compared to $4.5 million and $19.0 million for the same periods in 2019.

Net Loss: Net loss was $11.5 million for the fourth quarter of 2020 compared to a net loss of $13.8 million for the same period in 2019. For the year ended December 31, 2020, net loss was $50.1 million, or basic and diluted net loss per share attributable to common stockholders of $1.02, compared to a net loss of $57.4 million, or basic and diluted net loss per share attributable to common stockholders of $1.71, for the year ended December 31, 2019.

Conference Call

The Aptinyx management team will host a conference call and webcast today at 5:00 p.m. EDT to review its financial results and highlights for the full year 2020 and to provide other business updates. To access the live conference call, please dial (833) 772-0394 (domestic) or (236) 738-2205 (international) and refer to conference ID 4846816. A live audio webcast of the event will be available on the Investors & Media section of Aptinyx's website at https://ir.aptinyx.com. A replay of the webcast will be archived on Aptinyx's website for 30 days following the event.

About Aptinyx

Aptinyx Inc. is a clinical-stage biopharmaceutical company focused on the discovery, development, and commercialization of proprietary synthetic small molecules for the treatment of brain and nervous system disorders. Aptinyx has a platform for discovery of novel compounds that are believed to work through a unique

mechanism to modulate—rather than block or over-activate—NMDA receptors and enhance synaptic plasticity, the foundation of neural cell communication. The company has three product candidates in clinical development in central nervous system indications, including chronic pain, post-traumatic stress disorder, and cognitive impairment. Aptinyx is also advancing additional compounds from its proprietary discovery platform, which continues to generate a rich and diverse pipeline of small-molecule NMDA receptor modulators with the potential to treat an array of neurologic disorders. For more information, visit www.aptinyx.com.

Forward-Looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to, statements regarding the company's business plans and objectives, including future plans or expectations for NYX-2925, NYX-783, and NYX-458, therapeutic effects of the company's product candidates and discovery platform, expectations regarding the design, implementation, timing, and success of its current and planned clinical studies, including providing updated guidance with respect thereto, the timing for the company's receipt and announcement of data from its clinical studies, the timing and outcome of discussions with FDA and other regulatory agencies, expectations regarding its preclinical development activities, expectations regarding its uses and sufficiency of capital, the company's growth and the anticipated contribution of its executive officers and management to its operations and progress, and its expectations regarding its uses of capital, expenses, future accumulated deficit and other fourth quarter and year end 2020 financial results, and the effect of the COVID-19 pandemic on the foregoing. Risks that contribute to the uncertain nature of the forward-looking statements include: the effect of the COVID-19 pandemic on our business and financial results, including with respect to disruptions to our clinical trials, business operations, and ability to raise additional capital; the success, cost, and timing of the company's product candidate development activities and planned clinical studies; the company's ability to execute on its strategy; positive results from a clinical study may not necessarily be predictive of the results of future or ongoing clinical studies; regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time-consuming, and inherently unpredictable; regulatory developments in the United States and foreign countries; the company's estimates regarding expenses, future revenue, and capital requirements; the company's ability to fund operations into 2023; as well as those risks and uncertainties set forth in the company's most recent quarterly report on Form 10-Q and subsequent filings with the Securities and Exchange Commission, including our upcoming Annual Report on Form 10-K for the year ended December 31, 2020. All forward-looking statements contained in this press release speak only as of the date on which they were made. Aptinyx undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

APTINYX INC.
CONDENSED BALANCE SHEETS
(in thousands)
(Unaudited)

Assets	**December 31, 2020**	**December 31, 2019**
Current Assets:		
Cash and cash equivalents	$ 141,028	$ 98,849
Restricted cash	179	179
Accounts receivable	257	444
Prepaid expenses and other current assets	8,140	5,637
Total current assets	149,604	105,109
Property and equipment and other long-term assets	1,002	1,370
Total assets	$ 150,606	$ 106,479
Liabilities and stockholders' equity		
Current Liabilities:		
Accounts payable	$ 1,209	$ 1,555
Accrued expenses and other current liabilities	3,374	3,341
Total current liabilities	4,583	4,896
Other long-term liabilities	114	272
Total liabilities	4,697	5,168
Stockholders' equity	145,909	101,311
Total liabilities and stockholders' equity	$ 150,606	$ 106,479

APTINYX INC.
CONDENSED STATEMENTS OF OPERATIONS
(in thousands, except per share data)
(Unaudited)

	Three Months Ended December 31,		Year Ended December 31,	
	2020	**2019**	**2020**	**2019**
Revenues				
Collaboration revenue	$ —	$ 918	$ 1,564	$ 3,669
Operating expenses				
Research and development	6,786	10,598	32,835	44,330
General and administrative	4,775	4,533	19,494	18,952
Total operating expenses	11,561	15,131	52,329	63,282
Loss from operations	(11,561)	(14,213)	(50,765)	(59,613)
Other income	73	435	712	2,203
Net loss and comprehensive loss	$ (11,488)	$ (13,778)	$ (50,053)	$ (57,410)
Net loss per share - basic and diluted	$ (0.20)	$ (0.41)	$ (1.02)	$ (1.71)
Weighted average shares outstanding - basic and diluted	58,882	33,692	48,866	33,556

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