Issuer Free Writing Prospectus filed pursuant to Rule 433 supplementing the Prospectus dated May 27, 2009 Registration No. 333-158405

## AMICUS THERAPEUTICS, INC.

Up to 4,946,524 Shares Of Common Stock, Par Value \$0.01 Per Share

Warrants To Purchase up to 1,854,946 Shares Of Common Stock, Par Value \$0.01 Per Share

## INDICATIVE TERMS

Dated February 25, 2010

By reading the information contained within this document, the recipient hereof agrees with Amicus Therapeutics, Inc., or Amicus, and Leerink Swann LLC, or the Placement Agent, to maintain in confidence such information, together with any other non-public information regarding Amicus obtained from Amicus, the Placement Agent or their respective agents during the course of the proposed financing and to comply with the recipient's obligations under applicable U.S. and state securities laws.

Amicus Therapeutics, Inc.
FOLD/NASDAQ Global Market
Aggregate of (i) up to 4,946,524 shares (Shares) of Amicus's common stock \$0.01 par value per share (Common Stock), and (ii) warrants to purchase up to 1,854,946 shares of Common Stock (Warrants). The Shares and the Warrants will be sold together in units, with each unit consisting of one Shar and a Warrant to purchase 0.375 of a share of Common Stock. The units will not be issued or certificated. The Shares and the Warrants are immediately separable and will be issued separately.
The exercise price of the Warrants will be \$4.43 per share of Common Stock. The Warrants are exercisable any time on or after the date that is six months after of the date they are issued and expire on the fourth anniversary of the date they are issued. The Warrants shall have the terms and conditions substantially as set forth in the form of Warrant provided to investors.
\$3.74 per unit
Approximately \$17.2 million after deducting the placement agency fee and all other estimated offering expenses (based on the sale of 4,946,524 units at a public offering price of \$3.74 per unit)
Based on the public offering price of \$3.74 per unit and after giving effect to the 4,946,524 shares of Common Stock sold as part of the units in this offering, Amicus's adjusted net tangible book value per share of Common Stock as of September 30, 2009 would have been \$54.4 million, or \$1.97 per share. This represents an immediate increase in net tangible book value per share of Common Stock of \$0.33 to existing stockholders and immediate dilution of \$1.77 per share of Common Stock to new investors in this offering.

the units in this offering.

The foregoing calculation does not take into effect the further dilution to new investors that could occur upon the exercise of the Warrants sold as part of

Use of Proceeds:

Forward Looking Statements:

Amicus intends to use the net proceeds from the sale of units in this offering to further advance the development of its lead product candidate, Amigal, including the initiation of the Phase 3 study to support registration in the European Union and the completion of certain activities required for the submission of a license application globally, as well as for general corporate matters.

Amicus may also invest the net proceeds temporarily in deposits with major financial institutions, money market funds, notes issued by the United States government, fixed income investments, which can be readily purchased and sold using established markets, and United States bond funds, which can be readily purchased and sold using established markets, until it uses them for their intended purpose.

These Indicative Terms contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Those statements are therefore entitled to the protection of the safe harbor provisions of these laws. These forward-looking statements, which are usually accompanied by words such as "may," "might," "will," "should," "could," "intends," "estimates," "predicts," "potential," "continue," "believes," "anticipates," "plans," "expects" and similar expressions, involve risks and uncertainties, and relate to, without limitation, statements about Amicus's product candidates, its market opportunities, its strategy, its competition, its projected revenue, expense levels and cash spend and the adequacy of its available cash resources. These statements are only predictions based on current expectations and projections about future events. There are important factors that could cause Amicus's actual results, level of activity, performance or achievements to differ materially from those expressed or forecasted in, or implied by, such forward-looking statements, including those factors referred to in "Risk Factors" below.

Amicus's business, financial condition, results of operations and prospects may change. Although Amicus believes that the expectations reflected in these forward-looking statements are based upon reasonable assumptions, no assurance can be given that such expectations will be attained or that any deviations will not be material. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed herein may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. Amicus disclaims any obligation or undertaking to disseminate any updates or revision to any forward-looking statement to reflect any change in its expectations with regard thereto or any change in events, conditions or circumstances on which any such statement is based.

You should read these Indicative Terms completely and with the understanding that Amicus's actual future results may be materially different from what it expects. You should assume that the information appearing herein is accurate as of the date set forth above only. Amicus qualifies all of the information presented herein, and particularly its forward-looking statements, by these cautionary statements.

**Business Overview:** 

Amicus is a biopharmaceutical company focused on the discovery, development and commercialization of orally-administered, small molecule drugs known as pharmacological chaperones. Pharmacological chaperones are a novel, first-in-class approach to treating a broad range of diseases including lysosomal storage disorders and diseases of neurodegeneration. Amicus's goal is to become a leading biopharmaceutical company in this area. Its current strategic priorities are advancing:

- the Phase 3 development of its lead product candidate, Amigal for Fabry disease;
- the preclinical and clinical development of pharmacological chaperone/enzyme replacement therapy combination therapy; and
- the preclinical evaluation of the use of pharmacological chaperones for diseases of neurodegeneration.

Amicus's novel approach to the treatment of human genetic diseases consists of using pharmacological chaperones that selectively bind to the target protein, increasing the stability of the protein and helping it fold into the correct three-dimensional shape. This allows proper trafficking of the protein within the cell, thereby increasing protein activity, improving cellular function and potentially reducing cell stress. Amicus has also demonstrated in preclinical studies that pharmacological chaperones can further stabilize normal, or "wild-type," proteins. This stabilization could lead to a higher percentage of the target proteins folding correctly and more stably, which can increase cellular levels and improve cellular function, making chaperones potentially applicable to a wide range of diseases. Amicus's lead product candidate, Amigal (migalastat hydrochloride) for Fabry disease, is in Phase 3 development.

Amicus's other clinical stage product candidates are AT2220 (1-deoxynojirimycin HCl) for Pompe disease, which is currently in Phase 1 testing and remains on partial clinical hold, and Plicera (afegostat tartrate) for Gaucher disease, which Amicus does not plan to advance into Phase 3 development at this time. Amicus is conducting preclinical studies in diseases of neurodegeneration, including Parkinson's and Alzheimer's disease. Although Fabry, Gaucher and Pompe are relatively rare diseases, they represent substantial commercial markets due to the severity of the symptoms and the chronic nature of the diseases. The worldwide net product sales for the five currently approved therapeutics to treat Fabry, Gaucher and Pompe disease were approximately \$2.2 billion in 2008, as publicly reported by the companies that market these therapeutics.

Fabry and other lysosomal storage disorders are among certain human diseases that are caused by mutations in specific genes that, in many cases, lead to the production of proteins with reduced stability. Proteins with such mutations may not fold into their correct three-dimensional shape and are generally referred to as misfolded or unstable proteins. Misfolded or unstable proteins are often recognized by cells as having defects and, as a result, may be eliminated prior to reaching their intended location in the cell. The reduced biological activity of these proteins leads to impaired cellular function and ultimately to disease.

The current standard of treatment for Fabry, Gaucher and Pompe diseases is enzyme replacement therapy, or ERT. This type of therapy compensates for the reduced level of activity of specific enzymes through regular infusions of recombinant forms of the enzyme. Instead of adding enzymes from an external source by intravenous infusion, Amicus's approach uses orally-administered small molecule pharmacological chaperones to improve the function of the enzyme that is made by the patient's own body. Amicus believes its product candidates may have advantages over ERT relating to bio-distribution and ease of use, potentially improving treatment of these diseases.

In addition, Amicus has increasingly focused on the use of pharmacological chaperones in combination with ERT, which it believes may address certain key limitations of ERT. The use of pharmacological chaperones in combination with ERT may significantly enhance the safety and efficacy of ERT by, among other effects, prolonging the half-life of infused enzymes in circulation, increasing uptake of the infused enzymes into cells and tissues, and increasing enzyme activity and substrate reduction in target tissues compared to that observed with ERT alone.

While its initial clinical efforts have focused on the use of pharmacological chaperones to treat lysosomal storage diseases, Amicus believes that its technology may be applicable to the treatment of certain diseases of neurodegeneration. Its lead preclinical program in this area is focused on Parkinson's disease and it has established initial proof-of-concept in animal models. Amicus's second preclinical program in this area is focused on Alzheimer's disease. In 2010, Amicus expects to complete advanced preclinical proof-of-concept studies in Parkinson's disease and complete initial proof-of-concept studies in Alzheimer's disease.

Amicus's Lead Product Candidate-Amigal for Fabry Disease:

Amicus's first key strategic priority is to advance its lead program, Amigal for Fabry disease. Amicus commenced a Phase 3 study of Amigal intended to support approval in the United States (Study 011) in the second quarter of 2009, and treatment of the first patient began in the fourth quarter of 2009. Amicus expects to complete enrollment by the end of 2010 and to have preliminary results from this study in mid-2011. Study 011 is a 6-month, randomized, double-blind trial comparing Amigal to placebo in approximately 60 subjects. The surrogate primary endpoint is the change in the amount of kidney interstitial capillary GL-3, the substrate that accumulates in the cells of Fabry patients. Subjects to be enrolled are Fabry patients who have never received ERT or who have not received ERT for at least 6 months, and who have a mutation responsive to Amigal. Amicus intends to seek Accelerated Approval for Amigal according to Subpart H regulations. The key elements of this study design and regulatory path were agreed to with the U.S. Food and Drug Administration (FDA) in the second guarter of 2009.

In addition, Amicus expects to commence a separate Phase 3 study (Study 012) during 2010 to support approval of Amigal in the European Union. Study 012 will be an 18-month, randomized, open-label study comparing Amigal to ERT in approximately 60 subjects. The primary outcome of efficacy will be renal function as measured by glomerular filtration rate (GFR).

In February 2010, Amicus presented preliminary data from its ongoing Phase 2 extension study of Amigal, which is designed to evaluate the long-term safety and efficacy of Amigal. Among the endpoints being evaluated are two measures of renal function, estimated glomerular filtration rate (eGFR) and proteinuria. Preliminary data indicate that eGFR has remained stable out to 2-3 years for all subjects in the extension study and the average annual rate of change in eGFR in subjects identified as responders to Amigal, excluding hyperfiltrators, was +2.0 mL/min/1.73m<sup>2</sup>. Additionally, trends of reduced proteinuria continued to be observed in subjects identified as responders to Amigal. In addition, the data indicate that treatment with Amigal continues to be generally well-tolerated, with no drug-related serious adverse events. Nineteen subjects continue to receive treatment in the extension study. Amicus previously reported in March 2009 that subjects identified as responders to Amigal at the completion of the Phase 2 studies continued to maintain elevated levels of the target enzyme (a-Gal A), as measured in white blood cells, and reduced levels of the target substrate (kidney GL-3), as measured in urine. A reduction of GL-3 levels was also observed in interstitial capillary cells from kidney biopsies.

Chaperone-ERT Combination Therapy:

Another of Amicus's key strategic priorities is the advancement of the preclinical and clinical development of pharmacological chaperone-ERT combination therapy. When used as a monotherapy, pharmacological chaperones are designed to selectively bind to target enzymes in patient cells, thereby increasing protein stability and allowing for increased transport to lysosomes, where the enzyme performs its natural function of degrading substrate. When used in combination with ERT, Amicus believes that these binding and stabilization properties may improve key characteristics of the infused enzymes used in ERT, thereby increasing ERT's safety and efficacy. As previously reported, in 2009, Amicus conducted initial preclinical studies using pharmacological chaperones in combination with ERT. At several scientific conferences, Amicus presented data from these studies which demonstrated that the addition of a pharmacological chaperone to ERT has the potential to address key limitations of ERT, such as a lack of stability in circulation which can reduce safety and efficacy.

In February 2010, Amicus presented new data from preclinical studies that evaluated the combination of Amigal and an ERT, and another pharmacological chaperone, AT2220 (1-deoxynojirimycin HC1) and a different ERT, in mouse models of Fabry and Pompe disease, respectively. Studies of both combinations demonstrated that co-administration of the chaperone with ERT resulted in prolonged half-life of the administered enzyme in circulation, increased enzyme activity in cells and greater substrate reduction in target tissues compared to that seen with ERT alone.

Amicus intends to initiate a Phase 2 study with Amigal in combination with ERT for Fabry disease before the end of 2010. Additionally, Amcius is evaluating options to advance chaperone-ERT combination therapy programs for Pompe disease and Gaucher disease and is conducting pre-clinical combination studies for the treatment of these diseases.

Diseases of Neurodegeneration:

Amicus's final key strategic priority is advancing its pharmacological chaperone technology to develop treatments for diseases of neurodegeneration. Amicus believes the knowledge it has gained from exploring the use of pharmacological chaperones in rare genetic diseases can be applied to these non-lysosomal storage disease applications, and that its small molecule approach may be especially well-suited for treating diseases that affect the brain. For these applications, Amicus believes pharmacological chaperones may be used to further stabilize normal, or "wild-type," proteins and may therefore increase the cellular amounts and activities of specifically chosen target proteins that may be important for the treatment of neurodegenerative diseases. In addition, recent population genetics studies have established a link between being a Gaucher carrier and developing Parkinson's disease. In particular, these studies demonstrate that Gaucher carriers have an estimated five-fold increased risk for Parkinson's disease, and that carriers tend to develop Parkinson's at an earlier age. Amicus's lead pre-clinical program for Parkinson's disease is leveraging the knowledge it has gained from its Gaucher program to advance the use of pharmacological chaperones for the treatment of Parkinson's disease.

Amicus has completed initial proof-of-concept studies in animal models of Parkinson's disease and recently presented data from preclinical studies that evaluated the chaperone AT2101 in appropriate mouse models. These studies demonstrated that treatment with AT2101 increased the activity of βglucocerebrosidase (GCase), prevented accumulation of  $\alpha$ -synuclein in the brain and improved motor function as assessed in various behavioral tests. Amicus also reported that it has developed new compounds that improve on the properties of AT2101 and expand the range of doses and regimens that show motor improvement in mouse models of the disease. Amicus expects to complete advanced preclinical proof-of-concept studies in Parkinson's disease and report additional data during 2010. Additionally, Amicus recently announced that it has initiated a second preclinical neurodegenerative disease program for Alzheimer's disease. Amicus's work in Alzheimer's also builds on the understanding of pharmacological chaperones it has developed over the past several years and its work in Parkinson's disease. Amicus expects to complete initial proof-of-concept studies in Alzheimer's disease and report data during 2010.

Pharmacological Chaperone Technology:

In the human body, proteins are involved in almost every aspect of cellular function. Proteins are linear strings of amino acids that fold and twist into specific three-dimensional shapes in order to function properly. Certain human diseases result from mutations that cause changes in the amino acid sequence of a protein, and these changes often reduce protein stability and may prevent them from folding properly. The majority of genetic mutations that lead to the production of less stable or misfolded proteins are called missense mutations. These mutations result in the substitution of a single amino acid for another in the protein. Because of this type of error, missense mutations often result in proteins that have a reduced level of biological activity. In addition to missense mutations, there are also other types of mutations that can result in proteins with reduced biological activity.

Proteins generally fold in a specific region of the cell known as the endoplasmic reticulum (ER). The cell has quality control mechanisms that ensure that proteins are folded into their correct three-dimensional shape before they can move from the ER to the appropriate destination in the cell, a process generally referred to as protein trafficking. Misfolded proteins are often eliminated by the quality control mechanisms after initially being retained in the ER. In certain instances, misfolded or unstable proteins can accumulate in the ER before being eliminated.

The retention of misfolded proteins in the ER interrupts their proper trafficking, and the resulting reduced biological activity can lead to impaired cellular function and ultimately to disease. In addition, the accumulation of misfolded proteins in the ER may lead to various types of stress on cells, which may also contribute to cellular dysfunction and disease.

Amicus uses pharmacological chaperones to selectively bind to a target protein and increase its stability. The binding of the chaperone molecule helps the protein fold into its correct three-dimensional shape. This allows the protein to be trafficked from the ER to the appropriate location in the cell, thereby increasing cellular amounts and protein activity, improving cellular function and potentially reducing cell stress.

Amicus's proprietary approach to the discovery of pharmacological chaperone product candidates involves the use of rapid molecular and cell-based screening methods combined with its understanding of the intended biological function of proteins implicated in disease. Amicus uses this knowledge to select and develop compounds with desirable properties. In many cases, Amicus is able to start with specific molecules and classes of compounds already known to interact with the target protein but not used previously as therapies. This can greatly reduce the time and cost of the early stages of drug discovery and development.

Amicus believes its technology may be broadly applicable to a wide range of diseases for which protein stabilization and improved folding may be beneficial.

Preliminary Financial Results for the Three and Twelve Months Ended December 31, 2009:

The following information is preliminary and has been prepared by Amicus's management. Ernst & Young LLP, Amicus's independent registered public accounting firm, has not completed any audit, review or similar procedures with respect to the unaudited preliminary financial results presented below. Accordingly, Ernst & Young LLP does not express an opinion or any other form of assurance with respect to such preliminary financial results. Amicus expects the audit of its financial results and other financial statements for the year ended December 31, 2009 to be completed immediately prior to the filing of its Annual Report on Form 10-K for the year ended December 31, 2009.

During the course of the preparation of its complete, consolidated financial statements as of and for the year ended December 31, 2009, the completion of its annual fiscal year-end closing procedures and analyses and the completion of the audit of its financial statements, Amicus may identify items that would require it to make adjustments to the preliminary financial results presented herein. The unaudited preliminary financial results presented herein are not necessarily indicative of the results to be expected for any future period.

On February 16, 2010, Amicus reported its unaudited preliminary financial results for the fourth fiscal quarter and year ended December 31, 2009. Amicus's cash spend for the quarter ended December 31, 2009 was \$11.1 million. Amicus's cash, cash equivalents and marketable securities were \$78.2 million as of December 31, 2009, and Amicus reiterates its expectations that its cash spend will be \$40 to \$50 million in 2010.

Revenue for the quarter ended December 31, 2009 was \$49.5 million, which represented revenue received under Amicus's license and collaboration agreement with Shire Pharmaceuticals Ireland Ltd., or Shire. Upon signing the collaboration agreement in 2007, Shire paid Amicus an initial, nonrefundable license fee of \$50.0 million that was being recognized as revenue on a straight-line basis over the period of performance obligations under the collaboration agreement, or 18 years from the date of such agreement. In connection with the mutual termination of the Shire collaboration agreement on October 29, 2009, Amicus recognized \$44.7 million of previously deferred revenue on the upfront payment from Shire. In addition, Amicus received a \$5.2 million termination payment from Shire as a full and fair settlement of all development cost-sharing obligations, approximately \$4.7 million of which was recognized as research revenue during the quarter ended December 31, 2009, and \$0.5 million was applied to a receivable for reimbursable research and development costs incurred during the previous quarter ended September 30, 2009.

Net income for the quarter ended December 31, 2009 was \$33.0 million, or \$1.45 per diluted common share, compared to a net loss of \$14.2 million, or \$0.63 per diluted common share, for the quarter ended December 31, 2008. Net loss for the year ended December 31, 2009 was \$6.6 million, or \$0.29 per diluted common share, compared to net loss of \$39.4 million, or \$1.75 per diluted common share for the year ended December 31, 2008. The variances between periods were attributable to the termination of the Shire collaboration agreement and the resulting recognition of previously deferred revenue discussed above.

Research and development expense for the quarter ended December 31, 2009 was \$10.1 million, representing a decrease of \$3.7 million, or 27%, from \$13.8 million for the quarter ended December 31, 2008. The decrease was due primarily to a \$2.6 million non-recurring license fee incurred during the quarter ended December 31, 2008 and a reduction in costs incurred in connection with the development of AT2220 for the treatment of Pompe disease during the quarter ended December 31, 2009.

General and administrative expense for the quarter ended December 31, 2009 was \$4.3 million, representing a decrease of \$0.7 million, or 14%, from \$5.0 million for the quarter ended December 31, 2008. The decrease was due primarily to reduced consulting and personnel costs.

Restructuring charges incurred for the quarter ended December 31, 2009 in connection with Amicus's corporate restructuring were approximately \$1.5 million. The restructuring charges were attributable to employment termination costs of approximately \$0.9 million, consisting of one-time severance payments and benefit continuation, and a charge for facility consolidation of approximately \$0.7 million, consisting of future minimum lease payments and a write-off of certain fixed assets in a vacated facility.

Risk Factors:

Investing in Amicus's securities involves a high degree of risk and uncertainty. Please see the risk factors under the heading "Risk Factors" in Amicus's Annual Report on Form 10-K for the year ended December 31, 2008, as supplemented and updated by the risk factors in Amicus's Quarterly Reports on Form 10-Q for the quarters ended June 30, 2009 and September 30, 2009, respectively, as such discussions may be amended or updated in subsequent reports filed by Amicus with the Securities and Exchange Commission, or SEC.

Before making an investment decision, you should carefully consider these risks as well as other information Amicus includes or incorporates by reference into its registration statement (Registration Statement Number 333-158405) (including a prospectus) that was declared effective by the SEC on May 27, 2009. The risks and uncertainties Amicus has described are not the only ones facing Amicus. Additional risks and uncertainties not presently known to Amicus or that Amicus currently deems to be immaterial may also affect its business operations. If any of such risks and uncertainties actually occur, Amicus's business, financial condition, and results of operations could be severely harmed. This could cause the trading price of Amicus's common stock to decline, and you could lose all or part of your investment.

Lock-Up Agreements:

Amicus and each of its directors and executive officers and certain of its stockholders have entered into lock-up agreements with the Placement Agent providing that they will not, among other things, sell or otherwise transfer or dispose of any shares of Amicus's common stock without the prior written consent of Leerink Swann LLC, for a period of 90 days, with respect to Amicus, or 60 days, with respect to directors, executive officers and stockholders of Amicus, from the date of the prospectus supplement related to this offering, which period may be extended under certain circumstances.

The lock-up provisions summarized above are subject to customary exceptions, including, with respect to directors, executive officers and stockholders of Amicus, transfers of shares of Amicus's common stock as bona fide gifts or pursuant to a Rule 10b5-1 trading plan, and with respect to Amicus, the issuance of shares of Amicus's common stock or options to purchase Amicus's common stock, or shares of Amicus's common stock upon exercise of options, pursuant to its equity incentive plans.

Insider Participation: Amicus's Chairman and Chief Executive Officer will purchase 29,612 units

in this offering.

Settlement Date: March 2, 2010

Placement Agent: Leerink Swann LLC

The Placement Agent will receive a fee of 5.7% of the gross proceeds of the sale of units in this offering.

Amicus has filed a registration statement (Registration Statement Number 333-158405) (including a prospectus) with the SEC for this offering to which this communication relates. Before you invest, you should read the prospectus in that registration statement and other documents Amicus has filed with the SEC that are incorporated by reference into the prospectus for more complete information about Amicus and this offering. You may get these documents for free by visiting EDGAR on the SEC Web site at www.sec.gov. Alternatively, Amicus or the Placement Agent will arrange to send you the prospectus upon your request by calling Leerink Swann LLC, toll free, at 1-800-808-7525, Ext. 4814.