UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

SCHEDULE 13D

(Rule 13D-101)

Under the Securities Exchange Act of 1934 (Amendment No. 6)*

OPKO Health, Inc.

(Name of Issuer)

Common Stock, par value \$0.01 per share (Title of Class of Securities)

68375N103 (CUSIP Number)

Kate Inman General Counsel, Secretary OPKO Health, Inc. 4400 Biscayne Boulevard Miami, Florida 33137 Telephone: (305) 575-4138

(Name, address and telephone number of person authorized to receive notices and communications)

November 8, 2018 (Date of event which requires filing of this statement)

If the filing person has previously filed a statement on Schedule 13G to report the acquisition which is the subject of this Schedule 13D, and is filing this schedule because of Rule 13d-1(e), Rule 13d-1(f) or Rule 13d-1(g), check the following box \Box

The information required on the remainder of this cover page shall not be deemed to be "filed" for purpose of Section 18 of the Securities Exchange Act of 1934 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the *Notes*).

(1)	NAMES OF REPORTING PERSONS							
	The Chiin Hsiung Hsiao Family Trust A							
(2)	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (SEE INSTRUCTIONS)							
	(a)							
(3)	SEC USE ONLY							
(4)	SOURCE OF FUNDS (SEE INSTRUCTIONS)							
	N/A							
(5)	CHECK IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(D) OR 2(E) \Box							
(6)	CITIZENSHIP OR PLACE OF ORGANIZATION							
(0)	CHIZENSHII OKTEACE OF OKOANIZATION							
	Florida							
	(7) SOLE VOTING POWER							
NUMBER SHARE								
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OWNED EACH								
REPORTI	NG (9) SOLE DISPOSITIVE POWER							
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VV 1111.	1,000,000 Shares (10) SHARED DISPOSITIVE POWER							
	(10) SIMIKED DISI OSITIVE TOWER							
(11)	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON							
	1,000,000 Shares							
(12)	CHECK IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (SEE							
	INSTRUCTIONS) □							
(13)	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)							
	0.2%							
(14)	TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)							
	00							

(1)	NAMES OF REPORTING PERSONS							
	The Chiin Hsiung Hsiao Family Trust B							
(2)	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (SEE INSTRUCTIONS) (a) \Box (b) \Box							
(3)	SEC USE ONLY							
(4)	SOURCE OF FUNDS (SEE INSTRUCTIONS)							
	N/A							
(5)	CHECK IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(D) OR 2(E) \Box							
(6)	CITIZENSHIP OR PLACE OF ORGANIZATION							
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(11)	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON							
	1,000,000 Shares							
(12)	CHECK IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS) \Box							
(13)	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)							
	0.2%							
(14)	TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)							
_	00							

(1)	NAMES OF REPORTING PERSONS							
	Hsu Gamma Investment, L.P.							
(2)	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (SEE INSTRUCTIONS)							
	(a) □ (b) □							
(3)	SEC USE ONLY							
(4)	SOURCE OF FUNDS (SEE INSTRUCTIONS)							
	AF, OO							
(5)	CHECK IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(D) OR 2(E)							
(6)	CITIZENSHIP OR PLACE OF ORGANIZATION							
	Florida							
	(7) SOLE VOTING POWER							
NUMBER	OF 4,617,404 Shares							
SHARE BENEFICIA	(a) GYALDED VOEDDAG DOVED							
OWNED	ALLI (7)							
EACH								
REPORTI PERSO	(*)							
WITH								
	(10) SHARED DISPOSITIVE POWER							
(11)	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON							
	4,617,404 Shares							
(12)	CHECK IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (SEE							
	INSTRUCTIONS) □							
(13)	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)							
	0.8%							
(14)	TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)							
	PN							

(1)	NAMES OF REPORTING PERSONS						
	Jane Hsiao, Ph.D.						
(2)	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (SEE INSTRUCTIONS) (a) \Box (b) \Box						
(3)	SEC USE ONLY						
(4)	SOURCE OF FUNDS (SEE INSTRUCTIONS)						
	PF, OO						
(5)	CHECK IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(D) OR 2(E)						
(6)	CITIZENSHIP OR PLACE OF ORGANIZATION						
	United States of America						
	(7) SOLE VOTING POWER						
NUMBER							
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OWNED	ALL I						
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(11)	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON						
(1.2)	33,901,103 Shares						
(12)	CHECK IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS) □						
	Notice flore)						
(13)	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)						
	5.007						
(14)	5.8% TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)						
(17)	THE OF REPORTING LERSON (SEE INSTRUCTIONS)						
	IN						

This Amendment No. 6 (the "Amendment") amends and supplements the statement on Schedule 13D filed on February 14, 2008, as amended by Amendment No. 1 to the Schedule 13D filed on August 21, 2008, as amended by Amendment No. 2 to the Schedule 13D filed on October 1, 2009, as amended by Amendment No. 3 to the Schedule 13D filed on March 22, 2013, as amended by Amendment No. 4 to the Schedule 13D filed on September 16, 2013, as amended by Amendment No. 5 to the Schedule 13D filed on December 18, 2015 (together, the "Original Schedule 13D"), by Jane Hsiao, Ph.D. ("Dr. Hsiao"), The Chiin Hsiung Hsiao Family Trust A ("Trust A"), The Chiin Hsiung Hsiao Family Trust B ("Trust B"), and Hsu Gamma Investment, L.P. ("Hsu Gamma"). This Amendment is filed pursuant to the Joint Filing Agreement executed by the reporting persons listed on the cover pages to this Amendment. (Exhibit 1 to Amendment No. 1 to the Schedule 13D filed on August 21, 2008 is hereby incorporated by this reference.)

ITEM 3. Source and Amount of Funds or Other Consideration.

Item 3 is amended by adding the following paragraphs to the end of the item:

Dr. Hsiao acquired 573,066 shares of Common Stock, for investment purposes on November 8, 2018 for a purchase price of \$2,000,000. Dr. Hsiao used personal funds to make the acquisition.

ITEM 4. Purpose of Transaction.

Item 4 is amended by adding the following paragraphs to the end of the item:

On November 8, 2018, Dr. Hsiao and the Issuer entered into a stock purchase agreement (the "November 2018 Stock Purchase Agreement"), pursuant to which Dr. Hsiao acquired 573,066 shares of Common Stock from the Issuer in a private placement for an aggregate purchase price of approximately \$2,000,000 or \$3.49 per share (the "Private Placement"). The Private Placement closed on November 13, 2018. The shares issued in the Private Placement were offered and sold in reliance upon an exemption from registration under Section 4(a)(2) of the Securities Act of 1933, as amended (the "Securities Act"), for "transactions by an issuer not involving a public offering". An affiliate of Dr. Phillip Frost, the Issuer's Chairman and Chief Executive Officer, and two other investors acquired an aggregate of 25,931,232 shares of Common Stock from the Issuer in private placements that were dated concurrently with the Private Placement. The Reporting Persons disclaim beneficial ownership of the shares of Common Stock acquired in the other private placements, including the shares acquired by Dr. Frost, for purposes of Section 13 or otherwise.

ITEM 5. Interest in Securities of the Issuer.

Item 5 is deleted in its entirety and replaced with the following text:

(a)-(b) Dr. Hsiao may be deemed to beneficially own 33,901,103 shares of Common Stock, which consist of (i) 1,000,000 shares of Common Stock held by Trust A, (ii) 1,000,000 shares of Common Stock held by Trust B, (iii) 4,617,404 shares of Common Stock held by Hsu Gamma, and (iii) 27,283,699 shares of Common Stock held individually. The 27,283,699 shares of Common Stock individually held by Dr. Hsiao consist of 1,000,000 shares of Common Stock issuable upon conversion of a convertible note and options to purchase 937,500 shares of Common Stock, exercisable within 60 days of the date hereof. The 33,901,103 shares of Common Stock beneficially owned by Dr. Hsiao constitute 5.8% of the Issuer's outstanding shares of Common Stock, based upon 586,331,813 shares of Common Stock outstanding as of November 1, 2018 as reported by the Issuer, including 26,504,298 shares issued pursuant to certain stock purchase agreements dated November 8, 2018, and calculated in accordance with Rule 13d-3. Dr. Hsiao has sole voting and dispositive power over 33,901,103 shares of Common Stock.

Trust A beneficially owns 1,000,000 shares of Common Stock, which constitute 0.2% of the Issuer's outstanding shares of Common Stock, based on 586,331,813 shares of Common Stock outstanding as of November 1, 2018 as reported by the Issuer, including 26,504,298 shares issued pursuant to certain stock purchase agreements dated November 8, 2018, and calculated in accordance with Rule 13d-3. Dr. Hsiao is the sole trustee of

Trust A and holds sole voting and dispositive power with respect to the 1,000,000 shares of Common Stock held by Trust A.

Trust B beneficially owns 1,000,000 shares of Common Stock, which constitute 0.2% of the Issuer's outstanding shares of Common Stock, based on 586,331,813 shares of Common Stock outstanding as of November 1, 2018 as reported by the Issuer, including 26,504,298 shares issued pursuant to certain stock purchase agreements dated November 8, 2018, and calculated in accordance with Rule 13d-3. Dr. Hsiao is the sole trustee of Trust B and holds sole voting and dispositive power with respect to the 1,000,000 shares of Common Stock held by Trust B.

Hsu Gamma beneficially owns 4,617,404 shares of Common Stock, which constitutes 0.8% of the Issuer's outstanding shares of Common Stock, based on 586,331,813 shares of Common Stock outstanding as of November 1, 2018 as reported by the Issuer, including 26,504,298 shares issued pursuant to certain stock purchase agreements dated November 8, 2018, and calculated in accordance with Rule 13d-3. Dr. Hsiao is the general partner of Hsu Gamma and holds sole voting and dispositive power with respect to the 4,617,404 shares of Common Stock held by Hsu Gamma.

Dr. Hsiao is a member of The Frost Group, LLC, which holds 20,091,062 shares of Common Stock. Dr. Hsiao disclaims beneficial ownership of the shares of Common Stock and warrants held by The Frost Group, LLC.

- (c) In the last 60 days prior to the filing of this Amendment No. 6, Dr. Hsiao acquired a total of 573,066 shares of Common Stock in the Private Placement for an aggregate purchase price of approximately \$2,000,000, or \$3.49 per share. The Private Placement closed on November 13, 2018. The shares issued in the Private Placement were offered and sold in reliance upon an exemption from registration under Section 4(a)(2) of the Securities Act for "transactions by an issuer not involving a public offering".
- (d) Except as described herein, no other person is known by any Reporting Person to have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, any shares of the Issuer beneficially owned by them.
 - (e) Not applicable.

ITEM 6. Contracts, Arrangements, Understandings or Relationships with Respect to Securities of the Issuer.

Item 6 is amended in its entirety and replaced with the following text:

See Item 4 regarding the Stock Purchase Agreement, Second Stock Purchase Agreement, the Psilos Securities Purchase Agreement, the Third Stock Purchase Agreement, the V-Sciences Agreement, CRG Agreement, the Kennedy Agreement, the Fourth Stock Purchase Agreement, Warrant Agreement, and the Chung Chia Agreement and the November 2018 Stock Purchase Agreement.

Except as identified herein, there are no contracts, arrangements, understandings or relationships (legal or otherwise) between the Reporting Person and any other person with respect to any securities of the Issuer, including but not limited to transfer or voting of any of the securities, finder's fees, joint ventures, loan or option arrangements, puts or calls, guarantees of profits, division of profits or loss, or the giving or withholding of proxies.

ITEM 7. Materials to be Filed as Exhibits.

Item 7 is amended to add the following text to the end of the item:

Exhibit 9 Form of Stock Purchase Agreement, dated as of November 8, 2018, by and between the Issuer and Dr. Jane Hsiao.

SIGNATURES

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

The Chiin Hsiung Hsiao Family Trust A

Dated: November 20, 2018 By: /s/ Jane H. Hsiao, Ph.D.

Name: Jane H. Hsiao, Ph.D.

Title: Trustee

The Chiin Hsiung Hsiao Family Trust B

Dated: November 20, 2018 By: /s/ Jane H. Hsiao, Ph.D.

Name: Jane H. Hsiao, Ph.D.

Title: Trustee

Hsu Gamma Investment, L.P.

Dated: November 20, 2018 By: /s/ Jane H. Hsiao, Ph.D.

Name: Jane H. Hsiao, Ph.D. Title: General Partner

Dated: November 20, 2018 By: _/s/ Jane H. Hsiao, Ph.D.

Name: Jane H. Hsiao, Ph.D.

Title: Jane H. Hsiao, Ph.D., Individually

STOCK PURCHASE AGREEMENT

This Stock Purchase Agreement is dated as of November 8, 2018 (this " <u>Agreement</u> "), between OPKO Health, Inc., a Delaware corporation (the " <u>Company</u> "), and (the " <u>Purchaser</u> ").
WHEREAS, the Company desires to sell to Purchaser, and Purchaser desires to purchase from the Company, shares of the Company's common stock, par value \$.01 per share (the " <u>Common Stock</u> "), on the terms and subject to the conditions set forth in this Agreement (the " <u>Transaction</u> ").
NOW, THEREFORE, in consideration of the premises and the mutual covenants contained in this Agreement and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, and intending to be legally bound, the parties agree as follows:

Article 1

Purchase and Sale of Common Stock

- 1.2 <u>Closing</u>. The issuance, sale and delivery of the Shares (the "<u>Closing</u>") shall take place at the Company's offices in Miami, Florida on November 8, 2018, or as soon as possible thereafter (the "<u>Closing Date</u>"). As payment in full for the Shares being purchased at the Closing, Purchaser shall pay to the Company the Purchase Price by wire transfer. The obligation of the Company to deliver the Shares on the Closing Date as provided herein is subject to the approval for listing of the Shares by the NASDAQ Global Select Market.

Article 2

Additional Agreements

The Company and Purchaser shall cooperate with each other and use their respective commercially reasonable best efforts to take or cause to be taken all actions, and do or cause to be done all things, necessary, proper or advisable under this Agreement and applicable laws and regulations to consummate and make effective the sale of the Shares (the "Sale") and the other transactions contemplated by this Agreement as soon as practicable, including preparing and filing as promptly as practicable all documentation to effect all necessary applications, notices, petitions, filings and other documents and to obtain as promptly as practicable all permits, consents, approvals and authorizations necessary or advisable to be obtained from any third party and/or any governmental entity in order to consummate the sale or any of the other transactions contemplated by this Agreement.

Article 3

Representations and Warranties of the Company

The Company represents and warrants to Purchaser as of the date hereof as follows:

- 3.1 <u>Authorization of Agreements, etc.</u> The execution and delivery by the Company of this Agreement, the performance by the Company of its obligations hereunder, and the issuance, sale and delivery of the Shares have been duly authorized by all requisite corporate action and will not result in any violation of, be in conflict with, or constitute a default under, with or without the passage of time or the giving of notice: (a) any provision of the Company's Certificate of Incorporation, as amended, or Bylaws, as amended; (b) any provision of any judgment, decree or order to which the Company is a party or by which it is bound; (c) any material contract or agreement to which the Company is a party or by which it is bound; or (d) any statute, rule or governmental regulation applicable to the Company, except where such violation, conflict, or default would not have a material adverse effect on the Company.
- 3.2 <u>Valid Issuance of Common Stock</u>. The Shares have been duly authorized and, when issued, sold and delivered in accordance with this Agreement for the consideration expressed herein will be validly issued, fully paid and nonassessable with no personal liability attaching to the ownership thereof and will be free and clear of all liens, charges and encumbrances of any nature whatsoever except for restrictions on transfer under this Agreement and under applicable Federal and state securities laws.
- 3.3 <u>Validity</u>. This Agreement has been duly executed and delivered by the Company and constitutes the legal, valid and binding obligation of the Company, enforceable in accordance with its terms except (i) as limited by applicable bankruptcy, insolvency, reorganization, moratorium, and other laws of general application affecting enforcement of creditors' rights generally, and (ii) as limited by laws relating to the availability of specific performance, injunctive relief, or other equitable remedies.
- 3.4 <u>Brokers and Finders</u>. Neither the Company nor any of its subsidiaries, officers, directors or employees has employed any broker or finder or incurred any liability for any brokerage fees, commissions or finders' fees in connection with the Sale or the other transactions contemplated by this Agreement.

Article 4

Representations and Warranties of Purchaser

The Purchaser represents and warrants to the Company as of the date hereof as follows:

4.1 <u>Validity</u>. This Agreement has been duly executed and delivered by Purchaser and constitutes the legal, valid and binding obligation of Purchaser, enforceable in accordance with its terms except:

- (a) as limited by applicable bankruptcy, insolvency, reorganization, moratorium, and other laws of general application affecting enforcement of creditors' rights generally; and
- (b) as limited by laws relating to the availability of specific performance, injunctive relief, or other equitable remedies.

4.2 <u>Investment Representations.</u>

- (a) Purchaser is an "accredited investor" within the meaning of Rule 501 of Regulation D under the Securities Act of 1933, as amended (the "Securities Act") and was not organized for the specific purpose of acquiring the Shares;
- (b) Purchaser has sufficient knowledge and experience in investing in companies similar to the Company in terms of the Company's stage of development so as to be able to evaluate the risks and merits of its investment in the Company and it is able financially to bear the risks thereof and it has independently evaluated the merits and risks of its participation in the transaction contemplated hereby and, in so evaluating, has not relied upon any other person in connection with its decision to participate in such transactions;
- (c) it is the present intention that the Shares being purchased by Purchaser are being acquired for Purchaser's own account for the purpose of investment and not with a present view to or for sale in connection with any distribution thereof;
 - (d) Purchaser understands that:
- (i) the Shares have not been registered under the Securities Act by reason of their issuance in a transaction exempt from the registration requirements of the Securities Act pursuant to Section 4(2) thereof or Rule 505 or 506 promulgated under the Securities Act;
- (ii) the Shares must be held indefinitely unless a subsequent disposition thereof is registered under the Securities Act or is exempt from such registration;
 - (iii) the Shares will bear a legend to such effect; and
 - (iv) the Company will make a notation on its transfer books to such effect; and
- (e) the Company has made available to Purchaser all documents and information that the Purchaser has requested relating to an investment in the Company.
- 4.3 <u>Brokers and Finders</u>. The Purchaser has not employed any broker or finder or incurred any liability for any brokerage fees, commissions or finders' fees in connection with the Sale or the other transactions contemplated by this Agreement.

Article 5

Miscellaneous

5.1 Legend. Each certificate that represents Shares shall have conspicuously endorsed thereon the following legends:

THIS STOCK HAS NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "SECURITIES ACT"), OR ANY STATE SECURITIES LAWS. THIS STOCK MAY NOT BE OFFERED OR TRANSFERRED BY SALE, ASSIGNMENT, PLEDGE OR OTHERWISE UNLESS (A) A REGISTRATION STATEMENT FOR THE STOCK UNDER THE SECURITIES ACT IS IN EFFECT OR (B) THE COMPANY HAS RECEIVED AN OPINION OF COUNSEL, WHICH OPINION IS SATISFACTORY TO THE COMPANY, TO THE EFFECT THAT SUCH REGISTRATION IS NOT REQUIRED UNDER THE SECURITIES ACT OR THE RELEVANT STATE SECURITIES LAWS.

- 5.2 <u>Brokerage</u>. Each party hereto will indemnify and hold harmless the other against and in respect of any claim for brokerage or other commissions relative to this Agreement or to the transactions contemplated hereby, based in any way on agreements, arrangements or understandings made or claimed to have been made by such party with any third party.
- 5.3 <u>Parties in Interest</u>. All representations, covenants and agreements contained in this Agreement by or on behalf of any of the parties hereto shall bind and inure to the benefit of the respective successors and assigns of the parties hereto whether so expressed or not
- 5.4 <u>Notices</u>. All notices, requests, consents, demands, and other communications under this Agreement shall be in writing and shall be deemed to have been duly given on the date of service if served personally on the party to whom notice is to be given, on the date of transmittal of services via telecopy to the party to whom notice is to be given (with a confirming copy delivered within 24 hours thereafter), or on the third day after mailing if mailed to the party to whom notice is to be given, by first class mail, registered or certified, postage prepaid, or overnight mail via a nationally recognized courier providing a receipt for delivery and properly addressed as follows:

If to the Company: OPKO Health, Inc.

4400 Biscayne Blvd. Miami, FL 33137

Attn: Kate Inman, General Counsel

If to the Purchaser: To the address specified on the signature pages hereto.

Any party may change its address for purposes of this paragraph by giving notice of the new address to each of the other parties in the manner set forth above.

- 5.5 Governing Law. This Agreement shall be governed by and construed in accordance with the laws of the State of Florida for all purposes and in all respects, without regard to the conflict of law provisions of such state.
- 5.6 Entire Agreement. This Agreement constitutes the sole and entire agreement of the parties with respect to the subject matter hereof.
- 5.7 <u>Counterparts</u>. This Agreement may be executed in two or more counterparts (including facsimiles), each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.
- 5.8 <u>Amendments and Waivers</u>. This Agreement may be amended or modified, and provisions hereof may be waived, only with the written consent of the Company and the Purchaser.
- 5.9 <u>Severability</u>. If any provision of this Agreement shall be declared void or unenforceable by any judicial or administrative authority, the validity of any other provision and of the entire Agreement shall not be affected thereby.
- 5.10 <u>Titles and Subtitles</u>. The titles and subtitles used in this Agreement are for convenience only and are not to be considered in construing or interpreting any term or provision of this Agreement.

[Signatures on Following Pages]

NOW THEREFORE, the Company and Purchaser have executed this Stock Purchase Agreement as of the date first above written.

OPKO HEALTH, INC.

By: /s/ Steven D. Rubin

Name: Steve D. Rubin

Title: Executive Vice President

Address: 4400 Biscayne Boulevard Miami, FL 33137

INVESTO	R:			
By: Name: Address:				