UNITED STATES
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SCHEDULE 14A

PROXY STATEMENT PURSUANT TO SECTION 14(a) OF THE SECURITIES EXCHANGE ACT OF 1934

Filed by the Registrant ☒ Filed by a party other than the Registrant ☐
Check the appropriate box:

☐ Preliminary Proxy Statement

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☐ Definitive Proxy Statement

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Sema4 Holdings Corp.

(Name of Registrant as Specified In Its Charter)

(Name of Person(s) Filing Proxy Statement, if other than the Registrant)

Payment of Filing Fee (Check the appropriate box):

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(1) Title of each class of securities to which transaction applies:

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EXPLANATORY NOTE

This Schedule 14A filing relates to the proposed acquisition of GeneDx, Inc., a New Jersey corporation ("GeneDx"), by Sema4 Holdings Corp. ("Sema4" or the "Company") pursuant to that certain Agreement and Plan of Merger and Reorganization (the "Merger Agreement") between the Company, GeneDx, and the other parties thereto (the transactions contemplated by the Merger Agreement, the "Acquisition").

The following communication was distributed on March 11, 2022 and is filed herewith.

- Q&A with the Journal of Precision Medicine transcript

Q&A TRANSCRIPT

A Questions and Answers Session with Isaac Ro of Sema4 Holdings Corp. on Strengthening its Market-Leading AI-Driven Genomic and Clinical Data Platform

A recent press release announced that Sema4 and OPKO Health signed a definitive agreement for Sema4 to acquire OPKO's wholly owned subsidiary, GeneDx, a leader in genomic testing and analysis. Following completion of the acquisition, Sema4 will be optimally positioned to partner with health systems and biopharma companies to transform even further the standard of care throughout the patient health journey while also strengthening its AI-driven genomic and clinical data platform. Both companies have long been driven by generating and accessing large databases and applying a variety of data analytical techniques to derive insights about patients' health. We noted especially Sema4's focus on patient-centered health intelligence. Given this activity, we contacted Sema4 about addressing how the long-term plans for the company will further increase its clinical presence while maintaining its technology prowess.
Along these, we put a set of questions to Isaac Ro, CFO at Sema4, with a focus on three topics – the platform of algorithms, healthcare partnerships, and the patient's journey. We approached Sema4 on learning of the deal to acquire GeneDx. As you read on, you'll see we covered that news as well as a host of other topics during our discussion!

JPM: How does Sema4's recent acquisition of GeneDx add to Sema4's platform for more comprehensive database? For example, novel algorithms or capabilities to harvest data from the clinic?

Isaac: A couple of foundational capabilities are needed to build a platform of algorithms. One of them is access to extremely high-resolution genomic data. Today, we are at the point where genetic testing is a rapidly growing industry that's been enabled by the advent of Illumina's NextGen sequencing technology. The application of that technology, however, tends to be very narrow in a clinical context, meaning that many scientists and physicians tend to look only at a handful of genes, sometimes only one. And we, of course, know that many other scientists and physicians would want to look at the entire genome if they had all the relevant information. Today, we are moving towards a whole genome analysis, but we are not quite there yet.

We are in this interim phase of genome exploration that may turn out to be very long lived, namely, understanding the exome - the encoded portion of the genome. What makes GeneDx special is that they have perfected the commercialization of clinical exome analysis better, faster, and cheaper than any other company. This gives us an engine for acquiring enormous amounts of genomic data at the exome level. To date, GeneDx has sequenced over 300,000 exomes - nobody's done anywhere close to that amount. That is the primary asset in the deal.

The second piece of the GeneDx value stream, the massive repository of exome data they've assembled, can be very quickly subsumed into our existing database and platform of algorithms. Basically, it's like putting high octane fuel into a fighter jet. We are going to have a whole new level of scale of data and analytical power. Taken together, we view GeneDx's capabilities and exome records as "hidden" assets that give us this turbocharged trajectory on our platform. This has been a long-term trend and it is exciting that we're at another point of market inflection relative to where we've been over the last 20 years.

JPM: What is Sema4's strategy to integrate molecular diagnostics data with patient's clinical data? And what types of clinical data would be included in that integration?

Isaac: There's a tendency to assume that technology is, by itself, the key to making all this happen. But then there is implementation, which in healthcare is very difficult, especially when you have something that's distinctly different and clearly breakthrough. It takes years for adoption to play out in the hands of everyday physicians and patients.

How do you crack that code? I think one of the brilliant things that Eric Schadt, our Founder and CEO, did in conceiving Sema4 was to change the go-to-market strategy typically seen in this industry. If you look over the last 15 or so years, we see a successful industry of companies built up with basically the same playbook - set up a lab with a cool test that provides breakthrough insights in, say, oncology, then hire a group of salespeople, 50 to 100, of specialists who target the top 20% or so of early adopter oncologists. They go to them and say, "Hey, how would you like to ride the wave of the future?" In doing that, you can get to a very nice level of scale; so, we now have a dozen plus publicly traded companies - most are smaller cap, most have revenue less than a couple hundred million - which is respectable but limited.

Take cancer. For example, 80% of cancer patients are not sent to an academic setting; they're sent to a community hospital. For that 80% of people, the access to technology is still limited, not because technology isn't good, but because access to quality care is beyond the technology.

Instead, Sema4's strategy is to approach a specific group of health systems, which fit criteria that we think make them perfect partners for us. We say, "Let us be your collaborator. Let us be your partner. It's not going to be a traditional vendor customer relationship. Let's work together mutually to invest resources in time and people to bring this to life."

To date, we have partnered with four health systems, all of whom share a few enabling characteristics. First, they are integrated payer and provider systems, which makes it easier for them to effect change. Second, they are already users of advanced genomic technologies, so this is not a new thing for them in concept. And third, and this is important for us, they're willing to share patient data with us in a collaborative way that most partners do not typically see.

When you hit all three characteristics, it's super exciting and we've achieved that with these four health systems. And of course, Eric would tell you that we always approach these counterparts with creating a partnership with a research-driven mindset being our key offering to them. Many of these health systems are premier institutions, but they are not necessarily among the top decile of NIH grant recipients. They have ambitions to be bigger research institutions but they may not have the ability to do it themselves. We can catalyze that, and that resonates with their missions.

JPM: Centrellis®, Sema4's health intelligence platform, appears to be core to Sema4's capabilities. How will Sema4 be powered up by access to GeneDx data and Centrellis capabilities?

Isaac: Centrellis combines several important capabilities that, together, make the platform special. Keep in mind - it's not just the technology component; it starts with people and talent. We have over 160 computational biologists, people with MD and PhD level degrees who sit at the core of the platform to curate, annotate, and process the data inputs. If you've spent any time with healthcare data, you learn quickly that it tends to be dirty, inconsistent, and not easily manipulated and analyzed. And while AI is an incredibly powerful tool, it's still the case of

“garbage in, garbage out.” If you don't have clean, well-curated, well-annotated data, then what AI can tell you is very limiting. You still need world class scientific know-how and capability that sits on top of your cloud and your computing resources, especially as cloud storage and computing power is becoming more and more available, almost as a commodity.

Along with NGS (Next Generation Sequencing), we are riding powerful technological tailwinds, but my point is that you need people to harness it. So, say now you have the people and the technology - the third thing you need is access to high-quality data. In general, access to patient data is tricky because there's a lot of data for purchase in the marketplace, but those data are typically limited by clinical context. It's one thing to have a snapshot of someone's genetic code but with no other information about their diagnosis, their treatment history or future, or physician interpretation with a proper diagnosis. Without all those things, it's just information. So, in an ideal world, you would want not only a snapshot of patient data, but you would also want those data over a period of time.

Access to longitudinal data sets becomes very important. The only way we see to gain access to these data is to have a high level, trusting relationship with the provider. Our go-to-market strategy for the health systems starts with building a relationship with the physician - our user. You need to have that relationship for the data to be dimensionalized and, of course, scalable over time. So those are the three things we've done to make Centrellis special. Some companies can circle one or two of those three concentric circles in the Venn diagram, but no one else currently covers all three, and certainly not at the necessary scale.

JPM: Can you expand on the experience of the people at Sema4 in the relevant disciplines?

Isaac: Experience is extremely important to us. It brings intangibles that start with respect for the privacy and the sanctity of the data we host. In fact, we use the word “access” because we don't believe we own the patient data. Data belongs to the patient. We are privileged to have access to it, and that requires trust, security, and investment in that security.

We make sure that the physician and the user experience are governed by those values. We put ourselves in the shoes of a patient. In the case of women going through a pregnancy, we provide them tools that can be accessed on a smartphone or with a simple web interface, all those soft touch things that make the experience better with educational tools.

We engage not just in education for the patient, but also the physician. Physicians are increasingly overwhelmed with new information and technology; they need help understanding how to use these tools (information and technology), as well as the circumstances for which tools are applicable. We serve those purposes while keeping security and a research collaboration mentality foremost in mind.

That's why we've been able to get this unfettered, extremely rare level of access with high rates of consent. When we ask patients for consent to access their medical records, they say yes at unusually high rates because we've put all this together over time in a way that resonates with the health system partnership approach.

Our engagement with health systems is different in many ways, not just the fact that it's not a traditional sales call. But it's also typically from the top down where our CEO is going to the CEOs of these health systems and saying, "Let's architect something that allows you to accomplish a big part of your agenda as a health system administrator and work with you there from the top down." When you do that, you get a different level of buy-in. Once we've got that level of buy-in, it becomes a very different relationship.

Now, of course, every department in a health system is different and has different agendas. You've got to create not just sponsorship from the top down, but also champions within, at the department level. When you do that, you come up with specific scopes of work, for example, in women's health, cancer or rare disease.

That's how we put these relationships together. In doing all that, it allows for a much higher level of trust and collaboration out of the gate. As the CFO, I can tell you in numbers that trust can be expressed by how health systems are investing their resources – person hours and, in some cases, millions of their own dollars. Most health systems are non-profit, so this is a non-trivial investment for them.

JPM: What are the top two or three lessons learned from partners that Sema4 uses to improve its performance and platforms?

Isaac: It is important to remember we are at the infancy of this industry's evolution. When we talk about partners, we also think of them as learning-based partnerships. We're both in it, not only to make an impact, but also to learn. The nature of the industry is not a one-size fits all model by any stretch, and it won't be anytime soon. If you've met with one health system, you've met with one health system. I liken it to a systems integration type business model. Think of it as a McKinsey or a Deloitte coming in and doing a big ERP upgrade to a global company.

It's that kind of a close relationship that's consultative in nature but iterates over a long period of time with a dedicated hub and spoke team mindset. You do all those things because you just don't know exactly when and how it's going to land. And the whole thing will happen in chapters, but the whole book end to end is hard to write. When we think about where we are today in 2022, I suspect that in two or three years, we may see developing a small, medium, and large way to define how things are different.

There's been an extraordinary uptake and incredibly encouraging levels of feedback on the impact that we're already having. We talked on our third quarter earnings call about the first six months with Northshore University HealthSystem in Chicago and their extraordinary rates of compliance for cancer risk assessment that are multiples of what they had before they partnered with us. They've been doing this for years, so there is clearly a sea change. We'll see how well it sticks, but we feel good about the progress so far.

JPM: As for partners, are you talking to systems that offer multi-stage coverage? Or is Sema4 currently targeting at a local level for partnerships? What do you see in terms of regional differences?

Isaac: Let's go back to the comment I made about the market structure of health systems. They're all different. However, you can place categories at either end of the spectrum.

At the one end of the spectrum, you have, say, 50 or so of the nation's strongest, most sophisticated health systems who are very well resourced and very sophisticated in what they're doing in this field. They might ask, "What about working with Sema4?" They may say, "What they're doing is cool, but we can do what they do ourselves, or maybe we already are. So, why would we need a commercial partner?"

At the other end of the spectrum, you're going to have a large tail of community health systems that, even if they wanted to implement something like this, they just don't have the ability to do it. It's just too heavy of a lift.

Like any distribution curve, most opportunities lie for us in the middle range, where you find large, integrated payer provider systems that use genomics and are willing to share data. If your company fits that trifecta, then you are probably a good partner for us. That middle chunk is a universe of health systems that we think is more than big enough, certainly multiples bigger, than we can realistically service anytime soon. For us, this business growth opportunity goes about as far as the eye can see, and that's great. We don't expect to be the ideal solution for everyone. That's not how healthcare works and that's not our ambition, at least not any time soon. Maybe someday down the road!

We are heading in the right direction. We've also just taken the business model in this industry and turned it on its head, and we'll head toward this universe of companies that look and feel similar to where we are. I remind investors and external audiences that Eric conceived of the business as a data-first culture, and that's who we are today.

We have resources and assets attractive to this universe of companies, including things like a lab that we're very proud of and a franchise that is very strong. We've got a huge sales force that's done a great job, going toe to toe with the other public companies and diagnostics outfits. But we don't aspire to be purely a diagnostic company. We want to be a data company that happens to have a great diagnostic business, not the reverse. That's a stark contrast to what you see elsewhere in the industry, where it's mostly diagnostic companies who have grown up and done very well and now are trying to become data companies.

I would submit that it's probably harder to do the former. We'll see how it all plays out, but there may possibly be convergence from opposite directions. And then on top of all that, you have data companies who have good know-how on software and analysis, but maybe don't understand genomics deeply enough. The genomics piece, as evidenced by the GeneDx deal, is a market that is moving and evolving so fast that it's difficult to be a primary player with primary know-how in the wet lab and still claim that you can harness all technology well.

We are moving to the exome world and will eventually move to the whole genome world. We want to be a company that has a primary role in making transitions happen and isn't just a customer of the data feeds - that's going to be a limited way to live. We know about great data and software companies out there, but we still think you need to have a fully vertically integrated business model - you need the lab, you need the data scientists, you need, of course, the data platform, and you need the relationships with health systems. You need all of those pieces to do what we're doing.

JPM: To what extent has Sema4 made progress in extending and keeping in the loop with patients? Does Sema4 continue to receive information throughout the patient journey for treatments and outcomes? The critical point at the end is, what is the outcome of that patient? And how does that feed back into the Sema4 platform?

Isaac: We very much believe in being with a patient on a relational basis through a healthcare journey - and that is part of the reason we started with women's health. Women and potential parents come in seeking to conceive through a fertility process that requires carrier screening. What we do best is support those who go through that fertility process and progress to a pregnancy, then continue that support with newborn screening and documenting the mother's health journey.

For the newborn, you might have a need to test for rare disease, which is where GeneDx fits in and why GeneDx is so valuable. GeneDx is by far the market leader for clinical exome

sequencing of newborns to screen undiagnosed rare disease. Rare disease is not as rare as implied by the name; any one condition may be a small percent of the population but the cumulative effect of the variety of rare diseases prevalent in a population can be significant.

Currently, many cases go undiagnosed because technologies were not available (for example, sequencing and better annotation). We're now entering this amazing era where testing is potentially available to everyone. We want to be a big part of driving that forward and extend our relationship with the family into the newborn's life. We started to evolve our marketing to say that we're a family health company post transaction, supporting multiple members of the family, not just the mother. If we can do that writ large, you can imagine a database at population scale across large catchment areas where you have families and extended families all connected into the network.

Here's where the value to drug discovery becomes exciting. Instead of searching for proverbial needles in a massive global haystack - the 20 children across the world who have this one diagnosed disease – we prefer to say, "We found a case in this one area and started to look at the genomic profiles and medical records of the people where this child lives." Can we find patterns in the noise? Can we learn something about a rare disease that way?

We aim to follow patient journeys writ large over time and across populations - treatment, diagnosis to gain longitudinal perspectives. We want to have that level of dimensionality in the rare disease context for an individual as well as at population scale. This allows us to talk to drug companies about clinical trial enrollment, pipeline development - things that you could not do before are now possible. That is, in our estimation, an extremely powerful catalyst for value creation and for potential treatments where none exist today.

JPM: In line with Sema4's focus on family health, could you discuss Sema4's plans for genetic counselling and how this capability will be coordinated with healthcare partners?

Isaac: Let's step back and put ourselves in the shoes of a physician, that feeling of being overwhelmed with all this data and what does it mean? Even with a well-curated AI-powered data platform like Sema4's platform, the physician will still take delivery of a complex information packet that may require handholding in some cases. We decided to offer a value-added service to give physicians more tools to enhance *their* experience, as well as the patients. And increasingly, those tools are made available through a web and smartphone interface, because that's just the way people operate these days, especially when you think about what's changed during the pandemic. Telehealth has taken off.

This trend has been accelerated by the pandemic. Healthcare can now reach more patients directly with high resolution feedback on patients' genetics. We see it as an area of continued investment for us, and another reason why we believe you need to have genetic counselors and the relationship with the health system in this fully vertically integrated business model.

We're exiting a phase of infancy in the clinical NGS market where companies like Illumina have done incredible things. NGS has given rise to a number of companies that are doing a lot of good for patients. In cancer, in women's health, those are the most mature areas today and we are starting to see different types of innovation in these and other areas.

Tests are starting to converge. Several companies have very strong offerings in tumor profiling, Noninvasive prenatal testing (NIPT), and hereditary risk assessment. Now the question becomes, how do you have a greater impact clinically? Many companies tend to focus on price,

service, and quality, but these dimensions start to be taken for granted. Instead, we asked, "What about the physician experience? What about the patient experience? What about clinical context? What about actionability?"

Diagnostic testing has been around for a long time but, historically, a diagnostic test identified the patient’s condition but not enough depth to indicate a treatment – precision medicine. The doctor needed to adjudicate actionability. And now, the equation's flipping where the mass of data is more than a doctor can digest. That's why genetic counseling becomes important and why companies like us become more relevant. It's an exciting time to start thinking about the evolution of business models and we see ourselves as pioneers in market evolution.

JPM: Both companies, GeneDx and Sema4, have genetic counseling. How will these capabilities be merged? How will this function be leveraged by your healthcare system partners?

Isaac: We expect the completion of the Sema4-GeneDx deal in Q2 2022. During this period, we are highly constrained by what we're allowed to do when it comes to integration. We can do a lot of preparation, but we can't take a lot of action.

So, in answer to that question, I can say that the combined company’s goal would be to drive clinical exome sequencing into the market as quickly as possible. We're not alone in that vision. Other companies are starting to do it, but we think we're going to have a huge running start. As a combined company, our attention will focus on how to support the physicians and patients with this quantum leap in data volume and content.

We see that genetic counseling will only become bigger and more diversified - for example, GeneDx in the rare disease market and Sema4 on the women's health side. We are both somewhat small but growing players in oncology. Those three therapeutic areas are where we seek to build out our genetic counseling capabilities. We come with critical mass on both sides, so that gives us a huge opportunity to stay in the lead once we're done. That's the best I can say today. We’re super-excited to see how it plays out once the deal closes in Q2.

JPM: Any final comments?

Isaac: I would just like to say one last thing, which is to acknowledge that we know we're not the only ones working on cool stuff. We are riding a wave on a sea change in the entire healthcare ecosystem, from global drug companies leaning hard into the ways these technologies can improve drug development to a cottage industry of software companies - all trying to capitalize on digital health and moving towards this future state driven by data, relationships, and platform technologies.

And while we’re vertically integrated, we’re also seeking those who work with all ranges of constituencies for opportunities to partner. Right now, we're working first and foremost on closing the Sema4-GeneDx deal. In the meantime, our corporate development team is busy looking for other entities with whom we can work. Stay tuned.

Cautionary Statement Regarding Forward Looking Statements

This communication contains certain forward-looking statements within the meaning of the federal securities laws with respect to the proposed transactions, including statements regarding the anticipated benefits of the transactions, the anticipated timing of the transactions, expansion plans, projected future results and market opportunities of Sema4. These forward-looking

statements generally are identified by the words “believe,” “project,” “expect,” “anticipate,” “estimate,” “intend,” “strategy,” “future,” “opportunity,” “plan,” “may,” “should,” “will,” “would,” “will be,” “will continue,” “will likely result,” and similar expressions. Forward-looking statements are predictions, projections and other statements about future events that are based on current expectations and assumptions and, as a result, are subject to risks and uncertainties. Many factors could cause actual future events to differ materially from the forward-looking statements in this communication, including but not limited to: (i) the risk that the transactions may not be completed in a timely manner or at all, which may adversely affect the price of Sema4’s securities, (ii) the risk that the transactions may not be completed by the acquisition deadline and the potential failure to obtain an extension of the acquisition deadline if sought by either of the parties, (iii) the failure to satisfy the conditions to the consummation of the transactions, including approval by the stockholders of Sema4 of the issuance of the stock consideration pursuant to the merger agreement, the ratification of the required consent condition, the satisfaction of the pre-closing restructuring conditions and the other conditions specified in the merger agreement, (iii) the inability to complete the private placement financing in connection with the transactions and the fact that Sema4’s obligation to consummate the mergers is not conditioned on the completion of the private placement financing, (iv) the occurrence of any event, change or other circumstance that could give rise to the termination of the merger agreement, (vi) the effect of the announcement or pendency of the transactions on Sema4’s or GeneDx’s business relationships, operating results and business generally, (vii) risks that the transactions disrupt current plans and operations of Sema4 or GeneDx and potential difficulties in Sema4 or GeneDx employee retention as a result of the transactions, (viii) the outcome of any legal proceedings that may be instituted against Sema4 or GeneDx related to the merger agreement or the transactions, (ix) the ability to maintain the listing of Sema4’s securities on the Nasdaq Global Select Market, (x) the price of Sema4’s securities may be volatile due to a variety of factors, including changes in the competitive and highly regulated industries in which Sema4 and GeneDx operate, variations in operating performance across competitors, and changes in laws and regulations affecting Sema4’s or GeneDx’s business, (xi) the ability to implement business plans, forecasts, and other expectations after the completion of the transactions, and identify and realize additional opportunities, (xii) the risk of downturns and a changing regulatory landscape in the highly competitive healthcare industry, and (xiii) the size and growth of the markets in which each of Sema4 and GeneDx operates. The foregoing list of factors is not exhaustive. You should carefully consider the foregoing factors and the other risks and uncertainties described in the “Risk Factors” section of Sema4’s Quarterly Report on Form 10-Q for the fiscal quarter ended September 30, 2021, filed with the U.S. Securities and Exchange Commission (the “SEC”) and other documents filed by Sema4 from time to time with the SEC. These filings identify and address other important risks and uncertainties that could cause actual events and results to differ materially from those contained in the forward-looking statements. Forward-looking statements speak only as of the date they are made. Readers are cautioned not to put undue reliance on forward-looking statements, and Sema4 assumes no obligation and does not intend to update or revise these forward-looking statements, whether as a result of new information, future events, or otherwise. Sema4 gives no assurance that either GeneDx or Sema4 or the combined company will achieve its expectations.

Additional Information and Where to Find It / Non-Solicitation

In connection with the proposed transactions, Sema4 intends to file a proxy statement with the SEC. The proxy statement will be sent to the stockholders of Sema4. Sema4 also will file other documents regarding the proposed transactions with the SEC. BEFORE MAKING ANY VOTING DECISION, INVESTORS AND SECURITY HOLDERS OF SEMA4 ARE URGED TO READ THE PROXY STATEMENT AND ALL OTHER RELEVANT DOCUMENTS FILED OR THAT WILL BE FILED WITH THE SEC IN CONNECTION WITH THE PROPOSED TRANSACTIONS AS THEY BECOME AVAILABLE BECAUSE THEY WILL CONTAIN IMPORTANT INFORMATION ABOUT THE PROPOSED TRANSACTIONS. Investors and security holders will be able to obtain free copies of the proxy statement and all other relevant documents filed or that will be filed with the SEC by Sema4 through the website maintained by the SEC at www.sec.gov.

The documents filed by Sema4 with the SEC also may be obtained free of charge at Sema4's investor relations portion of its website at www.sema4.com or upon written request to Sema4 Holdings Corp., 333 Ludlow Street, North Tower, 8th Floor, Stamford, Connecticut, 06902.

Participants in Solicitation

Sema4 and GeneDx and their respective directors and executive officers may be deemed to be participants in the solicitation of proxies from Sema4's stockholders in connection with the proposed transactions. Information about Sema4's directors and executive officers and their ownership of Sema4's securities is set forth in Sema4's filings with the SEC. To the extent that holdings of Sema4's securities have changed since the amounts printed in Sema4's Registration Statement on Form S-1 (File No. 333-258467), such changes have been or will be reflected on Statements of Change in Ownership on Form 4 filed with the SEC. A list of the names of such directors and executive officers and information regarding their interests in the acquisition will be contained in the proxy statement when available. You may obtain free copies of these documents as described in the preceding paragraph.

No Offer or Solicitation

This communication does not constitute an offer to sell or the solicitation of an offer to buy any securities, or a solicitation of any vote or approval, nor shall there be any sale of securities in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such jurisdiction..