White Paper
Fundamental Growth and Core Equity

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Investing in Sustainable Growth
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STATE STREET GLOBAL ADVISORS

Contents

Innovation Is Not Limited to the Tech Sector

Innovation and the pace of technological change have been recurring themes in the Fundamental Growth and Core Equity team's newsletters. Artificial Intelligence has consumed the market's attention for some time now, but the theme of change and innovation has not been limited to the tech sector.

In healthcare, the introduction of GLP-1 drugs to treat obesity may have a significant impact on people's health. This pharmaceutical innovation has parallels with Artificial Intelligence. Nvidia's GPU chips were used for many years to power graphics for gaming but they have found new life in supporting large language models for generative AI. Similarly, GLP-1[1] drugs were used in the treatment of diabetes but were then found to be quite useful for weight loss giving them a much broader and more profound appeal.

A second parallel is that in AI, the release of ChatGPT has driven a frenzy of activity across industries as companies weigh how AI might help or hurt their businesses. Similarly with GLP-1s, the potential impact on health has set off activity well beyond pharmaceutical companies to include those in the consumer, medical equipment, and health insurance sectors. Another recurring theme in our newsletters is that we find some companies are better than others at reacting and adapting to change. This is something we call quality. Our first article in this newsletter explores many of the second-order effects of the release of GLP-1s and looks at some of the companies that may benefit.

In our second article, we profile a less well-known company called Tetra Tech, an engineering and consulting firm that specializes in water and environmental related projects. The company is benefitting from secular themes such as infrastructure investment and adapting to climate change.

Fundamental Equity Analysis: Assessing the Investment Impact of Weight Loss Drugs

A crucial aspect of fundamental analysis is understanding industry structures and trends. The Fundamental Growth and Core (FGC) equity research team assess companies through our proprietary Confidence Quotient (CQ) process, a key elements of which is to look at a firm's Market Position to determine the moat, or competitive advantage, of their business model.

Whenever a new trend emerges, such as obesity-related drugs, our analysts must 1) determine the size of the market opportunity to establish current and prospective growth rates, 2) assess the competitive forces at play and 3) gain confidence in the sustainability of that growth. We believe that investors must look at cross-sector implications to determine if this is a secular trend that disrupts other industries. While the market can often be very quick at identifying a new trend that can negatively impact an industry, only a deep understanding of the fundamentals can lead to an accurate assessment of the trend's potential impact. A tendency among some market participants to leap to an early, and misleading, conclusion can create buying opportunities among quality companies for a well-informed investor.

Four FGC analysts have undertaken a deep assessment of the obesity drugs and the impact on the sectors they cover to determine the sustainability of these new drugs and any negative implications for other industries.

Oral Obesity Molecules: Game Changer?

Shalabh Gupta
Research Analyst —
Global Bio-Pharma

With their blockbuster drugs, Wegovy and Ozempic, biopharmaceutical companies Eli Lilly and Novo Nordisk have made great strides in the treatment of obesity. However, the first generation of these highly efficacious weight loss drugs are administered subcutaneously (e.g., via injection) and manufacturing constraints and the high manufacturing costs involved have resulted in limited patient uptake. And it is here where next-generation oral GLP-1s come in. Orally-taken treatments are simpler to manufacture and usually don't have cold-chain requirements for shipping and storage — the oral class represents a novel method to achieve broad penetration along with more favorable pricing, therefore bolstering them as weight-loss drugs for the wider population. We believe the markets are underestimating the market share that orals can garner once launched post-2027. The total obesity and diabetes market is estimated to reach $150 billion in sales by 2023, with obesity being the key driver of growth — we expect orals to account for at least two-thirds of the sales mix for obesity products.

Based on proprietary analysis and discussions with prescribers, we recognize that to unlock the vast commercial opportunity for orals, the GLP-1s have to be safe, efficacious, and easy to manufacture and scale up, as this would get primary care prescribers on board. Looking to the upcoming trials, we would categorize any asset that shows low-teens weight loss (13%+), low discontinuation rates (<5%) due to tolerability, and zero liver toxicities to be a clear winner. We are tracking the space closely as multiple companies are running clinical trials and we are identifying what we consider to be hidden gems like AstraZeneca, whose valuation does not appear to have priced in the opportunity for its obesity treatment. AstraZeneca trades at a 2025 price/earnings (P/E) multiple of 15x, which is a huge discount to names like Eli Lilly and Novo Nordisk, which are trading at 45x 2025 P/E.[2] We like the call-optionality of Astra's obesity franchise, where we could see key clinical data in June 2024 at the American Diabetes Association medical meeting.

In the near term, we are watching several clinical test results that could act as positive catalysts for the sector and the companies involved. Figure 1 shows the companies, the drug, and the test results time frame. This could be the defining year for obesity treatment options for the masses, as one of these molecules could have the ideal clinical profile and manufacturability. We believe the price-sensitive OUS (Asia and Europe) markets will be the biggest beneficiary of oral treatment and we expect very rapid uptake toward the end of the decade. Our understanding from surveys and prescribers in the US is that oral molecules will be initially used for maintenance (i.e., to maintain a target weight) post-GLP1 injectables. Once these molecules are widely available, we believe that their efficacy, pricing, distribution, and side-effect profile could drive their usage and penetration into frontline use. On a net-net basis, we consider oral molecules to be game-changing for widespread obesity treatment globally and we expect that the transformative product will be identified in 2024.

Company	Drug	Results Expected
Novo Nordisk	Amycretin (oral)	June 2024
Novo Nordisk	CB1R inverse agonist monlunabant	Phase 2 results: Late 2024/early 2025
Lilly	Orforglipron (oral)	H1 2025
Viking	VK2735 (oral)	Phase 1 28-Day results: Q1 2025
Pfizer	Reformulation of danuglipron	Phase 1 results: H1 2024
Amgen	AMG786	Phase 1 results: H1 2024
AstraZeneca/Eccogene	ECC5004	Phase 1/2 results: H1 2024
Roche/Carmot	CT-996	Phase 1 results: H1 2024
Structure	GSBR-1290	Phase 2a results: Q2 2024
Tern	TERN-601	Phase 1 results: H2 2024

Source: Company data.

Why Procedures Won't Go to Zero

Stephen Kao
Research Analyst — Global Healthcare Equipment

The initial reaction to GLP-1s seemed to suggest an expectation that these will cure all weight-related diseases, bringing medical procedures to zero, and taking Medical Device companies down with them. While few are questioning the efficacy of GLP-1s or that obesity is a risk factor for many health ailments, affordability is the single largest barrier to widespread adoption. To quote UnitedHealth CEO Dirk McMahon, "innovation that is not affordable is not innovative." According to the Congressional Budget Office, "at current prices, anti-obesity medications would cost the federal government more than it would save from reducing other health care spending...over the next 10 years." In other words, the benefit provided by reduced comorbidities does not justify the cost. To put some numbers around this, the average annual health expenditure for a non-obese American adult is $15,000. An obese adult costs 30–50% more, or $4,500–7,500 per annum.[3] This compares to $12,000 for an annual supply of GLP-1s, which may need to be taken in perpetuity. Bariatric surgery as one possible alternative represents a one-time cost between $17,000–26,000[4] and is a permanent solution that typically results in greater weight loss than GLP-1s.

Putting aside the monetary costs, just how effective are GLP-1s? Novo Nordisk's Select trial showed a 19% reduction in Major Adverse Cardiac Events (MACE). That's an impressive headline, but note it is a *relative* risk reduction (a percentage of a small percentage: 6.5% MACE occurrence with Wegovy vs 8.0% in the placebo arm (i.e., the absolute MACE reduction is only 1.5%). The discontinuation rate was higher than expected (17%) and the benefit was limited in patients with a body mass index over 35. So GLP-1s help, but they're not a cure-all.

Oral GLP-1s may represent an affordable future option, so what happens to procedures in the event of broad adoption? Statins provide a good corollary. This "wonder drug" was introduced in the mid-1990s to treat cholesterol. Since going generic in the mid-2000s, this affordable once-daily pill is taken by millions of people around the world. Similar to GLP-1s, statins show a MACE reduction of over 20%.[5] At the time, there were widespread fears this would significantly impair cardiac procedures, but device companies have continued to grow at healthy rates for the past two decades. The reality is GLP-1s and Devices are likely complementary rather than mutually exclusive. Here are some of the Device categories thought to be at greatest risk from GLP-1s and why the outlook may not be as dire as feared:

Hip/knee replacement It's logical to think heavier individuals experience more joint pain. However, the primary drivers of osteoarthritis are age, genetics, and joint injury. Obesity can act as an accelerator, but once the cartilage is damaged, it's irreversible; losing weight won't make a difference. Weight loss does result in longer life expectancy (risk factor #1: age) and likely leads to a more active lifestyle (more joint wear and tear). Furthermore, 10% of patients are too obese to undergo a large joint replacement. Weight loss would enable those patients to get surgery.[6]

Continuous glucose monitors (CGM) GLP-1s can slow the progression of type 2 diabetes, particularly the earlier these are taken. This arguably will impact the total addressable market at some point in the (distant) future, but 1) CGM penetration rates are still low, and 2) using CGMs in conjunction with GLP-1 therapy can lead to better outcomes.

Obstructive sleep apnea (OSA) 60–80% of OSA cases are correlated with BMI. Similar to CGMs, weight loss may ultimately shrink the TAM, but 1) penetration is low, and 2) CPAP devices are likely to be used in tandem with GLP-1s in many instances.

Consumers on GLP-1 Still Need to Eat

Nicolas Caron,
Research Analyst —
US Consumer Staples

As the enthusiasm for GLP-1 took off over the summer of 2023, the market valuations of Food and Beverages companies compressed — in some cases to historical lows versus the S&P 500 Index. The industry discovered firsthand the impact these drugs could have on business models by challenging their growth algorithms, which have proven to be so resilient for decades.

GLP-1 users do not stop eating completely, but there is a severe caloric reduction that happens on this drug. Sugary food and beverage and alcohol consumption appear to be the biggest losers of changing consumers' cravings, with some studies reporting 50%-to-100% consumption reduction in those categories which are a significant part of the offering of many Food and Beverage manufacturers[7] — consequently, there is a real risk for their business models as adoption rates increase. We believe this is a serious threat for the sector, but we also anticipate that companies can find ways to reduce the impact over time. First off, these companies typically have strong market positions due to their distribution network and the sizable shelf space they occupy within the major retailers. Lost volume in impacted categories could be offset with other products to better suit customers' taste, just like they transitioned to zero sugar over time for some key products. Merger and acquisition (M&A) activity could also bring new products and categories to help them retain dominant shelf space with retailers. Second, the negative impact on sales is likely to be a gradual development as GLP-1 adoption rates increase and this evolving headwind should be offset by higher growth in many emerging market countries where the rate of adoption of appetite-suppressing medication should be much slower.

We believe the initial stock market reaction last summer was too harsh and too early as GLP-1 adoption rates are still very low. We are mindful that GLP-1 drugs will remain a threat for Food and Beverage manufacturers, especially as we get more data on these medications. Study results confirming the effectiveness of the medication, or any indication of a successful oral version, would be a significant negative catalyst for sentiment. Therefore, despite strong current market positions we believe the upside potential in the short term will be limited at valuations that are depressed from historical highs in many cases.

Healthy Nutrition is Key for Sustained Weight Loss

Nicole Chanthasoto
Research Analyst — International Consumer Staples

The sudden sell-off in many of the Food and Beverage names implied that food consumption is in a structural decline amid anecdotes from retailers like Wal-Mart and surveys from data providers indicating that GLP-1 users have spent incrementally less at the grocery store.[8] However, the sell-off was also indiscriminate, which creates an opportunity for stockpickers to identify and buy the companies best positioned to defend against, or even grow alongside, a widespread use of GLP-1s at reasonable valuations.

Food and beverage manufacturers have already indicated ways to support users, from enhancing the effectiveness of weight loss by preserving muscle mass, bone density, and essential nutrients, to addressing currently-known adverse issues, most notably gastrointestinal symptoms.
The most crucial part of the GLP-1 experience is for the user to ensure that the weight loss, once off the drug, remains sustainable by maintaining a balanced diet. Food and beverage companies already offer and continue to revamp their product lines with options that are better portioned and nutritious with less sugar and/or low-to-zero calories. Companies with revenues mainly tied to the consumption of high fat, high calorific, and high sugar products, such as snacks, sweets, and other indulgent categories, are at a structural disadvantage in the longer term. Even alcoholic beverage companies sell non-alcoholic and low-calorie extensions of their longstanding flagship brands today.

Regardless of the outcomes of the use of GLP-1s, people are becoming more health-conscious — this is particularly the case among key demographics. Food and Beverage companies have been executing their ongoing “premiumization strategy,” which aims to get more consumers to pay more for higher-quality products, and categories complementary to GLP-1s will be a way to differentiate and ultimately maintain leading market positions in the industry.

The Bottom Line: Knowing Your Companies Pays Off

Identifying quality companies with sustainable growth at a reasonable price necessitates rigorous fundamental analysis. The FGC team follows a well-established research process, based on our proprietary Confidence Quotient framework. When a powerful and disruptive event like these weight-loss drugs hit the market, investors need to assess the broader implications for a company’s fundamentals. It’s always easier to paint with a “wide brush” on all stocks that can be impacted, whether positively or negatively, but only a diligent and rigorous analysis of companies’ market positions can help identify winners and losers. The FGC team has been guided by this fundamental process for over 20 years with great success.

US Infrastructure and the Water Opportunity

Noble Alden
Research Analyst

The US has historically underinvested in water infrastructure. Lead piping, periodic water main breaks, emerging contaminants, and dated wastewater and drinking water systems continue to present issues for the existing system. While the need for improvement to infrastructure is a key concern, it is not the only water-related challenge. Climate change also drives the need for additional investment in climate resiliency infrastructure for coastal communities impacted from rising sea levels and increased frequency of extreme weather events.

Unpacking Water Infrastructure Spending

Fortunately, recent attention from policy makers and corporate stakeholders has shined a light on this theme, and recent legislation aims to address these infrastructure challenges. The US Infrastructure Investment and Jobs Act (IIJA) signed into effect on November 15, 2021, allocates $550 billion of new federal funding across many key infrastructure sectors,[9] including an incremental $92 billion for water-related projects as shown in Figure 1. We believe water will remain a key focus for the public sector in the US as it is integral to maintaining clean water access for communities, is a key resource for the industrial economy, and is impacted by climate change. With the significant increase in spending that the IIJA brings, we believe it presents an attractive multi-year investment opportunity in an underappreciated area of infrastructure.

Figure 1
IIJA Water Funding Breakdown

General Water ($65 billion)

- **$24.4B** Drinking water improvements
- **$15.0B** Lead service lines replacement
- **$10.0B** Testing and water treatment
- **$6.0** Clean water and facilities development for protected Native American Indian land and communities
- **$1.3B** Tax incentive for water storage related construction
- **$8.3B** Water storage, recycling/reuse, desalination, and other improvements for western and rural communities

Resilience ($15 billion)

- **$7.7B** Investments in Resilience related to hurricane and storm risk management, flood risk management, and ecosystem restoration efforts in aquatic areas
- **$3.8B** Water storage and efficiency/reuse technology to combat drought in western geographies
- **$3.5B** Flood Mitigation Assistance Program

Port and Water Ways ($12 billion)

- **$8.8B** Funding for coastal ports and inland waterways
- **$2.25B** Port Infrastructure Development Program to address sea level elevation, flooding, extreme weather events, and energy efficiency
- **$1.4B** Other programs including marine highway programs, ferry terminal facilities, and shore housing survey and design

Source: State Street Global Advisors, Infrastructure Investment and Jobs Act (IIJA), US White House, as of November 15, 2021. The information contained above is for illustrative purposes only.

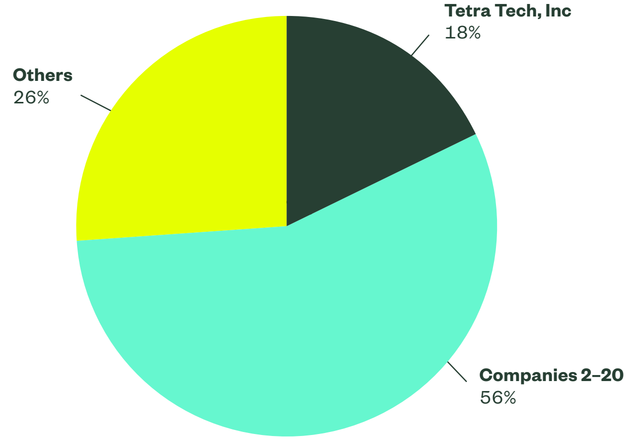
Finding Quality Growth in Infrastructure: Tetra Tech, Inc

Tetra Tech is an engineering and consulting services firm focused on providing unique professional expertise in the preliminary stages of infrastructure and other capital projects. Tetra Tech specializes in projects specifically related to water, environment, and climate. The company has the highest mix of exposure to water-related projects relative to industry peers. The company's water and environmental capabilities include research & development (5%), coastal and watershed management (60%), advanced water treatment (20%), high performance buildings (10%), and renewable energy (5%).

Quality Leader with a Durable Growth Runway

The Active Fundamental Equity team uses a proprietary Confidence Quotient (CQ) quality framework to evaluate the durable competitive advantage of a company. Tetra Tech exhibits strong quality attributes as measured in this framework. As an industry leader, the company has maintained a dominant 18% market share within their core water competency and has consistently been top-ranked in water infrastructure projects for the past 20 years. This strong brand strength is a key component of the Market Position element of CQ.

Figure 2
US Water Engineering Services Market Share (2022)



Source: Engineering News-Record, RBC Capital Markets, State Street Global Advisors.

Market Position Another component in our assessment of Market Position is the business model. Most engineering firms tend to have lower CQ scores due to a lack of competitive differentiation. However, we evaluate Tetra Tech with a strong market position due to its differentiated business model relative to other engineering companies. The company's specialized services in the front-end of the infrastructure project life cycle stray a bit further from more commoditized engineering work, are upstream from construction, and involve more technical project expertise. These services can include project permitting, early-stage planning and valuation, feasibility studies, research and development, and environmental compliance. In many cases, this type of early-stage consulting work is essential in laying the groundwork for the physical development of large-scale infrastructure projects. The company delivers these services by leveraging a highly-skilled workforce that primarily consists of scientists and engineers based in the US.

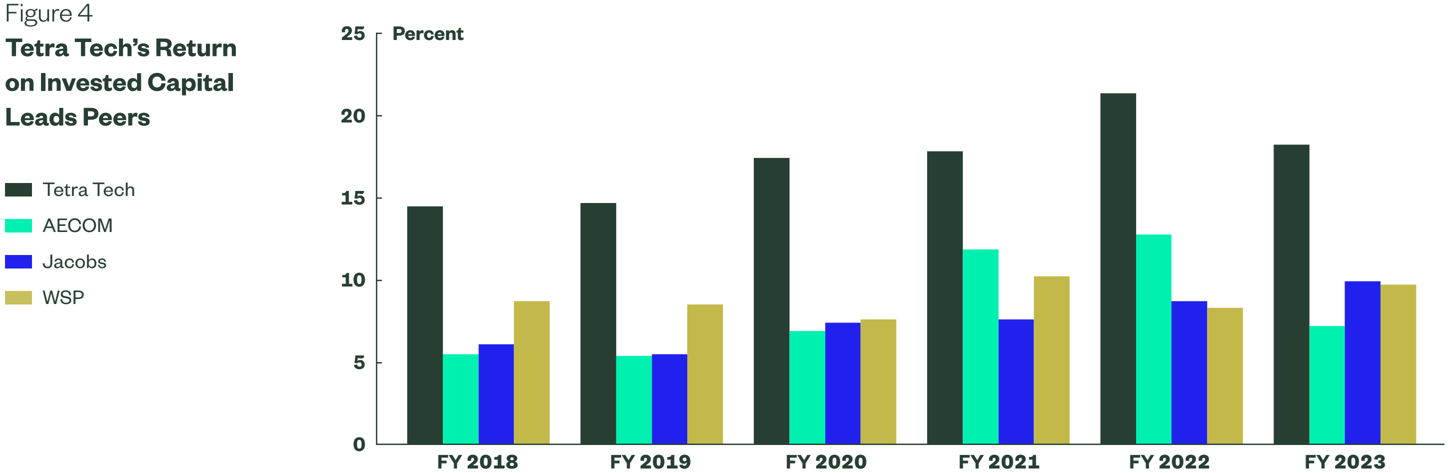
Figure 3
Tetra Tech's Project Scope

Project Lifecycle	Tetra Tech Services Mix %	Project Types
Phase 1 Project valuation, technology assessment, initial layout planning, permitting, feasibility, studies, site assessment & compliance.	65	• Renewable energy development • Ports & waterways • Drinking and waste water facilities • High performance buildings and facilities • Ecosystem and biodiversity management • Site remediation
Phase 2 Design and Engineering	35	
Phase 3 Construction		

Source: Tetra Tech Inc., State Street Global Advisors.

Tetra's leading position in front-end services is a key point of differentiation in the business model and leads to best-in-class returns relative to its peer group. The "asset light" business model and its deep subject matter expertise help the company execute scalable solutions for public and private sector clients. The use of proprietary home-grown software tools reinforces operational efficiency in the business and helps to increase project volumes without needing to scale labor at the same rate. The company's suite of home-grown software is referred to as the *Tetra Tech Delta* suite,[10] offering solutions that combine scientific and engineering expertise with complex analytical tools. The foundational use case for these tools has been developed from a deep repository of past projects, spanning 50 years.

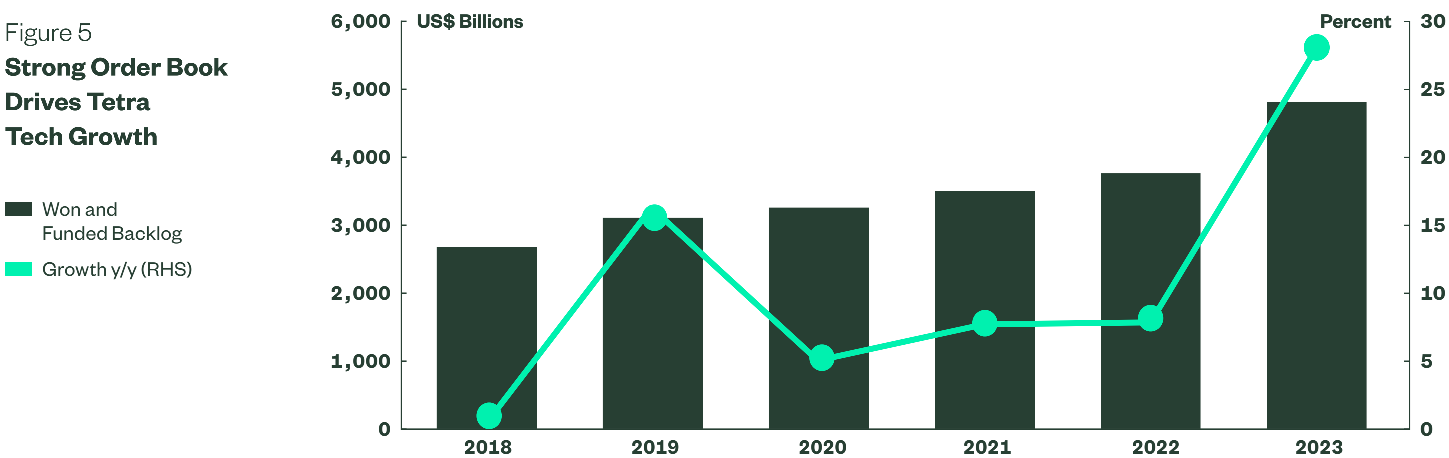
Figure 4
Tetra Tech's Return on Invested Capital Leads Peers



Source: Bloomberg Finance L.P., as of May 31, 2024.

Fundamental Momentum Tetra Tech's service offerings are strongly aligned with each category of water funding provided from the IIJA. Capabilities related to drinking and clean water, climate resiliency, and other environmental services meet many of the challenges that the IIJA seeks to address through infrastructure revitalization. However, the need for water related investment does not stop with the IIJA. According to Tetra Tech, global annual investment in water related infrastructure will need to double to $1.5T by 2030 in order to address 21st century challenges related to clean water, sanitation, climate adaptation, and emerging contaminants. This provides enhanced visibility into the company's future earnings growth. These factors indicate a strong fundamental momentum, another component of CQ.

Figure 5
Strong Order Book Drives Tetra Tech Growth



Source: Tetra Tech, as of May 2023.

Sustainability Tetra Tech is also positioned to benefit stakeholders in a world impacted by climate change. Many of the services Tetra Tech delivers enable sustainability. This includes helping private and public sector clients manage greenhouse gas reporting, energy usage, lower emissions footprint from standard business operations, and leverage sustainable building practices. We believe these competencies position the company to capitalize on climate transition in addition to legislative stimulus, as the need for private and public sector entities to manage energy efficiency and adapt to climate change increases over time.

Additional Sources

https://epa.gov/dwsrf/annual-allotment-federal-funds-states-tribes-and-territories.

https://epa.gov/cwsrf/clean-water-state-revolving-fund-cwsrf-allotments-federal-funds-states.

Contributor

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Endnotes

1 GLP-1 agonists are a class of medications that can help manage Type 2 diabetes and obesity.

2 Bloomberg forward consensus estimates.

3 UBS investor call, 9/25/23 discussing GLP-1 reimbursement for obesity. Dr. Andrew Baskin, guest speaker.

4 Crémieux, P. Y., et al (2008). A study of economic impact of bariatric surgery. The American Journal of Managed Care. Accessed from: https://ncbi.nlm.nih.gov/pubmed/18778174.

5 JP Morgan research note titled "Using History As A Guide; The Impact of Statins on MedTech & Implications for GLP-1s." November 16, 2023.

6 Zimmer Biomet, 3Q2023 earnings call.

7 Morgan Stanley AlphaWise, Downsizing Demand: Obesity Medications' Impact on the Food Ecosystem, August 7, 2023.

8 See: Doering, Christopher. "Consumers on weight-loss drugs buying less in certain grocery aisles, study finds." FoodDive. December 7, 2023. Link here: https://fooddive.com/news/consumers-on-weight-loss-drugs-buying-less-in-certain-grocery-aisles-study/701602/.

9 https://whitehouse.gov/wp-content/ uploads/2022/05/BUILDING-A-BETTER-AMERICA-V2.pdf.

10 https://tetratech.com/tetra-tech-delta/.

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* Pensions & Investments Research Center, as of December 31, 2022.
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