

The logo for PASI NEWS features the word "PASI" in a large, bold, blue serif font. A stylized blue and white graphic element resembling a sail or a leaf is positioned behind the "A". To the right of "PASI", the word "NEWS" is written in a smaller, blue, italicized serif font. Above "PASI", the text "since 1977" is written in a small, blue, sans-serif font. A horizontal line runs across the page below the logo.

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Market Update – *What is the “Market?”*

by David A. Jaffe, M.D.

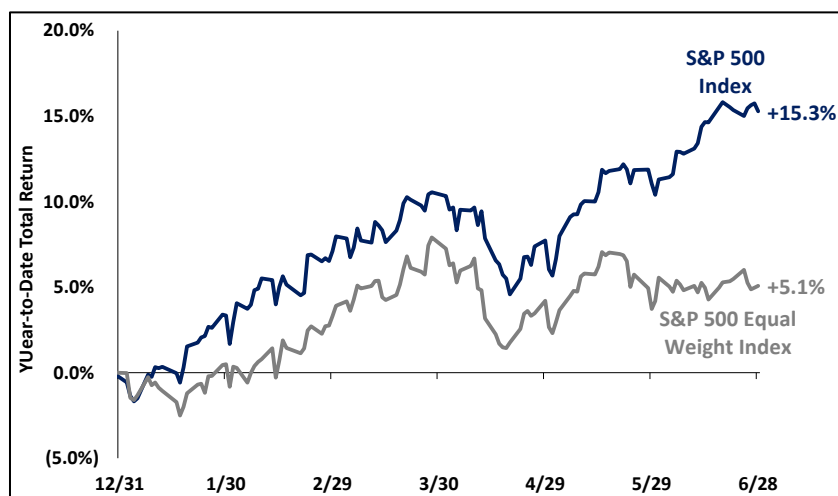
For years, my newsletter task has been to author our “Market Update.” Reporting stock and bond performance, recounting events which may have influenced those returns during the latest quarter, and offering comparison between PASI returns and those of the “market” has been pretty straightforward. Finding new adjectives to describe the same outcomes is often the most challenging part of the job (I heard today that the stock of Domino’s Pizza was “sliced.” Clever!)

While prudent investment diversification and risk management are central to our responsibilities, those elements are difficult to quantify. We recognize that first and foremost on the minds of investors is growth of their asset base, measured in dollars and percentage returns. In nominal terms, those figures are easy to calculate and share. Context, however, has become more and more complicated.

As we have discussed in previous newsletters and client meetings, calculation of the widely cited S&P 500 by sponsor Standard and Poor’s weights the contribution of individual companies based on their total stock market value (market capitalization or ‘market cap’). Thanks to stock price gains especially in the realm of artificial intelligence (AI), six technology companies are *each* valued at *over \$1 trillion* by investors: Amazon, Apple, Alphabet (Google), Meta (Facebook), Microsoft, and Nvidia. Technology businesses in aggregate now represent 44% of the total value of the S&P 500 and contributed 12.03% to the reinvested S&P 500 return of 15.29% for the first half of 2024!

Also produced by Standard and Poor’s, the Equal Weighted S&P 500 incorporates the stock returns of the same components, but without consideration for company size. With a first-half return of 5.08%, the equal stock weighting mutes the influence of the “mega-cap” technology companies and offers a broad measure of the overall economy. Of note, the gap between the

market cap weighted and equal weighted S&P 500 indexes is at the widest level since 1990.¹ Historically, when this gap reaches such an extreme level, it often presages the time when a more evenly balanced investment approach will regain favor.



Source: Bloomberg L.P. as of 6/30/2024

The challenge facing PASI and other managers favoring a portfolio based on broad industry diversification is that the commonly cited S&P 500 benchmark is now reminiscent of the “tech-heavy” Nasdaq of the 1990’s dot-com era, and less representative of the broad economy.

The PASI composite portfolio performed well in the first half of 2024, logging an average return of 7.57% YTD. This puts us ahead of the Equal Weighted S&P 500 return of 5.08%, while lagging the market cap weighted S&P 500 return of 15.29% by an admittedly wide margin (all include reinvested dividends).

Believing that the technology industry concentration of the S&P 500 lessens its value as a *comparative* benchmark, it is our plan to begin providing clients with both indexes for reference. Most importantly, we strongly encourage questions and discussion about this issue as we work to answer the question: “*What is the Market?*”

The “Magnificent Seven” Marches On

by Nathan Polackwich, CFA

In late 1999, when I was just beginning to learn about investing, I had an epiphany. Internet and technology stocks went up relentlessly practically every day. I wondered to myself, “Why couldn’t I just construct a portfolio focused on those stocks. Why did I have to own stodgy, old economy, “bricks and mortar” companies? Why should I own foreign stocks? What’s the point of bonds that pay me 5-6% a year when I could make that in a day or two with tech?”

¹ Dow Jones Market Data

To test my theory, I built a mock portfolio on Yahoo Finance consisting of companies like Cisco Systems, Microsoft, Intel, Dell, America Online, Oracle, Sun Microsystems, and a handful of others. I remember the day I created the portfolio it rose more than 5%. Warren Buffett had nothing on me!

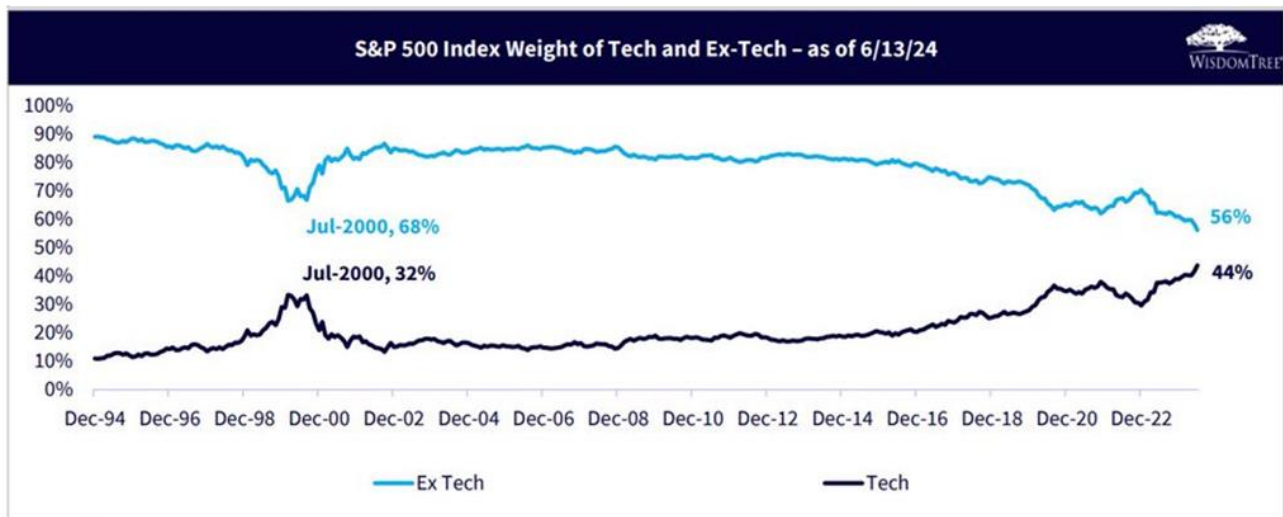
Thankfully, I didn't actually put real money into this portfolio. The stocks all peaked shortly thereafter when the Internet Bubble burst in the spring of 2000, suffering devastating declines over the next few years. In fact, between March 2000 and October 2002, the tech-heavy Nasdaq Index fell an excruciating 77%. It wasn't until 13 years later (April 2015) that the Nasdaq finally surpassed its early 2000 high.

What's fascinating about tech stocks' 15 year stretch in the proverbial wilderness is that 24 years later, even the most optimistic investors' hopes and dreams in 2000 concerning the growth and importance of the Internet were realized! Almost everyone on the planet is now constantly connected and peoples' online lives are as important as their time in the physical world (much to my chagrin). Yet despite the Internet's history-altering growth, tech stocks were a poor investment for a long time. Moreover, most of the tech companies that were dominant in early 2000 either no longer exist or remain a shadow of their former selves.

The late 1990s Internet Bubble is instructive and particularly relevant today as we're currently in the midst of the fourth great *growth* stock bubble of the last hundred years, this time inspired by advances in artificial intelligence (AI). The preceding two include the Roaring 20s (focused on new industries like autos, radio, consumer goods, electric, and telephone) and the Nifty Fifty stock bubble of the late 1960s/early 1970s (post WWII U.S. economic dominance culminating in a mania for high quality blue-chips).

Growth stock bubbles have typically been caused by significant shifts in the economy that disrupt the existing order. In his famous book, *Manias, Panics, and Crashes*, the economic historian Charles Kindleberger found that such displacements usually come from 1) the rise of a new global power like the United States in the 1920s, Japan in the 1980s, and China in the 2000s, or 2) excitement over new technologies that change the world such as railroads, automobiles, radio, computers, the Internet, and now artificial intelligence.

What makes the current mania particularly challenging for investors, however, is that it's mostly been confined to a very small group of mega-cap technology companies while the average stock has languished. This has led to a stock market that's now extraordinarily unbalanced. The so-called "Magnificent 7" – Nvidia, Microsoft, Apple, Alphabet (Google), Amazon, Meta (Facebook), and Tesla – today comprise fully 31% of the S&P 500. And technology stocks overall are 44% of the market! As can be seen in the chart below, even at the height of the Internet bubble tech stocks peaked at just 32% of the market.



Source: WisdomTree, FactSet, S&P. You cannot invest directly in an index. Historical forward P/E measured since 12/31/1994. Expanded Tech includes the Information Technology sector, Interactive Home Entertainment subindustry, Interactive Media & Services subindustry, Amazon, E-Bay, Etsy, and Netflix. Ex-Tech excludes the expanded tech companies.

Information technology is the most dynamic and fastest growing sector in the U.S. economy, but despite having such outsized representation in the stock market, it's still only 10% of U.S. Gross Domestic Product and a similar percentage of corporate profits. The stock market is not the economy.

And while advances in artificial intelligence have been incredible, the investment story is not as clearcut as investors seem to be assuming. What's happened so far is that the biggest technology companies and smaller venture-capital backed firms have been spending ungodly amounts of money on computing power (much of it directed toward Nvidia's high-capacity semiconductor chips) to build sophisticated machine learning models like ChatGPT. The models are impressive, but their impact on these companies' revenue and profits has thus far been negligible. Similarly, in the venture capital space, influential Silicon Valley investor Sequoia Capital recently estimated that while AI startups have collectively sunk \$50 billion into Nvidia chips alone, they've only generated about \$3 billion in revenue.

In the stock market there's been a feedback loop where mega-cap technology companies announce new AI initiatives and spending, which then propels both of their stocks (particularly Nvidia's) ever higher. Their strategy is to build large AI models that require massive data and computing power. Since only the biggest companies can afford such models, it's hoped this huge scale will provide an enduring and profitable competitive advantage. If true, then the smaller venture capital backed firms trying to compete in AI will fail, and it won't be long before their spending on AI hardware is severely curtailed.

Even if scale does win and large, general purpose AI models maintain their dominance, they still might not generate substantial profits for their mega-cap technology developers. In addition to being enormously expensive to construct, these models – from ChatGPT to Google's Gemini, Microsoft's Copilot, or Anthropic's Claude (heavily funded by Amazon) – exhibit similar capabilities. Such a lack of differentiation could prove a barrier to their ability

to command premium pricing in the marketplace. It's not enough to just develop great technology. A product has to offer a unique value proposition for customers to justify high enough pricing to support sustained profitability. Without clear superiority, these expensive AI models risk becoming commoditized services.

Further, more targeted AI models – which would require far less computing power and smaller data sets to solve specific problems – may prove more practical and cost effective for most applications in the long run. Such models would require significantly less expensive hardware than Nvidia's \$30K-\$40K chips. For instance, if CVS wants to create an AI chatbot for questions related to its pharmacy, it doesn't need a general purpose model trained on the entire Internet. Using an oversized solution for such a targeted task is analogous to flying a Boeing 747 half a mile to the beach.

In a recent report, the multinational investment bank Barclays noted that Wall Street analysts expect mega-cap technology companies building general purpose AIs to spend \$167 billion on hardware and inference (the actual running of models) through 2026. This staggering sum could support over 12,000 ChatGPTs! Additionally, given that the cost of inference continues to decline, this investment will likely be able to support far more than 12,000 large scale AI models within a few years. Barclays concludes that this extraordinary spending is more a reflection of companies' "fear of missing out" on the latest, greatest tech rather than a response to actual end market demand.

So who will be the biggest beneficiaries of AI? Obviously, Nvidia's been the clear winner so far. But it's highly questionable whether the current level of spending on AI can be maintained over the intermediate term let alone continue to grow at such a torrid rate. Moreover, Nvidia's dominance will be challenged if more targeted, less computationally demanding AI models become widespread. And even if the large scale, general models prevail, Nvidia's mega-cap technology customers will eventually slow their investment and seek cheaper sources of computing power, whether by developing their own chips (already happening) or turning to competing semiconductor companies like AMD and Intel.

Ultimately, we think the winners will be companies which – regardless of the industry in which they operate – have sustainable competitive advantages that will enable them to use AI technology to boost sales and cost efficiency while maintaining pricing power.

Take a company like PASI holding Stryker Corp, one of the world's leading medical device and technology companies, which manufactures a diverse range of products from knee, hip, and other joint replacements to surgical and patient handling equipment to its Mako robots that assist surgeons in performing more precise and less invasive procedures. Stryker enjoys a wide competitive moat due to 1) its innovative product portfolio, which provides a significant intellectual property advantage over competitors, 2) strong relationships with healthcare professionals thanks to extensive training and education programs and the Stryker brand's reputation for quality, and 3) the Company's global distribution network and manufacturing economies of scale. Stryker is already working on using AI to improve operating room efficiency and safety. For instance, its AI models can monitor surgeons' work in real-time,

ensuring adherence to planned steps and automatically detecting non-compliance with protocols. AI can help Stryker better manage its supply chain with improved demand forecasting, inventory level optimization, and more efficient distribution network routing. The models can even be used to predict manufacturing equipment failures before they occur. And because of its competitive advantages and pricing power, Stryker's use of AI to grow revenue and expand margins should flow directly to its bottom line, to the benefit of shareholders.

In contrast, businesses without a competitive moat are unlikely to see much of an increase in profits. The airlines, for instance, can use AI models to improve efficiency just like Stryker. But because they sell a commodity service and compete on price, their margins are unlikely to expand. Since every competitor in the industry will adopt similar technologies and improvements, any cost savings will likely be passed on to consumers in the form of lower prices. In this case, AI will serve more as a necessary tool for survival than a differentiator that can drive significant profit growth.

There's a popular saying, often apocryphally attributed to Mark Twain, that "history doesn't repeat itself, but it often rhymes." To me, the current AI buildout looks awfully reminiscent of the late 1990s/early 2000s race to expand Internet broadband networks, which led to a historic surge in business for telecom equipment manufacturers like Cisco Systems (the Nvidia of its day). Ultimately, however, the investment in network infrastructure far outpaced end user demand and the telecom companies' ability to monetize these networks, leading to a prolonged capacity glut and multiple bankruptcies across the industry.

The good news is that today's AI infrastructure boom is not fueled by debt like the telecom bubble 25 years ago, so there's little risk of a similar catastrophic collapse and cascading bankruptcies. Still, the mindboggling disparity between the hundreds of billions being spent on large-scale AI models and their trivial revenue generation will need to be resolved eventually.

AstraZeneca: Shaping the Future of Medicine

by Jeremy Goldberg, CFA, CFP®

In 1879, after over a thousand failed attempts, Thomas Edison successfully tested the first practical incandescent light bulb. This remarkable achievement illuminated homes and streets, transformed night into day, and revolutionized the way we live. Edison's tireless pursuit of innovation in the face of failure finds a parallel in pharmaceutical juggernaut and PASI portfolio company AstraZeneca (AZN), which has similarly turned obstacles into steppingstones for success. Faced with the loss of key drug patents a decade ago, AZN found itself at a crossroads. Blockbusters Nexium (reduces acid reflux) and Crestor (lowers cholesterol), which accounted for \$9.2 billion in sales or one-third of total revenues in 2014, lost patent protection in 2014 and 2016, respectively. In response, AZN embarked on a transformative journey through novel research and strategic acquisitions. By expanding its portfolio with innovative cancer treatments and rare disease therapies, AZN has emerged as a leader in the pharmaceutical industry.

Today, AZN operates through three main segments: Oncology, Rare Diseases, and Biopharmaceuticals, each playing a critical role in the company's strategy and growth. Excitingly, AZN is also poised to unveil groundbreaking treatments in its extensive drug pipeline, including a novel drug that could transform the weight-loss industry.

AZN's **Oncology** portfolio is foundational to its success, accounting for 39% of the company's \$43.8 billion of drug sales in 2023. This segment's strength is driven by key cancer treatments:

- **Tagrisso** and **Imfinzi** are both essential for treating non-small cell lung cancer (NSCLC). Their combined sales of \$6.3 billion in 2020 are expected to surpass \$12.5 billion by 2025. Recent trial results demonstrate that Tagrisso, the standard of care for early-stage NSCLC, reduced the risk of death by 51% compared to a placebo in the referenced trial, and significantly extended survival.² Imfinzi, effective in Stage III NSCLC, has shown marked improvements in survival rates across various cancer stages.³
- **Lynparza**, developed in partnership with Merck, targets cancers associated with the BRCA (Breast Cancer Gene) mutations. It is incredibly effective and extends the time patients with advanced ovarian cancer can live without progression to over 3 years on average vs. just under 1.5 years with standard treatments.⁴ Sales are projected to grow from \$1.8 billion in 2020 to \$3.4 billion by 2025, fueled by global approvals and broad effectiveness across diverse patient groups.
- **Calquence** targets blood cancers like chronic lymphocytic leukemia (CLL) and is marked by excellent safety and effectiveness. In clinical trials, it achieved a 90% response rate as a standalone therapy for previously untreated CLL, meaningfully reducing the risk of disease progression or death compared to traditional treatments.⁵ Sales have skyrocketed from \$522 million in 2020 to an estimated \$3.4 billion by 2025.

These flagship drugs not only represent significant revenue streams, but also reflect AZN's commitment to pioneering advancements in cancer treatment and enhancing patient outcomes.

The acquisition of Alexion Pharmaceuticals in 2021 for \$39 billion significantly bolstered AZN's **Rare Disease** portfolio. Alexion brought high-value, niche drugs such as Soliris and Ultomiris, which treat rare autoimmune disorders. These "orphan drugs," which target conditions that affect only a small number of people, command premium prices due to their exclusivity and limited competition:

² AZN Press Release (6/4/2023): *Tagrisso achieved unprecedented survival in early-stage EGFR-mutated lung cancer, with 88% of patients alive at five years in ADAURA Phase III trial*

³ AZN Press Release (5/4/2024): *Imfinzi significantly improved overall survival and progression-free survival for patients with limited-stage small cell lung cancer in ADRIATIC Phase III trial*

⁴ <https://www.lynparza.com/ovarian-cancer/home.html>

⁵ <https://www.calquence.com/why-calquence/how-effective-calquence-cll.html>

- **Soliris** is a groundbreaking treatment for disorders like neuromyelitis optica spectrum disorder (NMOSD), which cause severe damage to the body's cells and organs. Soliris blocks a part of the immune system that can mistakenly attack the body's own cells, protecting patients' organs from damage and greatly improving their health.
- **Ultomiris** is the advanced successor to Soliris, offering the same therapeutic benefits with less frequent dosing. Recent trials have shown that Ultomiris reduces the risk of relapse of NMOSD by 98.6%,⁶ a crucial feature as these rare diseases often involve severe and unpredictable relapses that can rapidly worsen patient outcomes. AZN is actively transitioning patients from Soliris to Ultomiris to capitalize on its enhanced efficacy and fewer dosing requirements.

When Alexion was acquired three years ago, Soliris and Ultomiris generated \$2.6 billion in sales, with 27% attributed to Ultomiris. By 2025, they are expected to generate a combined \$6.5 billion, with Ultomiris contributing approximately 70% of sales. This shift illustrates AZN's ability to expand its drug portfolio, while also strengthening its position in a market segment characterized by high demand and substantial opportunity.

AZN's **Biopharmaceutical** segment plays a key role in managing widespread health issues, particularly diabetes, respiratory conditions, and cardiovascular diseases. This segment is crucial not only for managing common diseases, but also for pushing the boundaries with innovative treatments:

- **Farxiga (Forxiga in the EU)** is an effective medication for lowering blood sugar levels in patients with Type 2 diabetes and also aids in managing heart failure and chronic kidney disease. Its diverse benefits contribute significantly to broader cardiovascular and renal health. Despite the upcoming patent expiration in the U.S. next year, AZN's management is confident it can maintain Farxiga's market strength through strong international sales and unique drug combinations. Sales are expected to surge from \$2 billion in 2020 to \$7.5 billion by 2025.
- **Symbicort** and **Breztri Aerosphere** are vital in respiratory care. Symbicort treats asthma and chronic obstructive pulmonary disease (COPD), and Breztri offers a more advanced approach to COPD management by integrating three active substances. Symbicort's patent expired last summer and sales of \$2.7 billion in 2020 are expected to fall to \$2.1 billion by 2025. Breztri, on the other hand, is expected to more than offset this with projected sales reaching \$1.1 billion by 2025 (up from just \$28 million in 2020), thanks to its ability to significantly improve symptom control and prevent exacerbations.

Building on these advancements, AZN is developing **ECC5004** in collaboration with Shanghai-based Eccogene. Positioned as a breakthrough treatment for obesity and Type 2

⁶ AZN Press Release (3/25/2024): *Ultomiris approved in the US for the treatment of adults with neuromyelitis optica spectrum disorder (NMOSD)*

diabetes, ECC5004 is an oral GLP-1 receptor agonist currently undergoing Phase I trials. Early results show that it is well-tolerated and effective, surpassing many existing treatments. Unlike other weight-loss medications, ECC5004 is rapidly absorbed and doesn't linger in the stomach, which helps minimize side effects like nausea, vomiting, and abdominal pain. Designed as a once-daily pill, ECC5004 is likely to be favored by patients over injectable options, offering significant market potential.

In AZN's drug trial pipeline, promising candidates include **datopotamab deruxtecan** (dato-DXd) and **camizestrant**. Dato-DXd is an antibody-drug conjugate (ADC) in Phase III trials that delivers potent chemotherapy directly to cancer cells, while sparing healthy cells and reducing side effects. Camizestrant, currently in Phase II and Phase III trials, provides a new pill-based treatment for advanced breast cancer sensitive to estrogen. It disrupts the growth mechanisms in cancer cells, and recent trial results suggest a significant improvement over existing therapies. These drugs, among others, are part of a broader strategy to diversify AZN's portfolio and reduce reliance on any single therapeutic area.

AZN has demonstrated impressive growth since its business hit a trough in 2018. At that time, sales were \$22 billion and profits were \$2.5 billion. By 2023, sales grew 107% (16% annually) to \$45.8 billion and profits soared 248% (28% annually) to \$8.4 billion. **More importantly, management expects this growth to continue, with a target of \$80 billion in total revenue by 2030.** This optimistic projection is underpinned by AZN's robust pipeline, which includes plans to launch 15 new medications by 2030 (including Dato-DXd and camizestrant) that each have peak sales targets of over \$5 billion annually.

From overcoming patent expirations in the mid-2010s to establishing itself as a leader in Oncology, Rare Diseases, and Biopharmaceuticals, AZN exemplifies the kind of dynamic company that aligns with our investment philosophy. Its industry leading and diverse drug portfolio, strong financials, and forward-looking growth strategy make it a compelling long-term opportunity. With estimated earnings per share growth of 13%, an above average dividend yield of 2.6%, and a reasonable valuation of 19x next 12-months' earnings estimates, we are excited about AZN's potential. Just as Thomas Edison's light bulb revolutionized the way we live, AZN's innovations are transforming the landscape of healthcare, illuminating the path to a brighter and healthier future.

Enhancing your Financial Planning Experience

Professional Advisory Services has long offered retirement planning projections and analysis as a courtesy to our clients. Committed to enhancing this service, we recently upgraded our financial planning software with advanced tools which expand our ability to model various financial scenarios and empower you with deeper insights and more flexible planning options. It is particularly valuable for those nearing retirement, helping determine the optimal age to retire, when to begin taking Social Security benefits, whether Roth conversions make sense for you, and how to efficiently manage the transfer of assets to your heirs. With three CFP®

professionals⁷ as part of our investment team, we can assess and compare the potential impact of different financial decisions in real-time, ensuring that recommended strategies are both well-informed and aligned with long-term goals.

If you're interested in exploring these new features and how they can benefit your financial planning, please reach out to your Portfolio Manager. We are here to support you in making the most informed and effective decisions for your financial well-being.

Hurricane Season – *It's That Time of Year Again*

Officially ranging from June 1st to November 30th, Hurricane Season is once again upon us. Our hurricane procedures include preparation of our physical office to minimize the impact of water intrusion and protecting the integrity of our central computer. Most of our team will be able to plug in phones and laptops and be ready to serve your needs quickly, limited only by availability of electricity. David's Montana office serves as remote backup. BNY will be alerted to initiate contingency processing for client needs.

While PASI has settled on a staffing structure minimizing “work from home” time, we surely have the experience, as well as resources and technology, to serve client needs remotely if required.

You can read our Disaster Recovery Policy on our website www.pa-services.com. Please follow the “contact us” tab; you will find a link to the policy on the bottom left area of that page. In the event that primary communications are affected by a storm, we will post updates and any important information on our website. If you have any questions about our contingency planning, please don't hesitate to call.

Disclosure

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⁷ CERTIFIED FINANCIAL PLANNER™