John F. Kennedy once said, “Change is the law of life, and those who only look to the past and present are certain to miss the future.” Very real words of wisdom and as I reflect on these, so too do I think about the past and present as the foundation for the future – the lessons learned, the people met, the wisdom gained, the accomplishments achieved. So too is the case with the VHL Alliance. I am honored to be working with a talented and committed group of individuals in the board, volunteers, staff, medical research teams, and everyone who is a part of our rich and diverse community, serving as the Chair of the Board for the coming year.

As I begin this role, I reflect on the accomplishments of the VHL Alliance and the incredible people involved. People have worked tirelessly towards advancements in research and medical care, towards supporting patients and families, to educating the world, to increasing awareness, and to striving towards our ultimate goal – finding a cure. In reflecting, so many accomplishments come to mind – Dr. William G. Kaelin, Jr.’s award of the Nobel Prize for Medicine, announcement of early data of clinical trials of a possible systemic treatment of VHL tumors, increased recognition of VHL, an international community

“I reflect on the accomplishments of the VHL Alliance…”

built to share resources, ongoing research, and stories of support... the list goes on and on. This, however, is not just about the past, rather this is taking all that has been developed and accomplished to date and looking to the future.

As we, hopefully, come through the pandemic in the coming months, we are re-structuring the Annual Family Meeting and the 14th International VHL Medical/Research Symposium to take them virtual – a means of continuing to provide the critical information and resource sharing, but also expanding reach and, hopefully, engaging more of our community to attend.

With a new strategic plan in hand (vhl.org/strategic-plan) as our compass, we continuously evaluate our communications and are seeking new ways to educate and increase awareness for VHL. We are working to increase funding and continuing to make substantive investment and progress in research. We are also engaging new parts of our community with a mindfulness and sense of inclusivity and progress.

All of this is to say that the future of the VHL Alliance is strong. It is built on the success of hard work and determination by many, supported with advancement of funding research by a broad community, and propelled forward by the commitment, perseverance and outlook by all those who are involved. I look forward to working with you all to ensure that the coming years are some of the best for the VHL Alliance!
A MESSAGE FROM THE VHL ALLIANCE

Our vision at the VHL Alliance is to cure cancer through VHL (von Hippel-Lindau), a disease that does not discriminate against race, ethnicity, socio-economics, geography, or gender. We value fairness and equality in access to medical care, but we know that many patients with VHL are undiagnosed and untreated, particularly people of color and those living in under-resourced communities.

As an organization, we agonize over our society's chronic failure to purge itself of racism. These events, coupled with the COVID-19 pandemic, have revealed the unacceptable racial inequities that still exist today. Unfortunately, we know these same disparities also exist in the diagnosis and treatment of VHL. We have a role to play in eliminating racism and addressing health disparities, in particular across the VHL community. We recognize the need to better reach medically underserved communities and their healthcare providers with information about VHL. We also recognize that we can't truly understand the impact of VHL on all patients and families without the voice of people from different backgrounds, privilege, and skin color. We are committed to addressing the gaps we have at the VHL Alliance to ensure we represent the full diversity of our patient community and work to improve access to regular and experimental medical care for underserved VHL patients.

In a very difficult year for our country and our world, our VHL community has celebrated breakthroughs that give us hope for treating this disease. These achievements belong to everyone.

GETTING INVOLVED WITH VHLA

by Danny B, patient, VHLA Ambassador

I t took more than ten years from my diagnosis with VHL at age 18 for me to finally get involved with a VHL Alliance event. As a de novo patient I was not even sure what it would be like to meet another person with VHL, but in early 2018 I started to see flyers about an upcoming Young Adult Retreat. I decided to attend as it was a short drive for me and coincided with the end of my school year as a teacher. It has been one of the most important experiences of my adult life.

As 2020 began and the COVID-19 pandemic arrived in the United States, I helped put on a virtual Coffee Against Cancer as a kick-off event for May’s VHL Awareness Month. As “hosts,” we invited friends, co-workers, and family members. I was so happy to see them feel comfortable enough to engage in a real conversation and ask questions about our different experiences with VHL. These events are often small and hosted by one person, but in this setting we were able to have patients from around the country attend and share their unique experiences. All of those I invited remarked on two takeaways: they were surprised at just how deeply the disease impacts our lives, and they couldn't help but notice the resilience of the patients and the strength of the community.

I also just recently attended the 2020 virtual edition of the Young Adult Retreat in early June. The quality of these events speaks to why the retreat I attended in 2018 prompted me to get more involved: the strength of VHLA and its community goes far beyond what I expected. While past events have allowed us to go out and explore Boston or share great meals, my strongest memories have always been the connections with other patients. Those connections were still a highlight as I saw familiar faces from the past and heard new voices chiming in.

The quality of the guest speakers was also up to its usual high standards. 2019 Nobel Laureate and VHL researcher Dr. William Kaelin was the headliner, and other experts like Dr. Othon Iliopoulos and Dr. Giselle Perez gave great talks and answered questions on managing the disease and its emotional impact. Superstar ambassadors (and sisters) Haley Miller and Emily Billcheck also joined to share how they have dealt with the challenges of VHL in their family.

Many of us know well the types of nuts-and-bolts resources that the VHLA can provide for patients, like details on care protocols or connections with physicians, but the events that they host and the community they help to foster are simply tremendous. I hope that if you have not yet connected with one of these events, large or small, that you find a way to attend or even host an event of your own!
VOICES RAISED ON A NATIONAL PLATFORM

VHLA COMMUNITY PARTICIPATES IN FDA “VHL PATIENT LISTENING SESSION”

by Jacqueline Z, patient

A VHL advocacy milestone was met after the Food and Drug Administration (FDA) granted to VHLA a “Patient Listening Session” which was held via teleconference this June. “It has been a long-term goal for the VHLA to secure this critical meeting at the FDA so that the VHL patient and caregiver voice can be shared for the first time in this setting,” noted Ilene Sussman.

Patient Listening Sessions serve as a forum where patients and advocates share their knowledge and unique experiences with the FDA so they can hear directly about conditions such as rare diseases. These meetings are disease-related and are not tied to a specific medical product, thus it is unrelated to the Merck (previously Peloton) trial.

True to the overarching goal of listening, representatives from the FDA divisions of drug, device, and biologics were present. Notably in attendance was Anand Shah, MD, the Deputy Commissioner for Medical and Scientific Affairs who serves as second in command at the FDA. The overall participation highlights the interest and dedication of the Agency to comprehensively hear directly from the VHL community.

In order to provide a representative picture of living with and managing VHL within a focused time frame, the agenda included a summary of the genetics and medical presentation, patient experiences, and a summary pulling all aspects together.

A medical review was presented by Eric Jonasch, MD, focusing on the unique VHL genetic pathways and the diversity of how VHL presents in each person. Special reference was made to how VHL can target up to 10 organs in the body (beyond the frequently discussed renal cell carcinoma) and how the spectrum can range from benign tumors that require surveillance, to organ masses that impact functioning and require surgical removal (often many times over), to cancerous tumors that require a variety of treatments.

It was important that patient stories covered the range of experiences in our community to most fully represent as many aspects as possible. To this end, seven patient stories were presented by six individuals, ages 14 - 52. Participants described disease presentation and progression, highlighted the significant impact on life and on families, and shared the challenges of living with VHL.

In closing, Ilene highlighted many key items about VHL including the variability in disease presentation across the multitude of organs, how the course of lives are changed with diagnosis impacting individuals and whole family units, and noted the significant emotional toll.

Results of a recent VHLA patient survey were summarized to amplify key topics including need and interest in treatments other than surgery. Further, heartfelt memories of VHLers lost too soon were shared as well as gratitude on behalf of the VHL community for the session. At the end of the meeting, several members of the FDA expressed sincere thanks for the time and eye opening information presented.

It is an honor that VHL is now a rare disease that has been incorporated in to the FDA’s Patient Listening Sessions. Such milestone efforts are at the heart of the VHLA’s vision of Curing Cancer through VHL. This session is seen as one way our community raises the patient voice especially since a summary will be available to the general public on the FDA website at a later date. With this FDA Patient Listening Session, please know that you were heard.

If you would like to more fully engage in supporting efforts to elevate patient voices and champion the cause for VHL, please contact the office at info@vhl.org.

Material from the Listening Session can be found at vhl.org/listening-Session.
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<td>(Endolymphatic sac tumors)</td>
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Notes:

Your clinician may suggest more frequent surveillance based on existing lesions. In such a circumstance, it is important to be seen by a VHL specialist.

1. Beginning at age 65, routine laboratory and radiologic screening for patients who have never had specific VHL manifestations may cease. With the exception of routine physical examination and ophthalmologic assessment, this applies to all other routine screening/surveillance tests in asymptomatic patients. However, patients presenting with signs/symptoms should be evaluated with appropriate testing/imaging regardless of age.
2. Age-appropriate history and physical examination to include: Neurologic examination, auditory and vestibuloneural questions and testing, visual symptoms, catecholamine excess symptom assessment (headaches, palpitations, diaphoresis, hyperactivity, anxiety, polyuria, abdominal pain).
3. Dilated, in-person eye examination, including ophthalmoscopy, to occur every 6-12 months based on quality of examination obtained (especially in a child) and perceived adherence to follow-up. Consider examination under anesthesia in young children in whom a detailed eye examination cannot be adequately obtained in the clinic. Consider including ultrawidefield photography and ultrawidefield fluorescein angiography, but these should not replace a dilated eye examination with a specialist with experience in retinal manifestations of VHL.
4. Plasma free metanephrines (preferred, due to its higher sensitivity) or fractionated 24-hour urinary free metanephrines.
5. Use macrocyclic/class II gadolinium-based contrast agents. MRI of the neuroaxis may be obtained at the same time as MRI abdomen, and may be performed under a single long anesthesia event, especially in children. However, both the neuroaxis protocol and the abdominal protocols should be obtained consecutively. It is NOT recommended to evaluate the spine solely using an abdominal protocol MRI, nor is it recommended to evaluate the abdominal organs solely using a neuroaxis protocol. See footnote #6 and #7 for how to combine these protocols.
6. Based on contraindications (metallic implants, renal failure, etc.), the following order of imaging priority applies: MRI (with and without contrast) > MRI (without contrast) > CT (with contrast) > CT (without contrast) > US (kidneys, adrenals and pancreas only) > Endoscopic US (pancreas only). See also footnote #5 and #7.
7. Timing of contrast administration when imaging multiple organ systems together should be as follows: Obtain non-contrasted images of CNS and abdomen first, then give contrast using a power injector and perform multi-phase contrast-enhanced imaging of the abdomen including pancreas and kidneys during the late
**CLINICAL TRIAL UPDATE**

*by Rachel Giles, MD, PhD, Dutch VHL Organization*

Results from a phase II international, multi-center clinical trial were presented by Dr. Eric Jonasch at this year’s American Society of Clinical Oncology (ASCO) Annual Meeting, held virtually from May 29-31, 2020. The study enrolled 61 patients with a genetic diagnosis of von Hippel-Lindau (VHL) disease, with one or more detectable RCC tumors, no prior cancer drug treatments, non-metastatic disease, and in reasonably good health. Patients were treated with a novel hypoxia inducible factor (HIF-2α) inhibitor (MK-6482, originally called PT-2977).

The study’s objective (end point) was defined as a demonstration of kidney tumor shrinkage of 30% or more. The reported data demonstrated that 28% of patients reached this objective while 87% of patients had a decrease their tumor size. No patients experienced disease progression while on treatment. The median time to response was 5.5 months. Fifty-eight patients of the 61 patients remain on treatment.

MK-6482 was well tolerated and most side effects were mild or moderate in nature. Less than 10% of patients had a severe adverse event and there were no life-threatening side effects.

"Patients with von Hippel-Lindau disease are at risk of developing several types of cancer and other tumors, and there are currently no approved therapies," said Dr. Eric Jonasch, the lead investigator. "We are encouraged by the results of this clinical trial and look forward to seeing further study of MK-6482 as we work to make this treatment option available for patients with VHL disease." These further studies include testing MK-6482 to see if it can prevent the development of new tumours in patients with VHL disease.

**RECENT VHL RESEARCH REVIEW**

*by Amit Tirosh, MD, VHL Clinical Care Center Sponsor, Sheba Medical Center*

Researchers in Japan published a paper that looked at a novel mechanism for the development of hemangioblastomas. A separate paper reported on the involvement of two key cancer-related pathways (EGFR and TGFα) in VHL-related hemangioblastomas while other researchers identified how VHL and a protein called Di-Ras2, can promote the growth of kidney tumors.

A report published in the Journal of Medical Genetics examined a possible connection between VHL mutation site and increased risk for pheochromocytomas. An additional study, presented the cases of 5 patients with VHL from the underreported Arab population, demonstrating that VHL has no geographic boundaries. A group from Spain published a report documenting the possible protective effect that a CNL5 gene mutation might have on the development of VHL manifestations.

A paper published in Radiology investigated whether diffusion-weighted MRI may be useful in identifying kidney tumors with higher growth rates in people with VHL. In addition, a report was published that looked into the use of different imaging techniques and found them to be complementary in providing the best possible imaging coverage for patients.

A meta-analysis looking into possible interventions for VHL-related brain lesions found that SRS (stereotactic radiosurgery) may be a good option for certain patients with VHL and limited surgical alternatives. A case report was published describing a spinal paraganglioma that presented as a hemangioblastoma, expanding our understanding of possible VHL manifestations.

More information can be found at vhl.org/research-update.
CLIPPERS AGAINST CANCER

by Seth H, patient, Board member

As we have come to know the VHL Alliance as both a pioneer in aiding patients and supporting VHL research, less well known is the extent to which our always creative volunteers will go in order to raise funds to advance the organization’s goals. From bowling nights to raffles, and distance runs to sponsored happy hours, we’ll try anything.

Roughly eight weeks into the COVID-19 lockdown, what started as a casual observation on a videoconference call about the unruliness of several patients’ hair styles, quickly turned into one of the strangest fundraisers in our organization’s history. How could this unique (and awkward) period be used to both raise funds and support our community? Fixing the growing messy hair seemed too tame, and led us to Clippers Against Cancer. Since the goal was a shaved head, no barber experience was necessary, and was actually discouraged. In addition, it was a fitting tribute to all of the VHLers who have been shaven for too many procedures. For those who were unable to get “scalped,” the idea of dyeing hair blue was deemed an inclusive and worthy alternative.

The best part of the campaign was that it was fun and cost nothing, especially in a time when fundraising of any sort has been quite difficult, and when everyone could use some levity. Anyone could join as long as photographic or video proof would be provided.

From here, 13 brave warriors set about raising funds for their journey. Goals were set, and exceeded. Little did we know how much people would be willing to donate to humiliate a family member or friend, while also supporting a good cause. Children (even toddlers) were eager to get payback on adults who weren’t always appeasing them, with the adults just as excited to exact a little revenge on their children that may have not always been on their best behavior during extended family time with no breaks. Thanks to the generosity of each of our donors, and a family member who took on the clippers for his already smooth-headed brother, Clippers Against Cancer was able to raise almost $33,000 to help fund the VHL Alliance. Without exception, this was also genuinely enjoyable for all who participated.

Not only has this been a successful fundraising campaign launch, but the freshly shorn heads and blue hair have proven to be an effective awareness tool, as well. They have been a great conversation starter with people who you may have never spoken with about VHL and the VHL Alliance. (Check out all of the new hairdos and get a glimpse of the fun by watching the video at vhl.org/clippers.)

While this wave of the fundraiser has finished, and the ability to get a haircut has increased nationwide, anyone who wants to participate is more than encouraged to take on the clippers! Interested? Please contact Heidi at heidi.leone@vhl.org to get more information.

Donate your car, truck, or boat to VHLA

We will handle the pick-up and you get a tax deduction!

vhl.org/give/ways-to-give/
Welcome VHLA’s Newest Board Members

July 1st kicked off VHLA’s new fiscal year (FY21). We welcome our newest members to the VHLA Board of Directors! This year’s Executive Committee consists of: Camron King, Chair; Stacy Lloyd, Vice Chair; Seth Horwitz, Treasurer; Emily Billcheck, Secretary. Returning Board members are: Jennifer Galenkamp, Doug Karle, Prashant Kudva, Kevin Nichols, Mark Pallansch, Connie Rath, and Julie Woodruff. For information on all board members, please visit vhl.org/about/people/board-of-directors.

Othon Iliopoulos, MD, PhD is an oncologist at Massachusetts General Hospital, where he serves as the Clinical Director of the VHL Disease/ Familial Renal Cell Cancer Program. Dr. Iliopoulos is an incoming VHLA Board Member, as well as the incoming Chair for the Clinical Advisory Council and the Research Council.

John Josey, PhD is a venture Partner at The Column Group. Previously he served as the President, Chief Executive Officer, and a member of the Board of Directors of Peloton Therapeutics, Inc. (inventor of MK-6284), until its acquisition by Merck in 2019.

Rod Miller is an NFP executive leader with experience in a variety of sectors and industries. Recognized for his transformative leadership, business development, and ability to develop exceptional organizations. As a caregiver, Rod is committed to the work of the VHL Alliance to not only bettering the quality of life for patients and families but to also move toward a cure for VHL.

Cary Schwanitz is a 30-year veteran of TV news. He currently works for KSL-TV, the NBC affiliate in Salt Lake City. Gail and Cary decided to leave their longtime home in New Mexico in 2019 to be near the VHL Clinical Care Center at the University of Utah. Cary and his three adult children have manifestations of VHL.

Rohan Nirody is a senior member of the private equity team at Viking Global Investors, L.P., where he currently helps lead the firm’s private healthcare investing practice. Rohan is grateful for all the support VHLA has provided to his family members who have VHL, and he looks forward to working with the organization to improve the lives of patients and advance research efforts.

JOIN US FOR THE VIRTUAL 2020 ANNUAL FAMILY WEEKEND!

Events Include:

- **Online Silent Auction**
  October 20-25

- **Teen Event**
  October 23

- **Educational Family Meeting**
  October 24

- **Virtual Team VHL Walk/Run**
  October 25

For more information and tickets, visit vhl.org/familyweekend
REGISTRATION NOW OPEN FOR TWO VIRTUAL MEETINGS!

October 23-25
vhls.org/familyweekend

October 29-31
vhls.org/symposium