Dr. Ponni Subbiah, MD, MPH

Chief Medical Officer, Indivior PLC

Statement to the President's Commission on Combating Drug Addiction and the Opioid Crisis

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Good afternoon. I am Dr. Ponni Subbiah, Chief Medical Officer at Indivior. Thank you for the privilege to address the President's Commission on Combating Drug Addiction and the Opioid Crisis. Indivior seeks to provide insight on: the patient journey, innovations in medication-assisted treatment for addiction, and policies to prevent addiction, accelerate evidence-based treatment and enable long-term recovery for patients.

Indivior is a global specialty pharmaceutical company. Our core focus is addiction medicine. We have a 20-year legacy of clinical and basic research, treatment development, health policy and patient advocacy. Our vision is that all patients have access to quality treatment for the chronic relapsing condition and co-occurring disorders of addiction.

We worked with the National Institutes of Health (NIH) and National Institute on Drug Abuse (NIDA) to develop the first buprenorphine-based opioid use disorder (OUD) treatment for patients in the United States (US). For more than a decade, we have worked together with policymakers, medical societies, patient advocacy groups, healthcare providers, payers and other stakeholders to educate on the disease of addiction and advocate for patient access to OUD treatment.

Today, we have a global portfolio of OUD treatments and a pipeline of product candidates to address unmet patient needs in OUD and other chronic conditions and co-occurring disorders of addiction, including alcohol use disorder (AUD) and schizophrenia.

In recent years, all levels of government have taken significant steps to address the disease of addiction:

> The **Drug Addiction Treatment Act in 2000** (DATA 2000) enabled millions of patients to seek buprenorphine-based treatment for opioid use disorder in the privacy of a physician's office.

The **2008 Mental Health and Substance Use Disorder Parity Act** prevented group health plans and health insurance issuers that provide mental health and substance use disorder benefits from imposing less favorable benefit limitations on those benefits than on medical/surgical benefits for other medical conditions. This was extended to individual insurance coverage under the Affordable Care Act.

The **2016 Surgeon General's Report on Alcohol, Drugs and Health: Facing Addiction in America** reviewed what is known about substance misuse and offered a vision for the future with policy and practice recommendations.

The **Comprehensive Addiction Care Act** (CARA) passed by Congress in 2016 is a comprehensive effort undertaken to address the opioid epidemic, establishing a strategy encompassing six pillars for a coordinated comprehensive response: prevention, treatment, recovery, law enforcement, criminal justice and overdose reversal. In addition, the Act authorizes for five years, nurse practitioners and physician assistants to obtain waivers to prescribe buprenorphine-based treatment for patients.

The **US Department of Health & Human Services** action in 2016 raised the maximum number of patients who can be treated by certain qualified physicians under DATA 2000 from 100 to 275 and enabled more patients to have access to treatment.

But it is clear much more is needed to effectively fight substance use disorders and the increasing -- and unacceptable -- number of human lives lost due to drug overdose.

In 2015 alone, the harm caused by drug use translated into an estimated 28 million years of healthy life lost worldwide due to premature death and disability[1]. Opioids were the most harmful drugs in this context, accounting for 12 million disability-adjusted life years (DALYs) or 70% of the negative health impact associated with drug use disorders (DUDs) worldwide[1].

In the US, the misuse of opioids, together with a significant increase in heroin and fentanyl use, accounted for approximately 25% of the estimated number of drug-related deaths worldwide in 2015[1]. Overdose deaths in the US were mostly driven by opioids and increased from 16,849 to 52,404 annually during the 1999-2015 period[1,2,3].

According to the 2016 National Survey on Drug Use and Health, in the US there were 20.1 million people aged 12 or older who suffered from substance use disorder[4], but many are not aware that addiction is a disease that can be medically treated[5]. Access to treatment of substance use

disorders and related conditions remains limited, and currently, only one in ten persons with a substance use disorder receives treatment[4].

The 2016 Surgeon General's Report states that "[w]idening access to highly effective medications treating opioid addiction – methadone, buprenorphine, and naltrexone – has been identified by the United States public health authorities as an essential part of tackling America's current prescription opioid and heroin crisis."[6] Scientific evidence shows that long-term use of maintenance medications like buprenorphine successfully reduces substance use and risk of relapse or overdose in addition to helping patients return to a healthy, functional life.[7] A 2014 article in the New England Journal of Medicine noted that "[e]xpanding access to [medication-assisted treatments] MATs is a crucial component of the effort to help patients recover."[8] Additionally, the National Institute on Drug Abuse stated that scientific research has established that medication-assisted treatment of opioid addiction increases patient retention and decreases drug use, infectious disease transmission, and criminal activity.[9]

The Patient Journey

The patient journey to treatment and recovery is complex.

Social Stigma: Social stigma, prejudice and misconceptions about addiction, coupled with feelings of guilt and shame, often prevent people from coming forward and seeking help. Addiction is often punished and criminalized. People with the disease of addiction are imprisoned, further discriminated against upon release, marked as felons and unwelcome by employers and communities. Even when people want to stop using illicit drugs, cravings and withdrawal symptoms of addiction can be so intense that generally there is only a small window of time when a person is emotionally and physically able to pursue treatment. The healthcare system, however, does not always allow treatment during that window due to structural barriers to care. Thus, the majority of those who need help go untreated.

Access to Evidence-Based Treatment: For those who do decide to take action, there are many obstacles to access treatment. Stigma surrounding the disease and treatment -- especially when treatment services are specialized instead of part of mainstream medicine -- is a significant barrier to accessing quality treatment. Prescribers for an effective medication-assisted treatment, buprenorphine, are often a scarce resource. The DATA 2000 law limits those who can prescribe to those certified by the Drug Enforcement Agency ("DEA")[10]. To reduce abuse, misuse and diversion, the law requires DEA to audit prescribers and it limits patient access and encourages physician oversight of the use of medication by capping the number of patients any certified provider can treat[10]. In 2016, the law was changed to allow nurse practitioners and

physician assistants to prescribe buprenorphine[11]. Also in 2016, regulations increased the number of opioid dependent patients allowed to be treated from 100 to 275 patients per physician. Regardless, prescribers who exceed their legal limits face loss of certification and DEA registration and other consequences.

Today in the US, there are more than 40,000 waivered physicians able to prescribe buprenorphine-based treatments[12]; however, according to Indivior internal analysis, only approximately half are actively prescribing buprenorphine[13]. Further, of the 40,000 physicians, less than 10% are approved to treat up to 275 patients[12]. In addition, most treating providers are heavily concentrated in urban areas resulting in treatment deserts in rural communities[14]. We need to take active steps to assure that increased patient treatment limits work to increase the number of patients with access to treatment.

Adherence to Treatment Plans: Once in treatment, challenges for patients continue. Patients have difficulty adhering to treatment plans when confronted with relapse due to the chronic nature of the disease. Affordability and lack of coverage for treatment, including proposed limits on treatment dose and duration, restrictions on treatment choice, and required prior authorization (imposed by payers and sometimes state policymakers) result in sub-optimal disease management[15]. Well-intended families, friends and communities pressure patients to stop taking addiction medicine due to misconceptions about the disease and treatment.

Mission to Pioneer Potentially Transformative Treatments

Indivior's core guiding principle -- focus on patient needs to drive decisions -- incentivizes our research and development to advance treatment innovation in the face of the growing addiction crisis. Putting the patient first defines Indivior's Research and Development (R&D) mission: stabilize drug delivery, decrease dosing frequency, increase treatment adherence and retention, decrease diversion and misuse, improve management of overdose, and treat the comorbidities of addiction.

Our science is constantly expanding our mechanistic understanding of addiction so we can develop novel approaches to treatment and new methodologies to support measurement of clinical response.

For example, Indivior is developing RBP-6000, a new investigational buprenorphine sustained-release formulation using the ATRIGEL® delivery system. The Food and Drug Administration (FDA) granted RBP-6000 Priority Review in June, and the product is currently under review by the FDA, with FDA's stated PDUFA date of November 30, 2017.

RBP-6000 was thoughtfully designed with the following objectives: (1) provide sustained plasma levels of buprenorphine that translate into high mu-opioid receptor occupancy in the brain to suppress withdrawal symptoms and reduce the subjective and objective effects of illicit opioids; (2) deliver once-monthly buprenorphine at plasma levels that are consistent across the entire 1-month period; (3) reduce risks of diversion and misuse; and (4) enhance adherence to treatment.

If approved, RBP-6000 would represent the first once-monthly injectable buprenorphine treatment for adults with moderate to severe opioid use disorder as part of a complete treatment plan to include counseling and psychosocial support. We believe the medication has the potential to transform treatment for these OUD patients.

The President's Commission on Combating Drug Addiction and the Opioid Crisis reported in July that as many as forty percent of those with substance use disorders have a mental health condition[16]. Epidemiological and clinical studies have shown that psychiatric disorders are highly co-morbid with substance use disorders. For example, nearly half of all patients diagnosed with schizophrenia have co-occurring substance use disorders[17]. To help address this challenge, Indivior is developing a once-monthly sustained release injectable formulation of risperidone (RBP-7000), the leading medication to treat schizophrenia.

Indivior is also focusing on new molecular targets with mechanisms of action involved in craving; these are likely to be useful across other substance use disorders, including pipeline development of medications to treat Alcohol Use Disorders (AUD).

We recognize the social and economic burdens of substance use disorders on families, communities, payers, government and society. Indivior invests in prospective health economics and outcomes research as part of clinical development plans to better understand patient outcomes beyond clinical efficacy and safety. For example, for opioid use disorder treatment, Indivior has studied improvement in health status and health-related quality of life, medication satisfaction, decrease in healthcare resource utilization, improvement in employment status and health insurance, as well as decrease in co-morbid drug use and psychiatric associations.

More collaborative research efforts will be required on the pharmacogenomics of substance use disorders including how to characterize and quantify pharmacotherapy response, for example, efficacy, nonadherence, treatment duration, concurrent medications use, and how to define patients' characteristics -- such as differential diagnosis, illness course and co-morbidities.

Indivior welcomes the opportunity for public-private partnership because we believe that collaborative, concerted efforts may ultimately result in the reduction and cessation of drug use, preventing future harms associated with the abuse of drugs, and improving the quality of life and well-being of patients with substance use disorders and co-occurring mental health disorders.

Public Policies to Lead Recovery from Addiction

Indivior respectfully recommends that the Commission consider aggressive policies that can accelerate social change, prevent addiction, accelerate treatment and enable recovery for people, families and communities. Our recommendations are aligned with our own corporate commitments, actions and investments in patients.

End the stigma of addiction: People with substance use disorders are not "addicts," nor criminals who deserve to be punished. They are fathers, mothers, sisters, brothers and friends who have been exposed to and become dependent on opioid painkillers, alcohol or other addictive substances and who risk being socially marginalized as a result. They deserve to be treated with dignity, respect and, like any other person with a chronic relapsing condition, medically treated.

Stigma Recommendations:
Indivior has long believed that education about substance use disorders can and will improve patient treatment and access. We join the Commission[16] in its recommendation to mandate increased education on substance use disorders and treatment.

- *Disease and Treatment Education*: Accelerate public, healthcare provider and patient education on the disease of addiction and evidence based treatment, including all FDA approved medication-assisted treatments – methadone, buprenorphine and naltrexone.
- *Medical Education*: Promote addiction and evidence-based treatment education in medical, physician assistant and nursing schools and as a core requirement for continuing medical education programs within the healthcare system.

Accelerate and expand access to evidence-based treatments: We should do more to accelerate and expand access to all evidence-based treatments available today and new innovations in addiction science and treatments that have the potential to transform treatment for patients and expand healthcare provider and patient medication choices.

As the Commission reported, of the current low percentage of substance use disorder patients who do seek treatment in conventional drug treatment facilities, only ten percent are offered medication-assisted treatments.[16] As the Commission noted with respect to prison studies,

patients on medication-assisted treatment stay in treatment longer and do better than those who try recovery without medication[16]. Education, coupled with federal requirements, can combat the common but misplaced belief among treatment providers that medication-assisted treatment does not constitute true recovery or sobriety; only abstinence equals recovery.

No one who overdoses should ever leave a hospital emergency department without a path to evidence based treatment, including psychosocial support and counseling resources.

Also, progress that has been made already has not yet realized its full potential, specifically the vision of the Mental Health/Substance Use Disorder Parity Act, nearly a decade on from passage with patients and families still struggling to achieve coverage at parity with other medical conditions.

Access Recommendations:

- *Expand Access to Medication-Assisted Treatment*: As the Commission recommends, federal health centers should have staff qualified to prescribe medication-assisted treatment[16]. Prior Authorization requirements and processes must be consistent with the urgency of opioid dependent patients' decisions to seek treatment and their immediate needs. Regulatory or statutory changes are needed to reduce barriers to payment for medication-assisted treatment, such as treatment choice restrictions and prior authorization requirements that interrupt and delay treatment.
- *Remove Barriers to Innovative Treatments for Rapid Deployment and Wide Availability*: New buprenorphine long acting injectable medications are innovations in medication-assisted treatment for opioid addiction. Any ambiguity in current federal and state controlled substance distribution laws should be addressed to ensure patients and providers can realize the full value of these innovations.
- *Overdose Path to Treatment*: Help states and communities develop evidence-based protocols for emergency treatment providers to ensure people who overdose are accurately assessed and offered an immediate pathway and options for treatment at this key intervention point for people with substance use disorders.
- *Enforce the Parity Act*: We join the Commission[16] in recommending enforcement of and compliance with the Mental Health and Substance Use Disorder Parity Act: 1) health plans should demonstrate to state and federal regulators prospectively as a condition of approval fully aligned contract standards with federal and state parity laws, and 2) regulators should develop model contract standards that fully inform patients of their mental health and substance use disorder benefits and rights under the Parity Act.

Prevent Addiction, Encourage Recovery, Help Save Lives: The patient journey from addiction to treatment and recovery is not traveled alone. According to a 2012 study by the Substance Abuse and Mental Health Administration (SAMHSA), 8.7 million children in the US, 17 years of age and younger, live in a home with at least one parent who had a substance use disorder in the past year[18]. Children impacted by a family member's addiction are at far greater risk than their peers to suffer from depression and anxiety as well as health and learning challenges[19]. Patients in treatment and their families require support from community services and employers to promote a healthy environment for recovery.

Recovery Recommendations:

- *Break the Cycle of Intergenerational Addiction*: Children living with a parent or an adult with a substance use disorders need trusted mentors, education and coping strategies. Prioritize funding for non-profit, state and local entities to support positive youth development programs that provide evidence-based life skills training, drug use prevention programs, therapeutic camps, after school programming, and other programs aimed at supporting these children in their daily lives.
- *Support Recovery Infrastructure*: There are 23 million Americans in recovery from substance use disorders[20]. Resources are needed to expand critical recovery infrastructure as more people enter treatment and reclaim their lives from addiction. Prioritize funding for recovery education, outreach programs and recovery support services, including housing. Engage the Department of Labor to educate employers to support people with substance use disorders and develop workforce readiness and job training programs for patients re-entering the workforce.

Conclusion

Thank you again for the opportunity to address the Commission. We hope you will consider our insights into the patient journey, innovations in medication-assisted treatment for addiction, and policies to prevent addiction, accelerate evidence-based treatment and enable long-term recovery for patients.

All of us together can transform addiction from a human crisis to a recognized and highly treated disease.

Addiction is a disease. It can be treated. One patient at a time.

Patients are waiting. We stand ready to support the Commission's work however we can. Thank you for your leadership.

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