

$$\begin{aligned} & \text{P}\ddot{\text{Y}}\text{P}^{\circ}\text{P}\pm\text{P}\gg\text{P}\mu\text{C},\text{PeP}\ddot{\text{e}}\text{P}\ddot{\text{I}}\text{P}\gg\text{P}^{\circ}\text{C}\dagger\text{P}\mu\text{P}\pm\text{Ps}: \text{PeC}\ddot{\text{T}}\text{C}\ddot{\text{r}}\text{P}\ddot{\text{I}}\text{P}\gg\text{C}-\text{C},\text{P}^{\circ}\text{P}\pm\text{P}\gg\text{P}\mu\text{C},\text{PeP}\ddot{\text{e}}, \text{P}\ddot{\text{I}}\text{PeC}\ddot{\text{T}}\text{P}\ddot{\text{e}}\text{C},\text{C}- \\ & \text{P}\ddot{\text{I}}\text{P}\gg\text{C}-\text{P}\ddot{\text{I}}\text{PePsP}\ddot{\text{I}}\text{PsC}\ddot{\text{T}}\text{PsP}\pm\text{PsP}\gg\text{PsPSPePsC}\ddot{\text{T}}\text{H}, \text{P}\pm\text{C}-\text{P}\gg\text{PsP}\ddot{\text{I}}\text{PsPePsP}\gg\text{C}\ddot{\text{H}}\text{PsC}\ddot{\text{T}}\text{C}\ddot{\text{r}}. \end{aligned}$$

$\text{P}_{\mu}\text{C}\overline{\text{H}}\text{P}_{\mu}\text{P}^{\circ}\text{C}\overline{\text{H}}\text{P}^{\circ}\text{C}$, $\text{P}^{\circ}\text{C}-\text{PrPsC}\overline{\text{H}}\text{P}^{\circ}\text{PjC}-\text{PeC}\overline{\text{H}}\text{Ps}\text{b}\overline{\text{H}}^{\circ}\text{C}\dagger\text{P}_{\mu}\text{PePsPjP}\pm\text{C}-\text{PSPsPIP}^{\circ}\text{PSP}\overline{\text{P}}\text{PN}_{\text{e}}$
 $\text{PsC}\overline{\text{H}}\text{P}^{\circ}\text{P}\rangle\text{CHbPSP}\overline{\text{P}}\text{PN}_{\text{e}}\text{PePsPSC},\text{C}\overline{\text{H}}\text{P}^{\circ}\text{C}\dagger\text{P}_{\mu}\text{PiC},\text{P}\overline{\text{e}}\text{PI}\text{P}^{\circ}$
 $\text{P}_{\mu}\text{C},\text{P}\overline{\text{e}}\text{PSC}-\text{P}\rangle\text{P}_{\mu}\text{C}\overline{\text{I}}\text{C},\text{C}\overline{\text{H}}\text{P}^{\circ}\text{PrC}-\text{PsP}\rangle\text{PsPj}\text{C},\text{P}^{\circ}\text{P}\overline{\text{i}}\text{C}\overline{\text{H}}\text{PsPiP}_{\mu}\text{C}\overline{\text{I}}\text{C},\text{PsPiP}_{\mu}\text{PSPsPj}$
 $\text{PrC}\overline{\text{H}}\text{PsC}\overline{\text{I}}\text{PiC}-\text{C}\overline{\text{H}}\text{P}_{\mu}\text{PSPsPSPsPj}.\text{Pj}\text{C},\text{P}_{\mu}\text{C}\overline{\text{H}}\text{P}^{\circ}\text{PiP}_{\mu}\text{PIC},\text{P}\overline{\text{e}}\text{C}\dagger\text{PSP}\overline{\text{e}}\text{C}\dots\text{PrPsP}^{\circ}\text{P}^{\circ}\text{C}\dots$
 $\text{PrC}\overline{\text{H}}\text{PsC}\overline{\text{I}}\text{PiC}-\text{C}\overline{\text{H}}\text{P}_{\mu}\text{PSPsPS}\text{P}\overline{\text{i}}\text{C}\overline{\text{H}}\text{PsC}\overline{\text{I}}\text{PIP}\rangle\text{C}\overline{\text{I}}\text{C}^{\circ}\text{P}^{\circ}\text{PSC},\text{P}\overline{\text{e}}\text{P}^{\circ}\text{PSPrC}\overline{\text{H}}\text{PsPiP}_{\mu}\text{PSPSC}-\text{C},\text{P}^{\circ}$
 $\text{PiPsPjC}-\text{C}\overline{\text{H}}\text{PSC}-\text{P}^{\circ}\text{PSC},\text{P}\overline{\text{e}}\text{PjC}-\text{PSP}_{\mu}\text{C}\overline{\text{H}}\text{P}^{\circ}\text{P}\rangle\text{PsPePsC}\overline{\text{H}}\text{C},\text{P}\overline{\text{e}}\text{PePsC}-\text{PrPSC}-$
 $\text{PIP}\rangle\text{P}^{\circ}\text{C}\overline{\text{I}}\text{C},\text{P}\overline{\text{e}}\text{PIPsC}\overline{\text{I}}\text{C},\text{C}-.\text{P}^{\circ}\text{C}-\text{PS}\text{PSP}_{\mu}\text{PjP}^{\circ}\text{C}^{\circ}\text{P}_{\mu}\text{C}\overline{\text{I}}\text{C},\text{C}\overline{\text{H}}\text{PsPiP}_{\mu}\text{PSPSPsC}-,$
 $\text{PiP}\rangle\text{C}\overline{\text{H}}\text{PePsPePsC}\overline{\text{H}}\text{C},\text{P}\overline{\text{e}}\text{PePsC}-\text{PrPSPsC}-\text{C},\text{P}^{\circ}$
 $\text{P}^{\circ}\text{PSC},\text{P}\overline{\text{e}}\text{PiP}\rangle\text{C}\overline{\text{H}}\text{PePsPePsC}\overline{\text{H}}\text{C},\text{P}\overline{\text{e}}\text{PePsC}-\text{PrPSPsC}-\text{P}^{\circ}\text{PeC},\text{P}\overline{\text{e}}\text{PIPSPsC}\overline{\text{I}}\text{C},\text{C}-.\text{PhC},\text{P}\overline{\text{I}}\text{P}_{\mu},$
 $\text{PrC}\overline{\text{H}}\text{PsC}\overline{\text{I}}\text{PiC}-\text{C}\overline{\text{H}}\text{P}_{\mu}\text{PSPsPS}\text{PjP}^{\circ}\text{C}^{\circ}\text{C}\overline{\text{I}}\text{C}\dots\text{PsP}\overline{\text{I}}\text{P}\overline{\text{e}}\text{PN}_{\text{e}}\text{C}_{\text{e}},\text{P}^{\circ}\text{C}\overline{\text{H}}\text{PjP}^{\circ}\text{PePsP}\rangle\text{PsPiC}-\text{C}\dagger\text{PSP}\overline{\text{P}}\text{PN}_{\text{e}}$
 $\text{PiC}\overline{\text{H}}\text{PsC}_{\text{e}}\text{C}-\text{P}\rangle\text{CHb}\text{C}-\text{P}^{\circ}\text{PiC}\overline{\text{H}}\text{P}\overline{\text{e}}\text{C}\overline{\text{H}}\text{PsPrPSP}\overline{\text{P}}\text{Pj}\text{PiC}\overline{\text{H}}\text{PsPiP}_{\mu}\text{C}\overline{\text{I}}\text{C},\text{P}_{\mu}\text{C}\overline{\text{H}}\text{PsPSPsPj}.$

P—PiC-PrPSPs PrP°PSPëC... PeP»C-PSC-C†PSPëC... PrPsCÍP»C-PrP¶PµPSCĤ PiPsPjC-CĤPSC-
P°PSC,PëPjC-PSPµCĤP°P»PsPePsCĤC,PëPePsC—PrPSC- PIP»P°CÍC,PëPIPsCÍC,C-
PíCĤPµPiP°CĤP°C,CÍ P°C-PrPsCĤP° PjC-PeCĤPs PíCĤPëP·PIPsPrCÍC,CĤ PrPs
PíPsPjC-CĤPSPsPiPs P°PSC,PëPjC-PSPµCĤP°P»PsPePsCĤC,PëPePsC—PrPSPsPiPs PIPiP»PëPICÍ.

P°CÍP»Ps PíCĤPsPIPµPrPµPSPs PrPIP° P±P°PiP°C,PsC†PµPSC,CĤPsPIPëC...,
PíPsPrPIC-PNëPSPëC... CÍP»C-PiPëC..., CĤP°PSPPrPsPjC-P·PsPIP°PSPëC..., PiP»P°C†PµP±Ps-
PePsPSC,CĤPsP»CĤPsPIP°PSPëC... PrPsCÍP»C-PrP¶PµPSPSCÍ PrP»CÍ PsC†C-PSPePë
PµC,,PµPeC,PëPIPsCÍC,C- C,P° P±PµP·PiPµPePë P·P°CÍC,PsCÍCÍPIP°PSPSCÍ
PíCĤPµPiP°CĤP°C,CÍ P°C-PrPsCĤP° PjC-PeCĤPs P¶C-PSPeP°Pj P· *acne vulgaris*
CÍPµCĤPµPrPSCĤPsPiPs CÍC,CÍPiPµPSCÍ. PµC-CÍP»CÍ 6 PjC-CÍCÍC†C-PI C,PµCĤP°PiC-C—,
PíPsCĤC-PIPsCÍPSPs P· PiP»P°C†PµP±Ps, PíCĤPµPiP°CĤP°C, PíCĤPsPrPµPjPsPSCÍC,CĤCÍPIP°PI
CÍC,P°C,PëCÍC,PëC†PSPs P·PSP°C†CÍC%PëPNë PµC,,PµPeC, P·PSPëP¶PµPSPSCÍ PSP° 15,6 %
(49,3 % PíPsCĤC-PIPsCÍPSPs P· 33,7 %) PeC-P»CĤPePsCÍC,C- P·P°PiP°P»CĤPSPëC...
PµP»PµPjPµPSC,C-PI, 18,5 % (40,6 % PíPsCĤC-PIPsCÍPSPs P· 22,1 %) PeC-P»CĤPePsCÍC,C-
PSPµP·P°PiP°P»CĤPSPëC... PµP»PµPjPµPSC,C-PI, C,P° 16,5 % (44,6 % PíPsCĤC-PIPsCÍPSPs P·
28,1 %) P·P°PiP°P»CĤPSPsC— PeC-P»CĤPePsCÍC,C- PIPëCÍPëPiP°PSCĤ. PŸP°PePsP¶
P±C-P»CĤC€PëPNë PIC-PrCÍPsC,PsPe CÍCÍP±BĤ™C°PeC,C-PI, 11,8 % (18,6 %
PíPsCĤC-PIPsCÍPSPs P· 6,8 %), P±CÍPI C-P· B«C†PëCÍC,PsCĤB» C,P° B«PjP°PNëP¶Pµ
C†PëCÍC,PsCĤB» C€PeC-CĤPsCĤ, CÍPeC- PsC†C-PSCĤPIP°P»PëCÍCÍ P·P° C€PeP°P»PsCĤ ISGA
(InvestigatorBĤ™ s Stated Global Assessment).

Pα°CĤPjP°PePsPeC-PSPµC,PëPeP°.

P°CĤPsCÍPiC-CĤPµPSPsPS

P°CÍPjPsPeC,CÍPIP°PSPSCÍ. PµPµCĤPsCĤP°P»CĤPSPs PíCĤPëPNëPSCÍC,PëPNë
PrCĤPsCÍPiC-CĤPµPSPsPS C€PIPëPrPePs C- PíPsPIPsC-CÍC,CĤ
PICÍPjPsPeC,CÍC°C,CĤCÍCÍ. PĤP°PeCÍPëPjP°P»CĤPSP° PePsPSC†PµPSC,CĤP°C†C-CÍ
CÍ CÍPëCĤPsPIP°C,C†C- PeCĤPsPIC-, C°Ps CÍC,P°PSPsPIPëC,CĤ 38 PSpI/PjP»,
PrPsCÍCÍPiP°C°C,CĤCÍCÍ PíCĤPëP±P»PëP·PSPs C†PµCĤPµP· 1-2 PiPsPrPëPSPë
PíC-CÍP»CÍ PsPrPSPsCĤP°P·PsPIPsPiPs PíPµCĤPsCĤP°P»CĤPSPsPiPs
P·P°CÍC,PsCÍCÍPIP°PSPSCÍ. P°C-PsPrPsCÍC,CÍPiPSC-CÍC,CĤ CÍC,P°PSPsPIPëC,CĤ
76-85 %. PĤPrPSPsC†P°CÍPSPµ PIP¶PëPIP°PSPSCÍ C—P¶C- PSPµ PIPiP»PëPIP°C°PSP°
P±C-PsPrPsCÍC,CÍPiPSC-CÍC,CĤ PrCĤPsCÍPiC-CĤPµPSPsPSCÍ.

P PsP·PiPsPrC-P». PµC-CÍP»CÍ PiPµCĤPsCĤP°P»CĤPSPsPiPs P·P°CÍC,PsCÍCÍPIP°PSPSCÍ
PePsPSC†PµPSC,CĤP°C†C-CÍ PrCĤPsCÍPiC-CĤPµPSPsPSCÍ PI CÍPëCĤPsPIP°C,C†C- PeCĤPsPIC-
P·PSPëP¶CÍC°C,CĤCÍCÍ, P° CÍPµCĤPµPrPSC-PNë PeC-PSC†PµPIPëPNë PíPµCĤC-PsPr
PSP°PiC-PIPIPëPIPµPrPµPSPSCÍ CÍC,P°PSPsPIPëC,CĤ PíCĤPëP±P»PëP·PSPs 31 PiPsPrPëPSCÍ.
P°CĤPsCÍPiC-CĤPµPSPsPS P·PiBĤ™ CÍP·CÍC°C,CĤCÍCÍ P·C- CÍPëCĤPsPIP°C,PePsPIPëPj
P°P»CĤP±CÍPjC-PSPsPj, PíCĤPë C†CĤPsPjCÍ PSPµ P·PiBĤ™ CÍP·CÍCĤC†PëCÍCĤ C-P·
PiP»PsP±CÍP»C-PSPsPj, C°Ps P·PiBĤ™ CÍP·CÍC° CÍC,P°C,PµPIC- PiPsCĤPjPsPSPë, C,P° P·
PePsCĤC,PëPePsC—PrPsP·PiBĤ™ CÍP·CÍCĤC†PëPj PiP»PsP±CÍP»C-PSPsPj. PŸC-P»CĤPePë 3-5 %
PNëPsPiPs P·P°PiP°P»CĤPSPsC— PeC-P»CĤPePsCÍC,C- PI CÍPëCĤPsPIP°C,C†C- PeCĤPsPIC-
PíCĤPëP±CÍPIP°C° CÍ PIC-P»CĤPSPsPjCÍ CÍC,P°PSC-. PŸPíCĤPëC†PëPSPµPSPµ
PµC,PëPSC-P»PµCÍC,CĤP°PrC-PsP»PsPj PiC-PrPIPëC°PµPSPSCÍ P°P—PŸPŸ PSPµ
PIPiP»PëPIP°C°PSP° P·PiBĤ™ CÍP·CÍPIP°PSPSCÍ PrCĤPsCÍPiC-CĤPµPSPsPSCÍ P·
PíCĤPsC,PµC—PSP°PjPë CÍPëCĤPsPIP°C,PePë PeCĤPsPIC-. PŸPµCĤPµPrPSC-PNë PsP±BĤ™C°Pj
CĤPsP·PiPsPrC-P»CÍ PrCĤPsCÍPiC-CĤPµPSPsPSCÍ CÍC,P°PSPsPIPëC,CĤ 3,7 B± 1,2 P»/PePi.

P_HPμC,P°P±PsP»C-P·Pj. P”C_HPsCΓPiC-C_HPμPSPsPS P·PSP°C‡PSPsC_H PjC-C_HPsC_H PjPμC,P°P±PsP»C-P·CrC”C,C_HCΓCΠ PiC-CΓP»CΠ PiPμC_HPsC_HP°P»C_HPSPsPiPs P·P°CΓC,P_sCΓC_rPIP°PSPSCΠ. P“PsP»PsPIPSPëPjPë PjPμC,P°P±PsP»C-C,P°PjPë Cr PiP»P°P·PjC- C” PePëCΓP»PsC,PSC- C„PsC_HPjPë PrC_HPsCΓPiC-C_HPμPSPsPSCr, C%Ps CrC,PIPsC_HC_HC_HC,C_HCΓCΠ PiC_HPë PIC-PrPeC_HPëC,C,C- P»P°PeC,P_sPSPsPIPsPiPs PeC-P»C_HC†CΠ, C,P° 4,5-PrPëPiC-PrC_HPsPrC_HPsCΓPiC-C_HPμPSPsPS-3-CΓC_rP»C_HC„P°C,, CΠPeC- CrC,PIPsC_HC_HC_HC,C_HCΓCΠ C€P»CΠC...PsPj PiC-PrC_HP°C,P°C†C-C— P· PiPsPrP°P»C_HC€PëPj CΓC_rP»C_HC„P°C,C_rPIP°PSPSCΠPj. P”C_HPsCΓPiC-C_HPμPSPsPS C,P°PePsP¶ C” PsP±B_H™ C”PeC,P_sPj PsPePëCΓPSC_HPIP°P»C_HPSPsPiPs PjPμC,P°P±PsP»C-P·PjCr, C%Ps PeP°C,P°P»C-P·CrC”C,C_HCΓCΠ CYP3A4. *In vitro* PrC_HPsCΓPiC-C_HPμPSPsPS PjPsP¶Pμ CΓP»P°P±PePs P°P±Ps PiPsPjC-C_HPSPs PiC_HPëPiPSC-C‡CrPIP°C,Pë C„PμC_HPjPμPSC,Pë C†PëC,P_sC...C_HPsPjCr P450: CYP1A1, CYP2C9, CYP2C19 C,P° CYP3A4.

P·PëPIPμPrPμPSPSCΠ P· PsCḡPiP°PSC-P·PjCṛ. PËPIPëPrPeC-Cl̇C,CḢ
PjPμC,P°P±PsP»C-C‡PSPsPiPs PeP»C-CḡPμPSCl̇Cṛ PrCḡPsCl̇PiC-CḡPμPSPsPSCṛ C-P·
Cl̇PëCḡPsPIP°C,PePë PeCḡPsPIC- Cl̇C,P°PSPsPIPëC,CḢ PiCḡPëP±P»PëP·PSPs 1,5 B± 0,2
PjP»/C...PI/PePi. P"ḡPsCl̇PiC-CḡPμPSPsPS PIPëPrC-P»CΠC"C,CḢCl̇CΠ Cṛ
PSPμP·PjC-PSPμPSC-PṄ C,,PsCḡPjC- C,C-P»CḢPePë Cṛ PrCṛP¶Pμ PSPμP·PSP°C‡PSC-PṄ
PeC-P»CḢPePsCl̇C,C-. PḡPμC,P°P±PsP»C-C,Pë PIPëPrC-P»CΠCḡC,CḢCl̇CΠ P·C- Cl̇PμC‡PμCḡ
C,P° PeP°P»PsPj Cṛ Cl̇PiC-PIPIC-PrPSPsC¶PμPSPSC- PIC-Pr 1,2 PrPs 1,4. PμPμCḡC-PsPr
PSP°PiC-PIPIPëPIPμPrPμPSPSCΠ PjPμC,P°P±PsP»C-C,C-PI P·C- Cl̇PμC‡PμCḡ C,P° PeP°P»PsPj
Cl̇C,P°PSPsPIPëC,CḢ PiCḡPëP±P»PëP·PSPs 40 PiPsPrPëPs.

ПҮС, Р°PS CҖC-PIPSsPIP°PiPё. PJPiCҖPsPrPsPIP¶ C†PёPeP»C† P·P°C†C, PsC†C†PIP°PSPSC¶
PjP°PeC†PёPjP°P»CHPSP° CҖC-PIPSsPIP°P¶PSP° PePsPSC†PµPSC, CҖP°C†C-C¶
PrCҖPsC†PiC-CҖPµPSPsPSC† PI C†PёCҖPsPIP°C, C†C- PeCҖPsPIC-, C%°Ps
C†C, P°PSPsPIPёC, CH PiCҖPёP±P»PёP·PSPs 70 PSPi/PjP», PrPsC†C¶PiP°C”C, CHC†C¶
PiC-C†P»C¶ 8 PrPSC-PI P·P°C†C, PsC†C†PIP°PSPSC¶. P C-PIPSC-
PrCҖPsC†PiC-CҖPµPSPsPSC† C† PeCҖPsPIC- PeC†PjC†P»CҖPIP°P»Pё C† 3 CҖP°P·Pё
C¶Pe PSP°C†P»C-PrPsPe C†PiC-PIPIC-PrPSPsCёPµPSPSC¶
C, PµCҖPjC-PSP°P»CHPSPsPiPs PiPµCҖC-PsPrC† PSP°PiC-PIPIPёPIPµPrPµPSPSC¶ C, P°
C-PSC. PuCҖPIP°P»C† PrPsP·C†PIP°PSPSC¶.

$$PhPeCH_2PuPjC-PiCH_2CzPiP\ddot{e} \quad PiP^{\circ}C\uparrow C-C''PSC,PsPe$$

P-C-PSPePë C-P· PiPsCfCrC€PuPSPSClIPiPë C„CrPSPeC†C-C— PSPëCfPsPe

P C-PIPSPsPIP°P¶PSP° PePsPSC†PµPSC, C¶P°C†C-Cl PrC¶PsC†PiC-C¶PµPSPsPSC† PI
 C†PëC¶PsPIP°C, C†C- PeC¶PsPIC- Cr P¶C-PSPsPe P· PSPëC¶PePsPIPsC¶
 PSPµPrPsC†C, P°C, PSC-C†C, C¶ P»PµPiPePsPiPs C†C, C†PiPµPSC¶ C, ClP¶PePsC†C, C-
 (PeP»C-C¶PµPSC† PeC¶PµP°C, PëPSC-PSC† 50-80 PjP»/C...PI) P±C†P»P°
 PiPsC¶C-PIPSC¶PSPSPsC¶ C-P· C†PëPj PiPsPeP°P·PSPëPePsPj PrP»Cl P¶C-PSPsPe C-P·
 PSPsC¶PjP°P»C¶PSPsC¶ C,, C†PSPeC†C-C" C¶ PSPëC¶PsPe (PeP»C-C¶PµPSC†
 PeC¶PµP°C, PëPSC-PSC† P±C-P»C¶C¶Pµ 80 PjP»/C...PI). P C-PIPµPSC¶
 PrC¶PsC†PiC-C¶PµPSPsPSC† PI C†PëC¶PsPIP°C, C†C- PeC¶PsPIC- P±C†PI Cr
 C†PµC¶PµPrPSC¶PsPjC† PSP° 37 % PIPëC‰PëPNe Cr P¶C-PSPsPe C-P· PSPëC¶PePsPIPsC¶
 PSPµPrPsC†C, P°C, PSC-C†C, C¶ C†PµC¶PµPrPSC¶PsPiPs C†C, C†PiPµPSC¶ C, ClP¶PePsC†C, C-
 (PeP»C-C¶PµPSC† PeC¶PµP°C, PëPSC-PSC† 30-50 PjP»/C...PI) PiPsC¶C-PIPSC¶PSPsC— P· C†PëPj
 PiPsPeP°P·PSPëPePsPj PrP»Cl P¶C-PSPsPe C-P· PSPsC¶PiP°P»C¶PSPsC¶ C,, C†PSPeC†C-C" C¶

PSPëCĤPsPe. P—P°CÍC,PsCÍCÍPIP°PSPSCĬ PrCĤPsCÍPíC-CĤPµPSPsPSCÍ
PíCĤPsPrPµPjPsPSCÍC,CĤCÍPIP°P»Ps PrPsP±CĤCÍ PíPµCĤPµPSPsCÍPëPjC-CÍC,Ch CÍ
PICÍC-C... PíCĤCÍPíP°C... PíP°C†C-C”PSC,PsPe. P”PsPIPµPrPµPSPs, C°Ps PíCĤPëPµPsPj
PrCĤPsCÍPíC-CĤPµPSPsPSCÍ PSPµ PjP°C” PeP»C-PSC-C†PSPs P·PSP°C†CÍC°PsPiPs
PµC,,PµPeC,CÍ PSP° PePsPSC†PµPSC,CĤP°C†C-CĤ PeP°P»C-CĤ PI CÍPëCĤPsPIP°C,C†C-
PeCĤPsPIC-.

P-C-PSPePë P· PíPsCĤCÍC€PµPSPSCĬPjPë C,,CÍPSPeC†C-C— PíPµC†C-PSPePë

Pj PrPsCÍP»C-PrP¶PµPSPSC- P·P°CÍC,PsCÍCÍPIP°PSPSCĬ PsPrPSPsCĤP°P·PsPIPsC— PrPsP·Pë
PeP»C-CĤPµPSCÍ PrCĤPsCÍPíC-CĤPµPSPsPSCÍ PíCĤPë PíPµCĤPsCĤP°P»CHPSPsPjCÍ
P·P°CÍC,PsCÍCÍPIP°PSPSC- P·PSPëP¶CÍPIP°PICÍCĬ PíCĤPëP±P»PëP·PSPs PSP° 50 % PI
PsCÍC-P± C-P· PíPsPjC-CĤPSPsCĤ PíPµC†C-PSPePsPIPsCĤ PSPµPrPsCÍC,P°C,PSC-CÍC,CĤ
PíPsCĤC-PIPSCĬPSPs P· PrPsP±CĤPsPIPsP»CHC†CĬPjPë P· PSPsCĤPjP°P»CHPSPsCĤ
C,,CÍPSPeC†C-C”CĤ PíPµC†C-PSPePë. P’PëCĬPIP»PµPSPµ PIC-PrC...PëP»PµPSPSCĬ
PeP»C-CĤPµPSCÍCÍ PrCĤPsCÍPíC-CĤPµPSPsPSCÍ PI PsCÍC-P± C-P· PíPsPjC-CĤPSPsCĤ
PíPµC†C-PSPePsPIPsCĤ PSPµPrPsCÍC,P°C,PSC-CÍC,CĤ PSPµ P·CÍPjPsPIP»CĤPIP°P»Ps
P±CÍPrCH-CĬPePëC... CĬPIPSPëC... PIC-PrPjC-PSPSPsCÍC,PµPNë C°PsPrPs
PePsPSC†PµPSC,CĤP°C†C-C— PeP°P»C-CĤ CÍ CÍPëCĤPsPIP°C,C†C- PeCĤPsPIC-. PkP°PIC-C,Ch
PíCĤPë PSP°CĬPIPSPsCÍC,C- C†CÍPeCĤPsPIPsPiPs PrC-P°P±PµC,CÍ C,P° PíCĤPë
CÍCÍPíCÍC,PSCHPsPjCÍ P·P°CÍC,PsCÍCÍPIP°PSPSC- CÍPíC-CĤPsPSPsP»P°PeC,PsPSCÍ (PrPIP°
C,,P°PeC,PsCĤPë, C°Ps PjPsP¶CÍC,Ch PíCĤPsPIPsPeCÍPIP°C,Pë PíC-PíPµCĤPeP°P»C-C”PjC-CĤ)
PSPµ CÍPíPsCÍC,PµCĤC-PíP°P»PsCÍCĬ PíC-PrPIPëC°PµPSPSCĬ PePsPSC†PµPSC,CĤP°C†C-C—
PeP°P»C-CĤ PI CÍPëCĤPsPIP°C,C†C- PeCĤPsPIC- PíPëC°Pµ PíPµCĤC...PSCCHPsC— PjPµP¶C-
PSPsCĤPjPë. PhC,P¶Pµ, PrCĤPsCÍPíC-CĤPµPSPsPS PrPsP±CĤPµ PíPµCĤPµPSPsCÍPëC,ChCÍCĬ
PsCÍPsP±P°PjPë P· PíPµC†C-PSPePsPIPsCĤ PSPµPrPsCÍC,P°C,PSC-CÍC,CĤ P»PµPiPePsPiPs C,P°
PíPsPjC-CĤPSPsPiPs CÍC,CÍPíPµPSCĬ (PeP»P°CÍ P’ P·P° PeP»P°CÍPëC,,C-PeP°C†C-C”CĤ
PŞP°PNëP»PrP°-PµBĤ™ CĤ).

P·C,PSC-C†PSC- PíCĤCÍPíPë. PkPµ CÍPíPsCÍC,PµCĤC-PíP°P»PsCÍCĬ PeP»C-PSC-C†PSPs
P·PSP°C†CÍC°PsC— CĤC-P·PSPëC†C- CÍ C,,P°CĤPjP°PePsPeC-PSPµC,PëC†C-
PrCĤPsCÍPíC-CĤPµPSPsPSCÍ P°P±Ps PµC,PëPSC-P»PµCÍC,CĤP°PrC-PsP»CÍ CÍ
P¶C-PSPsPe CĬPíPsPSCÍCHPePsC— PSP°C†C-PsPSP°P»CHPSPsCÍC,C- C,P°
C”PICĤPsPíPµPNëC†C-PI.

P·C,PëPSC-P»PµCÍC,CĤP°PrC-PsP»

P’CÍPjPsPeC,CÍPIP°PSPSCĬ. PµCĤPë PíPµCĤPsCĤP°P»CHPSPsPjCÍ
P·P°CÍC,PsCÍCÍPIP°PSPSC- PµC,PëPSC-P»PµCÍC,CĤP°PrC-PsP» C€PIPëPrPePs C-
PíPsPIPSC-CÍC,CĤ PICÍPjPsPeC,CÍC”C,ChCÍCĬ. PĤP°PeCÍPëPjP°P»CHPSP°
CÍPëCĤPsPIP°C,PePsPIP° PePsPSC†PµPSC,CĤP°C†C-CĬ, C°Ps PrPsCĤC-PIPSCĤC” 33
PíPePi/PjP», PrPsCÍCĬPíP°C”C,ChCÍCĬ PíCĤPsC,CĬPíPsPj 1 - 2 PíPsPrPëPS PíC-CÍP»CĬ
PsPrPSPsCĤP°P·PsPIPsPiPs PíPµCĤPsCĤP°P»CHPSPsPiPs P·P°CÍC,PsCÍCÍPIP°PSPSCĬ.
PhP±CÍPsP»CĤC,PSP° P±C-PsPrPsCÍC,CÍPíPSC-CÍC,Ch PIPSP°CÍP»C-PrPsPe
PíCĤPµCÍPëCÍC,PµPjPSPsC— PePsPSBĤ™ CĤPíP°C†C-C— C- PjPµC,P°P±PsP»C-P·PjCÍ
PíCĤPë PíPµCĤC€PsPjCÍ PíCĤPsC...PsPrP¶PµPSPSC- C†PµCĤPµP· PíPµC†C-PSPeCÍ
CÍC,P°PSPsPIPëC,Ch PíCĤPëP±P»PëP·PSPs 60 %. PhPrPSPsC†P°CÍPSPµ
PIP¶PëPIP°PSPSCĬ C—P¶C- P·PjPµPSC€CÍC” P±C-PsPrPsCÍC,CÍPíPSC-CÍC,Ch
PµC,PëPSC-P»PµCÍC,CĤP°PrC-PsP»CÍ PíCĤPëP±P»PëP·PSPs CÍ 25 %
PrPsCÍP»C-PrP¶CÍPIP°PSPëC... PíCĤPë PSPµP·PjC-PSPSC-PNë

$P \pm C - PsPrPsClC, CrPiPSPsClC, C - Cr C\eta P\mu C\epsilon C, P\epsilon.$

$P PsP \cdot PiPsPrC - P \gg$. $P C - PIP\mu PSC\eta P\mu C, P\epsilon PSC - P \gg P\mu ClC, C\eta P^\circ PrC - PsP \gg Cr Cr ClP\epsilon C\eta PsPIP^\circ C, C\uparrow C - P \cdot PjP\mu PSC\epsilon CrC''C, CHClC\uparrow C\uparrow PrPIP\mu C, P^\circ P \cdot PSPs, C, P\mu C\eta PjC - PSP^\circ P \gg CH\eta PSP^\circ C, P^\circ P \cdot P^\circ C \dots P^\circ C\eta P^\circ PeC, P\mu C\eta P\epsilon P \cdot CrC''C, CHClC\uparrow C\uparrow PiP\mu C\eta C - PsPrPsPj PSP^\circ PiC - PIPiP\epsilon PIP\mu PrP\mu PSPSC\uparrow, C\%Ps PiC\eta P\epsilon P \pm P \gg P\epsilon P \cdot PSPs PrPsC\eta C - PIPSC\eta C''$ 24 $PiPsPrP\epsilon PSP\epsilon.$
 $P \cdot C, P\epsilon PSC - P \gg P\mu ClC, C\eta P^\circ PrC - PsP \gg PjC - C\uparrow PSPs, PiC\eta PsC, P\mu PSP\mu ClPiP\mu C\uparrow P\epsilon C, C - C\uparrow PSPs, P \cdot Pi\eta C\uparrow C\uparrow P \cdot CrC''C, CHClC\uparrow C\uparrow P \cdot P^\circ P \gg CH\eta P \pm CrPjC - PSP^\circ PjP\epsilon ClP\epsilon C\eta PsPIP^\circ C, PeP\epsilon (PiC\eta P\epsilon P \pm P \gg P\epsilon P \cdot PSPs 98,5 \%) C, P^\circ C - PSPCrPeCrC'' P \cdot P \pm C - P \gg CH\eta C\epsilon P\mu PSPSC\uparrow PePsPSC\uparrow P\mu PSC, C\eta P^\circ C\uparrow C - C - P''P - P\check{Y}P\check{Y} C, P^\circ PePsC\eta C, P\epsilon PePsClC, P\mu C\eta PsC - PrP \cdot P\uparrow C\uparrow P \cdot CrC\eta C\uparrow PsPiPs PiP \gg PsP \pm CrP \gg C - PSP^\circ Cr ClP\epsilon C\eta PsPIP^\circ C, C\uparrow C - PeC\eta PsPIC-. PjC\uparrow PIPSP\epsilon P\mu PsP \pm \eta C''Pj C\eta PsP \cdot PiPsPrC - P \gg Cr ClC, P^\circ PSPsPIP\epsilon C, CH PiC\eta P\epsilon P \pm P \gg P\epsilon P \cdot PSPs 5 P \gg /PePi.$

$P\eta P\mu C, P^\circ P \pm PsP \gg C - P \cdot Pj$. $P \cdot C, P\epsilon PSC - P \gg P\mu ClC, C\eta P^\circ PrC - PsP \gg P \cdot PSP^\circ C\uparrow PSPsC\eta PjC - C\eta PsC\eta PjP\mu C, P^\circ P \pm PsP \gg C - P \cdot CrC''C, CHClC\uparrow C\uparrow Cr P\epsilon P\eta P\check{Y} C, P^\circ PiC\eta P\epsilon PiP\mu C\eta C\epsilon PsPjCr PiC\eta PsC \dots PsPrP\uparrow P\mu PSPSC - C\uparrow P\mu C\eta P\mu P \cdot PiP\mu C\uparrow C - PSPeCr.$
 $P \cdot C, P\epsilon PSC - P \gg P\mu ClC, C\eta P^\circ PrC - PsP \gg PjP\mu C, P^\circ P \pm PsP \gg C - P \cdot CrC''C, CHClC\uparrow C\uparrow, PiPsP \gg PsPIPSP\epsilon Pj C\uparrow P\epsilon PSPsPj, C\epsilon P \gg C\uparrow C \dots PsPj PiC - PrC\eta PsPeClP\epsilon P \gg C\eta PIP^\circ PSPSC\uparrow P^\circ C\eta PsPjP^\circ C, P\epsilon C\uparrow PSPsPiPs PeC - P \gg CHC\uparrow C\uparrow P \cdot CrC, PIPsC\eta P\mu PSPSC\uparrow Pj C\epsilon P\epsilon C\eta PsPePsPiPs ClPiP\mu PeC, C\eta P^\circ PiC - PrC\eta PsPeClP\epsilon P \gg CH\eta PsPIP^\circ PSP\epsilon C \dots C, P^\circ PjP\mu C, P\epsilon P \gg CH\eta PsPIP^\circ PSP\epsilon C \dots PjP\mu C, P^\circ P \pm PsP \gg C - C, C - PI, C\uparrow PeC - PiC\eta P\epsilon P \pm CrPIP^\circ C\eta C, CH Cr PIC - P \gg CH\eta PSPsPjCr ClC, P^\circ PSC - C, P^\circ C\uparrow Pe PePsP\eta C\uparrow C\eta PiP^\circ C, P\epsilon P \cdot PiP \gg C\eta PeCrC\eta PsPSC - PrP^\circ PjP\epsilon C, P^\circ ClCrP \gg CHC, P^\circ C, P^\circ PjP\epsilon. P\eta P\mu C, P^\circ P \pm PsP \gg C - C\uparrow PSP\epsilon P\mu PeP \gg C - C\eta P\mu PSC\uparrow P\mu C, P\epsilon PSC - P \gg P\mu ClC, C\eta P^\circ PrC - PsP \gg Cr ClC, P^\circ PSPsPIP\epsilon C, CH PiC\eta P\epsilon P \pm P \gg P\epsilon P \cdot PSPs 5 PjP \gg /C \dots PI /PePi.$

In vitro $P\mu C, P\epsilon PSC - P \gg P\mu ClC, C\eta P^\circ PrC - PsP \gg C'' P \cdot PIPsC\eta PsC, PSP\epsilon Pj C - PSPiC - P \pm C - C, PsC\eta PsPj CYP2C19, CYP1A1 C, P^\circ CYP1A2, P^\circ C, P^\circ PePsP\uparrow PSP^\circ PsClPSPsPIC - PjP\mu C \dots P^\circ PSC - P \cdot PjCr PrC - C - \eta C'' C - PSPiC - P \pm C - C, PsC\eta PsPj CYP3A4/5, CYP2C8 C, P^\circ CYP2J2.$

$P \cdot P\epsilon PIP\mu PrP\mu PSPSC\uparrow P \cdot PsC\eta PiP^\circ PSC - P \cdot PjCr$. $P \cdot C, P\epsilon PSC - P \gg P\mu ClC, C\eta P^\circ PrC - PsP \gg PjP^\circ P\mu P\uparrow P\mu PSP\mu PIP\epsilon PIPsPrP\epsilon C, CHClC\uparrow C\uparrow Cr PSP\mu P \cdot PjC - PSP\mu PSC - P\mu C, PsC\eta PjC-. P\eta P\mu C, P^\circ P \pm PsP \gg C - C, P\epsilon P\mu C, P\epsilon PSC - P \gg P\mu ClC, C\eta P^\circ PrC - PsP \gg Cr PIP\epsilon PIPsPrC\uparrow C, CHClC\uparrow C\uparrow C - P \cdot ClP\mu C\uparrow P\mu C\eta C, P^\circ P\uparrow PsPIC\uparrow C\eta Cr ClPiC - PIPIC - PrPSPsC\epsilon P\mu PSPSC - 4:6. P\mu P\mu C\eta C - PsPr PSP^\circ PiC - PIPiP\epsilon PIP\mu PrP\mu PSPSC\uparrow PjP\mu C, P^\circ P \pm PsP \gg C - C, C - PI ClC, P^\circ PSPsPIP\epsilon C, CH PjP^\circ P\mu P\uparrow P\mu 1 PrPsP \pm Cr.$

$P\check{Y}C, P^\circ PS C\eta C - PIPSPsPIP^\circ PiP\epsilon$. $P\check{Y}C, P^\circ PS C\eta C - PIPSPsPIP^\circ PiP\epsilon PrPsClC\uparrow PiP^\circ C''C, CHClC\uparrow C\uparrow Cr PrC\eta CrPiC - P\mu PiPsP \gg PsPIP\epsilon PSC - C\uparrow P\epsilon PeP \gg Cr P \cdot P^\circ ClC, PsClCrPIP^\circ PSPSC\uparrow, PePsP \gg P\epsilon PePsPSC\uparrow P\mu PSC, C\eta P^\circ C\uparrow C - C\uparrow P\mu C, P\epsilon PSC - P \gg P\mu ClC, C\eta P^\circ PrC - PsP \gg Cr PI ClP\epsilon C\eta PsPIP^\circ C, C\uparrow C - PeC\eta PsPIC - P \cdot P \pm C - P \gg CH\eta C\epsilon CrC''C, CHClC\uparrow C\uparrow Cr 2,0-2,3 C\eta P^\circ P \cdot P^\circ.$

$P''PsPeP \gg C - PSC - C\uparrow PSC - PrP^\circ PSC - P \cdot P \pm P\mu P \cdot PiP\mu PeP\epsilon$

$Pj P \gg P^\circ P \pm PsC\eta P^\circ C, PsC\eta PSP\epsilon C \dots C, PIP^\circ C\eta P\epsilon PS P\mu C, P\mu PeC, P\epsilon PrC\eta PsClPiC - C\eta P\mu PSPsPSC\uparrow C, P^\circ P\mu C, P\epsilon PSC - P \gg P\mu ClC, C\eta P^\circ PrC - PsP \gg Cr P \pm CrP \gg P\epsilon PsP \pm PjP\mu P\uparrow P\mu PSC - C, P^\circ PeP\epsilon PjP\epsilon, C\%Ps P^\circ ClPsC\uparrow C - C\eta PIP^\circ P \gg P\epsilon ClC\uparrow P \cdot PIC - PrPsPjPsC\eta C, P^\circ C\eta PjP^\circ PePsP \gg PsPiC - C\uparrow PSPsC\eta PrC - C''C\eta. P - PsPeC\eta P\mu PjP^\circ, PrPsClP \gg C - PrP\uparrow P\mu PSPSC\uparrow P \cdot PIP\epsilon C\uparrow PIP \gg P\mu PSPSC\uparrow C\eta P\mu PiC\eta PsPrCrPeC, P\epsilon PIPSPsC - C, PsPeClP\epsilon C\uparrow PSPsClC, C - Cr C, PIP^\circ C\eta P\epsilon PS PiPsPeP^\circ P \cdot P^\circ P \gg P\epsilon$

PSP°CΠIPISC-CTC,CH PIPePrPsCTPipmCtPeC,,C-CtPSPeC...
 PmPjP±CTC-PsC,PsPeCTPeCtPSPsPiPs C,P° C,,PmC,PsC,PsPeCTPeCtPSPsPiPs PIPiP»PePIC-PI.
 PmCTPe PmPeCTPisP·PeCtC-C—, C°Ps PimCTPmPIPeC°CrC” C,P°PeCr Cr C,PIP°CTPePS,
 CΠPeC- P·P°CTC,PsCTPsPICrPIP°P»Pe PictPmPiP°CTP°C, P'C-PrPsCTP° PjC-PeCTPs, Cr
 PrPmCΠPePeC... PIPePrC-PI C,PIP°CTPePS CTPisCTC,PmCTC-PiP°P»Pe PIPiP»PePI PSP°
 CTC,P°C,PmPICr PrPeC,,PmCTPmPSCtC-P°CtC-CH.

PlP»C-PSC-CtPSC- C...P°CTP°PeC,PmCTPeCTC,PePePe.

PuPsPeP°P·P°PSPSCI.

PmPmCTPsCTP°P»CHPSP° PePsPSC,CTP°CtPmPiCtC-CΠ.

PuCTPsC,PePisPsPeP°P·P°PSPSCI.

PlPsPjP±C-PSPsPIP°PSC- PipsCTPjPsPSP°P»CHPSC- PePsPSC,CTP°CtPmPiC,PePIPe (PlP“Pl)
 PSPm CTP»C-Pr P·P°CTC,PsCTPsPICrPIP°C,Pe PictPe PSP°CΠIPSPsCTC,C- C...PsCtP°
 P± PsPrPSPsPiPs C-P· PSPeP¶CtPmP·P°P·PSP°CtPmPSPeC... CTC,P°PSC-PI. Pj CTP°P·C-
 CΠPeC°Ps P±CrPrCH-CΠPePePn C-P· CtPeC... CTC,P°PSC-PI PIPePSPePeP°C”
 PIPiPmCTC¶Pm Pic-Pr CtP°CT P·P°CTC,PsCTCrPIP°PSPSCI PlP“Pl, PictPePnPsPj
 PictPmPiP°CTP°C,Cr CTP»C-Pr PSPmPiP°PnSPs PictPePipPePSPeC,Pe.

B· PkP°CΠIPISC-CTC,CH P°P±Ps CTPeP·PePe CTPsP·PIPeC,PeCr PIPmPSPsP·PSPsC—
 C,CTPsPjP±PsPmPjP±PsP»C-C— (P'PyP·):

o P'PyP· PSP° PrP°PSPePn CtP°CT, P·PsPeCTPmPjP° PIPSP°CTP»C-PrPsPe C,PmCTP°Pic-C—
 P°PSC,PePePsP°PicrP»CΠPSC,P°PjPe, P°P±Ps PI P°PSP°PjPSPmP·C- (PSP°PictPePeP»P°Pr,
 C,CTPsPjP±PsP· PIP»PeP±PsPePeC... PIPmPS (PyP“P') P°P±Ps C,CTPsPjP±PsPmPjP±PsP»C-CΠ
 P»PmPiPmPSPmPIPsC— P°CTC,PmCTC-C— (PyP·P·Ph));

o PIC-PrPsPjP° CTpiprPrPePsPIP° P°P±Ps PSP°P±CrC,P° CTC...PeP»CHPSC-CTC,CH PrPs
 P'PyP·, C,P°PeP° CΠPe CTPmP·PeCTC,PmPSC,PSC-CTC,CH PrPs P°PeC,PeIPsPIP°PSPsPiPs
 PictPsC,PmC—PSCr PŸ (Cr C,PsPjCr CtPeCTP»C- PjCrC,P°CtC-CΠ C,,P°PeC,PsCTP° V
 P>PmPnPrPmPSP°), PrPmC,,C-CtPeC, P°PSC,PeC,CTPsPjP±C-PSCr-III, PrPmC,,C-CtPeC,
 PictPsC,PmC—PSCr PŸ, PrPmC,,C-CtPeC, PictPsC,PmC—PSCr S;

o PIPmP»PePeC- PsPimCTP°C,PePIPSC- PIC,CTCrCtP°PSPSCI C-P· C,CTPePIP°P»PsCH
 C-PjPjPsP±C-P»C-P·P°CtC-C”CH (PrPePI. CTPsP·PrC-P» B«PhCTPsP±P»PePIPsCTC,C-
 P·P°CTC,PsCTCrPIP°PSPSCI»);

o PIPeCTPsPePePn CTPeP·PePe P'PyP· CtPmCTPmP· PSP°CΠIPISC-CTC,CH
 PjPSPsP¶PePSPPeC... C,,P°PeC,PsCTC-PI CTPeP·PePeCr (PrPePI. CTPsP·PrC-P»
 B«PhCTPsP±P»PePIPsCTC,C- P·P°CTC,PsCTCrPIP°PSPSCI»).

B· PkP°CΠIPISC-CTC,CH P°P±Ps CTPeP·PePe CTPsP·PIPeC,PeCr
 P°CTC,PmCTC-P°P»CHPSPsC— C,CTPsPjP±PsPmPjP±PsP»C-C— (PhPyP·):

o PSP°CΠIPISC-CTC,CH PhPyP· PSP° PrP°PSPePn CtP°CT P°P±Ps PI P°PSP°PjPSPmP·C-

(PSP°PīCḡPēPeP»P°Pr, C-PSC,,P°CḡPeC, PjC-PsPeP°CḡPrP°) P°P±Ps PSP°CḡIPSC-CḡC,CH PīCḡPsPrCḡPsPjP°P»CHPSPëC... CḡPēPjPīC,PSPjC-PI (PSP°PīCḡPēPeP»P°Pr, CḡC,PμPSPsPeP°CḡPrC-Cḡ);

o PīPsCḡCḡCēPμPSPSCḡ PjPsP·PePsPIPsPīPs PeCḡPsPIPsPsP±C-PiCḡ PSP° PrP°PSPëPNḡ C‡P°Cḡ P°P±Ps PI P°PSP°PjPSPμP·C-, PSP°CḡIPSC-CḡC,CH PīCḡPsPrCḡPsPjP°P»CHPSPëC... CḡPēPjPīC,PSPjC-PI (PSP°PīCḡPēPeP»P°Pr, C,CḡP°PSP·PëC,PSCḡPSP° C-CēPμPjC-C‡PSP° P°C,P°PeP° (TIA));

o PIC-PrPsPjP° CḡPīP°PrPePsPIP° P°P±Ps PSP°P±CḡC,P° CḡC...PēP»CHPSC-CḡC,CH PrPs PḡPḡP°, C,P°PeP° CḡPe PiC-PīPμCḡPiPsPjPsC‡PëCḡC,PμC—PSPμPjC-Cḡ C,P° P°PSC,PëC,C-P»P° PrPs C,,PsCḡC,,PsP»C-PiC-PrC-PI (P°PSC,PëC,C-P»P° PrPs PeP°CḡPrC-PsP»C-PiC-PSC-PI, PIPsPIC‡P°PePsPIPëPNḡ P°PSC,PëPePsP°PiCḡP»CḡPSC,);

o PjC-PiCḡPμPSCḡ C-P· PIPsPiPSPëC%PμPIPëPjPë PSPμPICḡPsP»PsPiC-C‡PSPëPjPë CḡPēPjPīC,PSPjP°PjPë PI P°PSP°PjPSPμP·C-;

o PIPëCḡPsPePëPNḡ CḡPēP·PëPe PḡPḡP· C‡PμCḡPμP· PSP°CḡIPSC-CḡC,CH PjPSPsPḡPëPSPSPëC... C,,P°PeC,PSCḡC-PI CḡPēP·PëPeCḡ (PrPëPI. CḡPsP·PrC-P» B«PhCḡPsP±P»PëPIPsCḡC,C- P·P°CḡC,PSCḡCḡPIP°PSPSCḡB») P°P±Ps C‡PμCḡPμP· PSP°CḡIPSC-CḡC,CH PsPrPSPsPiPs CḡPμCḡPNḡPsP·PSPsPiPs C,,P°PeC,PSCḡP° CḡPēP·PëPeCḡ, C,P°PePsPiPs CḡPe:

- C‡CḡPeCḡPsPIPëPNḡ PrC-P°P±PμC, C-P· CḡCḡPrPëPSPSPëPjPë CḡCḡPeP»P°PrPSPμPSPSCḡPjPë;

- C,CḡPḡPeP° P°CḡC,PμCḡC-P°P»CHPSP° PiC-PīPμCḡC,PμPSP·C-Cḡ;

- C,CḡPḡPeP° PrPëCḡP»C-PiPsPiCḡPsC,PμC—PSPμPjC-Cḡ.

B· PḡP°CḡIPSC-CḡC,CH C,CḡPḡPePsPiPs P·P°C...PIPsCḡCḡPIP°PSPSCḡ PīPμC‡C-PSPëPë PSP° PrP°PSPëPNḡ C‡P°Cḡ P°P±Ps PI P°PSP°PjPSPμP·C-, PīPsPePë PīPsPeP°P·PSPëPePë C,,CḡPSPëC‡C-C— PīPμC‡C-PSPëPë PSPμ PīPsPIPμCḡPSCḡP»PëCḡCḡ Cḡ PjPμPḡC- PSPsCḡPjPë.

B· PḡP°CḡIPSPëPNḡ CḡP°Pe PjPsP»PsC‡PSPsC— P·P°P»PsP·Pë PīPsC,PSC‡PSPëPNḡ P°P±Ps PI P°PSP°PjPSPμP·C-, CḡPePëPNḡ PjPsPḡPμ P±CḡC,Pë PiPsCḡPjPsPSPsC‡CḡC,P»PëPIPëPj (PrPëPI. CḡPsP·PrC-P» B«PhCḡPsP±P»PëPIPsCḡC,C- P·P°CḡC,PSCḡCḡPIP°PSPSCḡB»), PiC-PrCḡPsP·PrC-P» B«P—P»PsCḡPeC-CḡPSC- PSPsPIPsCḡC,PIPsCḡPμPSPSCḡB»).

B· PḡPëCḡPePsPIP° PSPμPrPsCḡC,P°C,PSC-CḡC,CH C,CḡPḡPePsPiPs CḡC,CḡPīPμPSCḡ P°P±Ps PiPsCḡC,CḡP° PSPëCḡPePsPIP° PSPμPrPsCḡC,P°C,PSC-CḡC,CH.

B· PḡP°CḡIPSC-CḡC,CH PīCḡC...P»PëPS PīPμC‡C-PSPëPë PSP° PrP°PSPëPNḡ C‡P°Cḡ P°P±Ps PI P°PSP°PjPSPμP·C- (PrPsP±CḡPsCḡPeC-CḡPSPëC... P°P±Ps P·P»PsCḡPeC-CḡPSPëC...).

B· P' C-PrPsPjC- P°P±Ps PiC-PrPsP·CḡCḡPIP°PSC- P·P»PsCḡPeC-CḡPSC- PīCḡC...P»PëPSPë (PSP°PīCḡPēPeP»P°Pr, CḡC,P°C,PμPIPëC... PsCḡPiP°PSC-PI), C%Ps C'' P·P°P»PμPḡPSPëPjPë PIC-Pr CḡC,P°C,PμPIPëC... PiPsCḡPjPsPSC-PI.

B· P'P°PiC-PSP°P»CHPSP° PeCḡPsPIPsC,PμC‡P° PSPμP·Ḃḡ™ CḡCḡPsPIP°PSPsC— PμC,C-PsP»PsPiC-C—.

В· РµС-РrPIPëC%PµPSP° C±CfC,P»PëPIC-ClC,CH PrPs PrC-CHC±PëC...
CтPµC±PsPIPëPS P°P±Ps PrPs P±CfPrCH-ClPePsPiPs P· PePsPjPiPsPSPµPSC,C-PI
PiCтPµPiP°CтP°C,Cf.

P>C-PeP°CтClCтCHPePëPNë P·P°ClC-P± P'C-PrPsCтP° PjC-PeCтPs
PiCтPsC,PëPiPsPeP°P·P°PSPëPNë PiCтPë PsPrPSPSc±P°ClPSPsPjCf P·P°ClC,PsClCfPIP°PSPSC- P·
P»C-PeP°CтClCтCHPePëPjPë P·P°ClPsP±P°PjPë, C%Ps PjC-ClC,ClC,CH
PsPjP±C-C,P°ClPIC-Cт/PiP°CтPëC,P°PiCтPµPIC-Cт/CтPëC,PsPSP°PIC-Cт C,P°
PrP°cP°P±CfPIC-Cт P°P±Ps P»C-PeP°CтClCтCHPePëPjPë P·P°ClPsP±P°PjPë, C%Ps
PjC-ClC,ClC,CH PiP»PµPeP°PiCтPµPIC-Cт/PiC-P±CтPµPSC,P°ClPIC-Cт P°P±Ps
ClPsC,,PsClP±CfPIC-Cт/PIPµP»PiP°C,P°ClPIC-Cт/PIPsPeClC-P»P°PiCтPµPIC-Cт (PrPëPI.
CтPsP·PrC-P» B«P'P·P°C"PjPsPrC-Cl P· C-PSCëPëPjPë P»C-PeP°CтClCтCHPePëPjPë
P·P°ClPsP±P°PjPë C,P° C-PSCëC- PIPëPrPë PIP·P°C"PjPsPrC-PNëB»).

***P'P·P°C"PjPsPrC-Cl P· C-PSCëPëPjPë P»C-PeP°CтClCтCHPePëPjPë
P·P°ClPsP±P°PjPë C,P° C-PSCëC- PIPëPrPë PIP·P°C"PjPsPrC-PNë.***

PŸP»C-Pr PsP·PSP°PNëPsPjPëC,PëClCl P· C-PSC,,PsCтPjP°C†C-C"CH C%PsPrPs
P»C-PeP°CтClCтCHPePsPiPs P·P°ClPsP±Cf, C%Ps P·P°ClC,PsClPsPICfC"C,CHClCl
PsPrPSPSc±P°ClPSPs, PrP»Cl PIPëClPIP»PµPSPSC PiPsC,PµPSC†C-PNëPSPëC...
PIP·P°C"PjPsPrC-PNë.

- P'PiP»PëPI C-PSCëPëC... P»C-PeP°CтClCтCHPePëC... P·P°ClPsP±C-PI PSP°
PiCтPµPiP°CтP°C, P'C-PrPsCтP° PjC-PeCтPs

P'P·P°C"PjPsPrC-C— PjPsP¶P»PëPIC- P· P»C-PeP°CтClCтCHPePëPjPë P·P°ClPsP±P°PjPë, C%Ps
C-PSPrCfPeCfCH,CH PjC-PeCтPsClPsPjP°P»CHPSC- C,,PµCтPjPµPSC,Pë. PiPµ
PiCтPëP·PIPµPrPµ PrPs P·P±C-P»CHCëPµPSPSC PiP»C-CтPµPSCfCf ClC,P°C,PµPIPëC...
PiPsCтPjPsPSC-PI, C%Ps P·C- ClPIPsPiPs P±PsPeCf ClPiCтPëC±PëPSClC" P·PjC-PSPë
C...P°CтP°PeC,PµCтCf PjPµPSCfC,CтCfP°P»CHPSPSc— PeCтPsPIPsC,PµC±C- C,P°/P°P±Ps
PIC,CтP°C,Pë PµC,,PµPeC,PëPIPsPSCfC,C- PePsPSC,CтP°C†PµPiC,PëPICf.

PŸPµCтP°PiC-Cl

P†PSPrCfPeC†C-Cl C,,PµCтPjPµPSC,C-PI PjPsP¶Pµ P±CfC,Pë PIPëClPIP»PµPSP° C±PµCтPµP·
PrPµPeC-P»CHPeP° PrPSC-PI P»C-PeCfPIP°PSPSCl. PëP°PeClPëPjP°P»CHPSP°
C-PSPrCfPeC†C-Cl C,,PµCтPjPµPSC,C-PI P·P°PiP°P»PsPj ClPiPsClC,PµCтC-PiP°C"C,CHClCl
C±PµCтPµP· PrPµPeC-P»CHPeP° C,PëP¶PSC-PI. PµC-ClP»Cl PIC-PrPjC-PSPë
P»C-PeCfPIP°PSPSCl C-PSPrCfPeC†C-Cl C,,PµCтPjPµPSC,C-PI PjPsP¶Pµ C,CтPëPIP°C,Pë
PiCтPëP±P»PëP·PSPs 4 C,PëP¶PSC-.

PµPsCтPsC,PePsClC,CтPsPePsPIPµ P»C-PeCáPIP°PSPSCl

P-C-PSPePë, ClPeC- PiCтPëPNëPjP°CHC,CH P»C-PeP°CтClCтCHPeC- P·P°ClPsP±Pë, C%Ps
C-PSPrCfPeCfCH,CH C,,PµCтPjPµPSC,Pë, PiPsPIPëPSPSC- C,PëPjC±P°ClPsPIPs
PIPëPePsCтPëClC,PsPICfPIP°C,Pë P±P°CтBт™C"CтPSPëPNë PjPµC,PsPr P°P±Ps C-PSCëPëPNë
PjPµC,PsPr PePsPSC,CтP°C†PµPiC†C— PrPsPrP°C,PePsPIPs PrPs PePsPjP±C-PSPsPIP°PSPëC...
PsCтP°P»CHPSPëC... PePsPSC,CтP°C†PµPiC,PëPIC-PI. P'P°CтBт™C"CтPSPëPNë PjPµC,PsPr
ClP»C-Pr PIPëPePsCтPëClC,PsPICfPIP°C,Pë PiCтPsC,ClPiPsPj CfClCHPsPiPs C,PµCтPjC-PSCf
P»C-PeCfPIP°PSPSCl PIC-PrPiPsPIC-PrPSPëPj PiCтPµPiP°CтP°C,PsPj C- C%Pµ

PŷPsPjCr PrP»CŬ PIPëCŬPIP»PµPSPSCŬ PiPsC,PµPSC†C-PNëPSPëC... PIP·P°C”PjPsPrC-PNë C,P°
 P±CrPrCH-ClPePëC... C-PSCëPëC... CŬPµPePsPjPµPSPPrP°C†C-PNë CŬP»C-Pr
 PsP·PSP°PNëPsPjPëC,PëCŬCŬ P· C-PSC,,PsCŬPjP°C†C-C”CŬ C%oPsPrPs PjPµPrPëC†PSPsPiPs
 P·P°CŬC,PscŬCŬPIP°PSPSCŬ P»C-PeP°CŬCŬCHPePsPiPs P·P°CŬPsP±Cr PrP»CŬ
 P»C-PeCrPIP°PSPSCŬ P’P†P>/P’P“Pŷ, C%oPs PiCŬPëPNëPjP°C”C,CHCŬCŬ PsPrPSPsC†P°CŬPSPs.
 Pj CŬP°P·C- PSP°CŬPIPSsCŬCŬ, C- P±CrPrCH-ClPePëC... CŬCŬPjPSC-PIC-PI PŬC-PSPeP°Pj
 PrPsPrP°C,PePsPIPs CŬP»C-Pr PIPëPePsCŬPëCŬCŬ,PsPICŬPIP°C,Pë P±P°CŬBŬ™C”CŬPSPëPNë
 PjPµC,PsPr PePsPSC,CŬP°C†PµPiC†C-C— PiCŬPë C,PµCŬP°PiC-C— C-PSPiC-P±C-C,PsCŬP°PjPë

РiСҗPsC,РµР°Р·Рё Р°Р±Ps C-PSiC-Р±C-C,PsСҗР°РјРё PSpµPSCrPeP»РµPsP·РёРrPSPsC—
Р·PIPсСҗPsC,PSPsC— C,СҗР°PSCrPeСҗРёРiC,Р°Р·Рё.

*P''C-СҗC±C- СҗРµC±PsPIPёPSPё, C%Ps P·PSPёP¶CзСҗC,Сҗ PeP»C-СҗРµPSCr РёРёPё
(C-PSiC-Р±C-C,PsСҗРё C,,РµСҗРјРµPSC,C-PI)*

РёР»Р»C-PSC-C±PSP° Р·PSP°C±CfC%C-СҗC,Сҗ PiPsC,РµPSC+C-PNёPSPsC— PIP·Р°C''РјPsPrC-C—
Р· C-PSiC-Р±C-C,PsСҗР°РјРё C,,РµСҗРјРµPSC,C-PI Р·Р°Р»»РёCёР°C''C,СҗCҗCҗ
PSPµP·Бҗ™ CҗCҗPsPIP°PSPsСҗ.

РёРrPSPsC±P°CҗPSPµ Р·Р°CҗC,PsCҗCҗPIP°PSPSCҗ CҗРёP»СҗPSPёC...
C-PSiC-Р±C-C,PsСҗC-PI CYP3A4 РјPsP¶Рµ PiC-PrPIPёC%PёC,Рё PiP»Р°Р·РјPsPIC-
PePsPSC+РµPSC,СҗР°C+C-C— РµCҗC,СҗPsPiРµPSCr Р°Р±Ps PiСҗPsPiРµCҗC,РёPSCr, Р°Р±Ps
PsP±PsC... PePsРјPiPsPSPµPSC,C-PI.

PJ PrPsCҗP»C-PrP¶РµPSPSC- Р±Р°РјР°C,PsСҗР°Р·PsPIPёC... PrPsP· PePsРјР±C-PSP°C+C-C—
PrСҗPsCҗPiC-СҗРµPSPs (3 РјPi/PrPsP±Cҗ)/РµC,РёPSC-Р»РµCҗC,СҗР°PrC-PsP»
(0,002 РјPi/PrPsP±Cҗ) C,Р° CҗРёP»СҗPSPsPiPs C-PSiC-Р±C-C,PsСҗР° CYP3A4
PeРµC,PsPePsPSP°Р·PsP»Cҗ, C%Ps Р·Р°CҗC,PsCҗPsPICrPIP°PICҗCҗ PsPrPSPsC±P°CҗPSPs,
PiСҗPsC,СҗPiPsРј 10 PrPSC-PI Р·Р±C-Р»СҗCёCҗPIP°P»PsCҗCҗ Р·PSP°C±РµPSPSCҗ AUC_(0-24h)
PrСҗPsCҗPiC-СҗРµPSPsPSCr C,Р° РµC,РёPSC-Р»РµCҗC,СҗР°PrC-PsP»Cҗ Cҗ
2,7 C,Р° 1,4 СҗР°Р°Р° PIC-PrPiPsPIC-PrPSPs.

Р·C,PsСҗРёPePsPeCҗРёP± Cҗ PrPsP°C... PIC-Pr 60 PrPs 120 РјPi/PrPsP±Cҗ
PiСҗPsPrРµРјPSPSCҗC,СҗCҗPIP°PI PiC-PrPIPёC%РµPSPSCҗ PiP»Р°Р·РјPsPIPёC...
PePsPSC+РµPSC,СҗР°C+C-PNё РµC,РёPSC-Р»РµCҗC,СҗР°PrC-PsP»Cҗ Cҗ 1,4-1,6 СҗР°Р°Р°
PIC-PrPiPsPIC-PrPSPs PiСҗРё PsPrPSPsC±P°CҗPSPsРјCҗ Р·Р°CҗC,PsCҗCҗPIP°PSPSC- Р· РёР»Р»PёPё,
C%Ps РјC-СҗC,РёC,Сҗ 0,035 РјPi РµC,РёPSC-Р»РµCҗC,СҗР°PrC-PsP»Cҗ.

- Р·PiP»РёPI PiСҗРµPiР°СҗР°C,Сҗ Р·C-PrPsСҗР° РјC-PeСҗPs PSP° C-PSCёC-
Р»C-PeР°СҗCҗСҗPeC- Р·Р°CҗPsP±Pё

РёРёPё РјPsP¶CҗC,Сҗ PIPiP»РёPIP°C,Рё PSP° РјРµC,Р°Р±PsP»C-Р·Рј CҗPePёC...
PrC-СҗC±PёC... СҗРµC±PsPIPёPS. Р·C-PrPiPsPIC-PrPSPs, PePsPSC+РµPSC,СҗР°C+C-C— Cҗ
PiP»Р°Р·РјC- PeСҗPsPIC- C,Р° Cҗ C,PeР°PSPёPSP°C... РјPsP¶CҗC,Сҗ Р°Р±Ps
PiC-PrPIPёC%CҗPIP°C,РёCҗCҗ (PSP°PiСҗРёPeP»Р°Рr, CҗРёPeP»PsCҗPiPsСҗРёPS), Р°Р±Ps
Р·PSPёP¶CҗPIP°C,РёCҗCҗ (PSP°PiСҗРёPeP»Р°Рr, Р»Р°РјPsC,СҗРёРrP¶PёPS).

РёР°Р° PiC-PrCҗC,Р°PIC- PrPsCҗP»C-PrP¶РµPSCҗ PIP·Р°C''РјPsPrC-C— *in vivo* Cҗ P¶C-PSPsPe-
PrPsP±СҗPsPIPsP»СҗC+C-PI, CҗPeC- Р·Р°CҗC,PsCҗPsPICrPIP°P»Рё PsРјPiСҗР°Р·PsP»,
CҗРёРјPIP°CҗC,Р°C,РёPS C,Р° РјC-PrР°Р·PsP»Р°Рј CҗPe CҗCҗCҗC,СҗР°C,Рё-РјР°СҗРµРµCҗРё,
PICҗC,Р°PSPsPIPsPSPs, C%Ps PeP»C-PSC-C±PSPs Р·PSP°C±CfC%Р° PIP·Р°C''РјPsPrC-Cҗ
PrСҗPsCҗPiC-СҗРµPSPsPSCr PI PrPsP·C- 3 РјPi Р· C-PSCёРёРјРё Р°PeC,РёPIPSёРјРё
CҗCҗCҗC,Р°PSC+C-CҗРјРё, C%Ps C-PSPrCҗPeCҗСҗC,СҗCҗCҗ CҗРёC,PsC...СҗPsРјPsРј P 450,
РјР°P»PsPNёРјPsPIC-СҗPSP°.

РёР»Р»C-PSC-C±PSC- PrР°PSC- CҗPIC-PrC±Р°C,Сҗ PiСҗPs C,Рµ, C%Ps
РµC,РёPSC-Р»РµCҗC,СҗР°PrC-PsP» PiСҗРёPiPSC-C±CҗC'' PeP»C-СҗРµPSCr
CҗCҗCҗC,СҗР°C,C-PI CYP1A2, C%Ps Р·C- CҗPiPsPiPs P±PsPeCҗ PIPёPeP»РёPeР°C''
CҗP»Р°Р±PeРµ (PSP°PiСҗРёPeP»Р°Рr, C,РµPsC,,C-Р»C-PS) Р°Р±Ps PiPsРјC-СҗPSPµ
(PSP°PiСҗРёPeP»Р°Рr, C,РёР·Р°PSC-PrPёPS) PiC-PrPIPёC%РµPSPSCҗ C—C...
PiP»Р°Р·РјPsPIPёC... PePsPSC+РµPSC,СҗР°C+C-PNё.

$$P \rightarrow P^0 P^\pm P_s C \bar{H} P^0 C, P_s C \bar{H} P S C - P^0 P S P^0 P \gg C - P \cdot P \ddot{e}$$

P—P°CÍC,PsCÍCÍPIP°PSPSCÍ PePsPSC,ЧҗP°C†PµPİC,PëPIPSPëC... CÍC,PµЧҗPsC—PrC-PI
PjPsP¶Pµ PİPİP»PëPIP°C,Pë PSP° ЧҗPµP·C†P»ЧҗC,P°C,Pë PrPµCІPеPëC...
P»P°P±PsCҗP°C,PsCҗPSPëC... P°PSP°P»C-P·C-PI, C,P°PePëC... CІPе P±C-PsC...C-PjC-C†PSC-
PİP°CҗP°PjPµC,ЧҗPë C,,C†PSPeC†C-C— PİPµC†C-PSPePë, C%PsC,PsPIPëPrPSPsC— P·P°P»PsP·Pë,
PSP°PrPSPëCҗPePsPIPëC... P·P°P»PsP·C- PSPëCҗPsPe, PSP° PePsPSC†PµPSC,ЧҗP°C†C-Чҗ C†
PİP»P°P·PjC- C,ЧҗP°PSCÍPİPsCҗC,PSPëC... P±C-P»PeC-PI, C,P°PePëC... CІPе
PİP»PsP±C†P»C-PS, C%Ps P·PIвҗ™ CІP·C†C” PePsCҗC,PëPePsCÍC,PµЧҗPsC—PrPë, PSP°
PePsPSC†PµPSC,ЧҗP°C†C-Чҗ C† PİP»P°P·PjC- PeCҗPsPIC- C,,ЧҗP°PeC†C-PNë
P»C-PİC-PrC-PI/P»C-PİPsPİCҗPsC,PµC—PSC-PI, PSP° PİPsPeP°P·PSPëPePë
PIC†PİP»PµPIPsPrPSPsPİPs PsP±PjC-PSC†, PePsP°PiC†P»CІC†C-C— C,P°
C,,C-P±CҗPëPSPsP»C-P·C†. P—P°P·PIPëC†P°PNë C,P°PeC- P·PjC-PSPë PİPµCҗPµP±C†PIP°CҗC,Чҗ
C† PjPµP¶P°C... PSPsCҗPjPë. P”CҗPsCÍPİC-ЧҗPµPSPsPS P·P±C-P»ЧҗC€C†C”
P°PeC,PëPIPSC-CÍC,Чҗ ЧҗPµPSC-PSC† C,P° P°P»ЧҗPrPsCÍC,PµЧҗPsPSC† C† PİP»P°P·PjC-
PeCҗPsPIC-, C%Ps C-PSPrC†PeC†C”C,ЧҗCÍCІ PNëPsPİPs PİPsPjC-ЧҗPSPsCҗ
P°PSC,PëPjC-PSPµЧҗP°P»PsPePsCҗC,PëPePsC—PrPSPsCҗ P°PeC,PëPIPSC-CÍC,Чҗ.

PhCÍPsP±P»PëPIPsCÍC,C- P·P°CÍC,PsCÍC¿PIP°PSPSCІ.

P C-C€PµPSPSCІ PİCҗPs PİCҗPëP·PSP°C†PµPSPSCІ PİCҗPµPİP°CҗP°C,C† P’C-PrPsCҗP°
PjC-PeCҗPs CÍP»C-Pr PİCҗPëPNëPjP°C,Pë P· C†CҗP°C...C†PIP°PSPSCІPj
C-PSPrPëPIC-PrC†P°P»ЧҗPSPëC... C,,P°PeC,PsCҗC-PI ЧҗPëP·PëPeC† P¶C-PSPePë, C%Ps
C-C†PSC†CҗC,Чҗ PSP° PrP°PSPëPNë PjPsPjPµPSC,, C† C,PsPjC† C†PëCÍP»C- C,,P°PeC,PsCҗC-PI
ЧҗPëP·PëPeC† ЧҗPsP·PIPëC,PeC† P’PŸP·, P° C,P°PePsP¶ ЧҗPëP·PëPeC† P’PŸP·,
PİPsPIвҗ™ CІP·P°PSPsPİPs P· PİCҗPëPNëPsPjPsPj PİCҗPµPİP°CҗP°C,C† P’C-PrPsCҗP°
PjC-PeCҗPs, PİPsCҗC-PIPSCІPSPs P· C-PSC€PëPjPë PљP”Pљ (PrPëPI. ЧҗPsP·PrC-P»Pë
B«PµЧҗPsC,PëPİPsPeP°P·P°PSPSCІB» C,P° B«PhCÍPsP±P»PëPIPsCÍC,C-
P·P°CÍC,PsCÍCÍPIP°PSPSCІB»).

PµPsPİPµЧҗPµPrP¶PµPSPSCІ

PµЧҗPë PSP°CІPIPSPsCÍC,C- P±C†PrCҗC-ІPеPëC... CÍC,P°PSC-PI P°P±Ps C,,P°PeC,PsCҗC-PI
ЧҗPëP·PëPeC†, P·P°P·PSP°C†PµPSPëC... PSPëP¶C†Pµ, CÍP»C-Pr PsP±PİPsPIPsCҗPëC,Pë P·
P¶C-PSPePsCҗ PrPsC†C-P»ЧҗPSC-CÍC,Чҗ P·P°CÍC,PsCÍCÍPIP°PSPSCІ PİCҗPµPİP°CҗP°C,C†
P’C-PrPsCҗP° PjC-PeCҗPs.

Pj ЧҗP°P·C- P·P°PİPsCÍC,ЧҗPµPSPSCІ P°P±Ps PİCҗPë PİPµCҗC€PëC... PİCҗPsCІPIP°C...
P±C†PrCҗC-ІPеPëC... C-P· PİPeP°P·P°PSPëC... CÍC,P°PSC-PI P°P±Ps C,,P°PeC,PsCҗC-PI
ЧҗPëP·PëPeC† P¶C-PSPeP°Pj ЧҗPµPePsPjPµPSPrC†C”C,ЧҗCÍCІ P·PIPµCҗPSC†C,PëCÍCІ PrPs
P»C-PeP°CҗCІ C,P° PİPëP·PSP°C†PëC,Pë PSPµPsP±C...C-PrPSC-CÍC,Чҗ
PİCҗPëPİPëPSPµPSPSCІ PİCҗPëPNëPsPjC† PİCҗPµPİP°CҗP°C,C† P’C-PrPsCҗP° PjC-PeCҗPs.

Pj ЧҗP°P·C- PİC-PrPsP·CҗCҗPIP°PSPsC— P°P±Ps PİC-PrC,PIPµЧҗPrP¶PµPSPsC— P’PŸP· P°P±Ps
PђPŸP· CÍP»C-Pr PİCҗPëPİPëPSPëC,Pë P·P°CÍC,PsCÍCÍPIP°PSPSCІ PљP”Pљ. PİPeC%Ps
ЧҗPsP·PİPsC†P°C,P° P°PSC,PëPePsP°PiC†P»CІPSC,PSP° C,PµЧҗP°PİC-CІ, CÍP»C-Pr
P·P°P±PµP·PİPµC†PëC,Pë P°P»ЧҗC,PµЧҗPSP°C,PëPIPSC† P°PrPµPePIP°C,PSC†
PePsPSC,ЧҗP°C†PµPİC†C-Чҗ C†PµЧҗPµP· C,PµЧҗP°C,PsPİPµPSPSPëPNë PİPİP»PëPI
P°PSC,PëPePsP°PiC†P»CІPSC,C-PI (PeC†PjP°CҗPëPSPë).

- PİPëCҗPeC†P»CІC,PsCҗPSC- ЧҗPsP·P»P°PrPë

P PëP·PëPe CĤPsP·PIPëC,PeCf P'PŷP•

P—P°CfC,PsCfCfPIP°PSPSCĬ P±CfPrCHb-CĬPePëC... PĽP“PĽ PĭC-PrPIPëC%oCfC” CĤPëP·PëPe CĤPsP·PIPëC,PeCf PIPμPSPsP·PSPsC— C,CĤPsPjP±PsPμPjP±PsP»C-C— (P'PŷP•) Cf PĬC-PSPsPe, CĬPeC- C—C... P·P°CfC,PsCfPsPICfCĤC,CH, PĭPsCĤC-PIPSCĬPSPs P· C,PëPjPë, CĬPeC- C—C... PSPμ P·P°CfC,PsCfPsPICfCĤC,CH. **PμCĤPμPĭP°CĤP°C,Pë, C%oPs PjC-CfC,CĬC,CH P»PμPIPSPSPsCĤPiPμCfC,CĤPμP», PSPsCĤPiPμCfC,PëPjP°C, P°P±Ps PSPsCĤPμC,PëCfC,PμCĤPsPS, P°CfPsC†C-CĤCĤC,CHCfCĬ P· PSPëPĬC±PëPj CĤPëP·PëPePsPj P'PŷP•. P—P°CfC,PsCfCfPIP°PSPSCĬ C-PSCëPëC... P»C-PëP°CĤCfCHPePëC... P·P°CfPsP±C-PI, C,P°PePëC... CĬPe P'C-PrPsCĤP° PjC-PëCĤPs, PjPsPĬPμ PĭCĤPëP·PIPsPrPëC,Pë PrPs PĭC-PrPIPëC%oPμPSPSCĬ CĤPëP·PëPeCf CfPrPIC-C†C-. P C-CëPμPSPSCĬ PĭCĤPs P·P°CfC,PsCfCfPIP°PSPSCĬ PĭCĤPμPĭP°CĤP°C,C-PI, PsPeCĤC-Pj C,PëC..., C%oPs PjP°CĤC,CH PSP°PNëPSPëPĬC±PëPNë CĤPëP·PëPe CĤPsP·PIPëC,PeCf P'PŷP•, CfP»C-Pr PĭCĤPëPNëPjP°C,Pë P»PëCëPμ PĭC-CfP»CĬ PsP±PiPsPIPsCĤPμPSPSCĬ P· PĬC-PSPëPsCĤ. PkPμPsP±C...C-PrPSPs PĭPμCĤPμPePsPSP°C,PëCfCĬ, C%oPs PIPsPSP° CfCfPIC-PrPsPjP»CĤC” CĤPëP·PëPe CĤPsP·PIPëC,PeCf P'PŷP•, P°CfPsC†C-PNëPsPIP°PSPëPNë C-P· P·P°CfC,PsCfCfPIP°PSPSCĬPj PĭCĤPμPĭP°CĤP°C,Cf P'C-PrPsCĤP° PjC-PëCĤPs, CfC,CfPĭC-PSCĤ PIPĭP»PëPICf PSP°CĬPIPSPëC... Cf PSPμC— C„P°PeC,PsCĤC-PI CĤPëP·PëPeCf C,P° C,PsPNë C„P°PeC,, C%oPs CĤPëP·PëPe P'PŷP• C” PSP°PNëPIPëC%oPëPj PĭCĤPsC,CĬPiPsPj PĭPμCĤCëPsPiPs CĤPsPeCf P·P°CfC,PsCfCfPIP°PSPSCĬ. P—P° PrPμCĬPePëPjPë PrP°PSPëPjPë CĤPëP·PëPe P'PŷP• PjPsPĬPμ P·CĤPsCfC,P°C,Pë PĭCĤPë PIC-PrPSPsPIP»PμPSPSC- P·P°CfC,PsCfCfPIP°PSPSCĬ PĽP“PĽ PĭC-CfP»CĬ PĭPμCĤPμCĤPIPë Cf 4 C,PëPĬPSC- P°P±Ps PrPsPICëPμ.**

Pj PrPIPsC... C-P· 10 000 PĬC-PSPsPe, CĬPeC- PSPμ PĭCĤPëPNëPjP°CĤC,CH PĽP“PĽ C,P° PSPμ C” PIP°PiC-C,PSPëPjPë, CĤPsP·PIPëPIP°C”C,CHCfCĬ P'PŷP• PĭCĤPsC,CĬPiPsPj CĤPsPeCf. PĥPrPSP°Pe Cf PePsPĬPSPsC— PsPeCĤPμPjPsC— PĬC-PSPëPë CĤPëP·PëPe PjPsPĬPμ P±CfC,Pë P·PSP°C†PSPs PIPëC%oPëPNë P·P°P»PμPĬPSPs PIC-Pr PSP°CĬPIPSPëC... Cf PSPμC— C„P°PeC,PsCĤC-PI CĤPëP·PëPeCf (PrPëPI. PSPëPĬC±Pμ).

P'CfC,P°PSPsPIP»PμPSPs¹, C%oPs C-P· 10 000 PĬC-PSPsPe, CĬPeC- P·P°CfC,PsCfPsPICfCĤC,CH PĽP“PĽ, C%oPs PjC-CfC,CĬC,CH PrCĤPsCfPĭC-CĤPμPSPsPS, Cf 9-12 PĬC-PSPsPe CĤPsP·PIPëPSPμC,CHCfCĬ P'PŷP• PĭCĤPsC,CĬPiPsPj PsPrPSPsPiPs CĤPsPeCf. PĭPμ PĭPsCĤC-PIPSCĤC”C,CHCfCĬ P· PĭPsPeP°P·PSPëPePsPj 6² Cf PĬC-PSPsPe, CĬPeC- P·P°CfC,PsCfPsPICfCĤC,CH PĽP“PĽ, C%oPs PjC-CfC,CĬC,CH P»PμPIPSPSPsCĤPiPμCfC,CĤPμP».

P' PsP±PsC... PIPëPĭP°PrPeP°C... PeC-P»CHPeC-CfC,CH PIPëPĭP°PrPeC-PI P'PŷP• P·P° CĤC-Pe P±CfP»P° PjPμPSCëPsCĤ, PSC-PĬ P·P°P·PIPëC†P°PNë PsC†C-PëCfC”C,CHCfCĬ PĭCĤPsC,CĬPiPsPj PIP°PiC-C,PSPsCfC,C- P°P±Ps Cf PĭC-CfP»CĬPiPsP»PsPiPsPIPsPjCf PĭPμCĤC-PsPrC-.

P'PŷP• PjPsPĬPμ PĭCĤPëP·PIPsPrPëC,Pë PrPs P»PμC,P°P»CHPSPëC... PSP°CfP»C-PrPeC-PI Cf 1-2 % PIPëPĭP°PrPeC-PI.

PĽC-P»CHPeC-CfC,CH PIPëPĭP°PrPeC-PI P'PŷP• PSP° 10 000 PĬC-PSPsPe P·P° PsPrPëPS CĤC-Pe

¹ P₁C- P_iPsPeP°P·PSPëPePë PsC, C₇PëPjP°PSPs PSP° PsC₇PSPsPIC- PIC₇C-C... PrP°PSPëC... P_μPiC-PrP_μPjC-PsP»PsPiC-C₇PSPëC... PrPsC₇P»C-PrP_μPSCH P· CrC₇P°C...C₇PIP°PSPSC₇Pj PIC-PrPSPsC₇PSPëC... C₇PëP·PëPeC-PI, P_iPsPIB₇™ C₇P·P°PSPëC... C-P· PiC₇PëPN₇PsPjPsPj C₇C-P·PSPëC... P₇P“P₇, P_iPsC₇C-PIPS₇C₇Ps C-P· P·P°C₇C,PsC₇C₇PIP°PSPSC₇Pj P₇P“P₇, C%Ps PjC-C₇C,C₇C,CH P»P_μPIPsPSPsC₇PiP_μC₇C,C₇P_μP».

² Pj C₇P_μC₇P_μPrPSC₇PsPjC₇ 5-7 PIPëPiP°PrPeC-PI PSP° 10 000 P_μC-PSPePs-C₇PsPeC-PI PSP° PsC₇PSPsPIC- C₇PsP·C₇P°C...C₇PSPeC₇ PIC-PrPSPsC₇PSPsPiPs C₇PëP·PëPeC₇ P·P°C₇C,PsC₇C₇PIP°PSPSC₇ P₇P“P₇, C%Ps PjC-C₇C,C₇C,CH P»P_μPIPsPSPsC₇PiP_μC₇C,C₇P_μP», P_iPsC₇C-PIPS₇C₇Ps P· C,P°PePëPj C₇ P_μC-PSPsPe, C₇PeC-PSP_μ P·P°C₇C,PsC₇PsPIC₇C₇C,CH P₇P“P₇ (PiC₇PëP±P»PëP·PSPs 2,3 - 3,6 PIPëPiP°PrPeC₇).

P_μP°PeC,PsC₇Pë C₇PëP·PëPeC₇ C₇PsP·PIPëC,PeC₇ P’P₇P•

P PëP·PëPe C₇PsP·PIPëC,PeC₇ PIP_μPSPsP·PSPëC... C,C₇PsPjP±PsP_μPjP±PsP»C-C₇PSPëC... C₇C₇PeP»P°PrPSP_μPSCH C₇ P_μC-PSPsPe, C₇PeC- P·P°C₇C,PsC₇PsPIC₇C₇C,CH P₇P“P₇, PjPsP_μP_μ P±C₇C,Pë P·PSP°C₇PSPs PIPëC%PëPN₇ PiC₇Pë PSP°C₇PIPSPsC₇C,C- PrPsPrP°C,PePsPIPëC... C,,P°PeC,PsC₇C-PI C₇PëP·PëPeC₇, PsC₇PsP±P»PëPIPs PjPSPsP_μPëPSPSPëC...

(PrPëPI. C,P°P±P»PëC₇C₇ 1).

P—P°C₇C,PsC₇C₇PIP°PSPSC₇ PiC₇P_μPiP°C₇P°C,C₇ P’C-PrPsC₇P° PjC-PeC₇Ps PiC₇PsC,PëPiPsPeP°P·P°PSP_μ P_μC-PSPeP°Pj C-P· PjPSPsP_μPëPSPSPëPjPë C,,P°PeC,PsC₇P°PjPë C₇PëP·PëPeC₇, C%Ps PjPsP_μP_μ PiC-PrPIPëC%PëC,Pë C₇PëP·PëPe C₇PsP·PIPëC,PeC₇ PIP_μPSPsP·PSPsPiPs C,C₇PsPjP±PsP·C₇ (PrPëPI. C₇PsP·PrC-P» B«P_μC₇PsC,PëPiPsPeP°P·P°PSPSC₇IB»). P_iPeC%Ps P_μC-PSPeP° PjP°C” P±C-P»CHC₇Pe_μ PsPrPSPsPiPs C,,P°PeC,PsC₇P° C₇PëP·PëPeC₇, P·C₇PsC₇C,P°PSPSC₇ C₇PëP·PëPeC₇ PjPsP_μP_μ P±C₇C,Pë P±C-P»CHC₇Pe_μPëPj, PSC-P_μ C₇C₇PjP° C₇PëP·PëPeC-PI, P°C₇PsC₇C-PN₇PsPIP°PSPëC... C-P· PePsP_μPSPëPj PsPeC₇P_μPjPëPj C,,P°PeC,PsC₇PsPj, C,PsPjC₇ C₇P»C-Pr PIC₇P°C...PsPIC₇PIP°C,Pë PrPs C₇PIP°PiPë P·P°PiP°P»CHPSPëPN₇ C₇PëP·PëPe C₇PsP·PIPëC,PeC₇ P’P₇P•. P_iPeC%Ps C₇PiC-PIPIC-PrPSPsC₇Pe_μPSPSC₇ PePsC₇PëC₇C,CH/C₇PëP·PëPe PSP_μC₇PiC₇PëC₇C,P»PëPIP_μ, PSP_μ C₇P»C-Pr PiC₇PëP·PSP°C₇P°C,Pë P₇P“P₇ (PrPëPI. C₇PsP·PrC-P» B«P_μC₇PsC,PëPiPsPeP°P·P°PSPSC₇IB»).

P₇P°P±P»PëC₇C₇ 1

P_μP°PeC,PsC₇Pë C₇PëP·PëPeC₇ C₇PsP·PIPëC,PeC₇ P’P₇P•

P_μP°PeC,PsC₇ C₇PëP·PëPeC₇
P_hP_μPëC₇C-PSPSC₇ (C-PSP_μPeC₇
PjP°C₇Pë C,C-P»P°
PiP_μC₇P_μPIPëC%CrC” 30 PePi/Pj²)

P_μC₇PëPjC-C,PeP°
P PëP·PëPe P·PSP°C₇PSPs
PiC-PrPIPëC%CrC”C,CHC₇C₇ PiC₇Pë
P·P±C-P»CHC₇Pe_μPSPSC- C-PSP_μPeC₇C₇ PjP°C₇Pë
C,C-P»P°.
P_hC₇PsP±P»PëPIPs PiPsC,C₇P_μP±C₇C” C₇PIP°PiPë
PiC₇Pë PSP°C₇PIPSPsC₇C,C- C-PSC₇PeC...
C,,P°PeC,PsC₇C-PI C₇PëP·PëPeC₇.

PŷCĤPĕPIP°P»P°
C-PjPjPsP±C-P»C-P·P°C†C-CĬ,
PIPμP»PĕPePμ PsPīPμCĤP°C,PĕPIPSPμ
PIC,CĤCfC±P°PSPSCĬ,
PsPīPμCĤP°C†C-CĬ PSP°
PSPĕP¶PSC-C... PeC-PSC†C-PIPeP°C...
P°P±Ps PsCĤPiP°PSP°C... C,P°P·P°,
PSPμPNĕCĤPsC...C-CĤCfCĤPiC-C±PSC-
PIC,CĤCfC±P°PSPSCĬ P°P±Ps
PsP±CĕPĕCĤPSP° C,CĤP°PIPjP°.

PμCĤPĕPjC-C,PeP°:
C,PĕPjC±P°C†PsPIP°
C-PjPjPsP±C-P»C-P·P°C†C-CĬ, Cf
C,PsPjCf C±PĕC†P»C-
PīPμCĤPμP»CHPsC,Pĕ > 4
PiPsPrPĕPS, C,P°PePsP¶
PjPsP¶CfC,CH P±CfC,Pĕ
C,,P°PeC,PsCĤPsPj CĤPĕP·PĕPeCf
CĤPsP·PIPĕC,PeCf P'PŷP·,
PsC†PsP±P»PĕPIPs Cf P¶C-PSPsPe P·
C-PSCĕPĕPjPĕ C,,P°PeC,PsCĤP°PjPĕ
CĤPĕP·PĕPeCf.
PŷC-PjPμPNĕPSPĕPNĕ P°PSP°PjPSPμP·
(P'PŷP· Cf PePsPiPsC†CH C-P·
CĤPsPrPĕC±C-PI P°P±Ps
P±P°C,CHPeC-PI, PsC†PsP±P»PĕPIPs
Cf PIC-PrPSPsC†PSPs
PjPsP»PsPrPsPjCf PIC-C†C-,
PSP°PiCĤPĕPeP»P°Pr, B Cf PIC-C†C-
PrPs 50 CĤPsPeC-PI).
P†PSCĕC- C†C,P°PSPĕ,
PīPsPIbĤ™ CĬP·P°PSC- P· P'PŷP·

P'C-Pe

Pj C,P°PePĕC... C†PĕC,CfP°C†C-CĬC...
CĤPμPePsPjPμPSPrCfC"C,CHC†CĬ
PīCĤPĕPīPĕPSPĕC,Pĕ P·P°C†C,PsC†CfPIP°PSPSCĬ
PīCĤPμPīP°CĤP°C,Cf (Cf CĤP°P·C- PīP»P°PSPsPiPs
PsPīPμCĤP°C,PĕPIPSPsPiPs PIC,CĤCfC±P°PSPSCĬ
C‰PsPSP°PNĕPjPμPSCĕPμ P·P° 4 C,PĕP¶PSC-) C,P°
PSPμ PIC-PrPSPsPIP»CĤPIP°C,Pĕ
P·P°C†C,PsC†CfPIP°PSPSCĬ CĤP°PSC-CĕPμ PSC-P¶
C±PμCĤPμP·B B B B B B B B 2 C,PĕP¶PSC-
PiC-C†P»CĬ PiPsPIPSPsPiPs PIC-PrPSPsPIP»PμPSPSCĬ
CĤCfC...PsPiPsC— P°PeC,PĕPIPSPsC†C,C-. P—
PjPμC,PsCĤ CfPSPĕPePSPμPSPSCĬ
PSPμP±P°P¶P°PSPsC— PIP°PiC-C,PSPsC†C,C-
C†P»C-Pr PIPĕPePsCĤPĕC†C,PsPICfPIP°C,Pĕ C-PSCĕC-
PjPμC,PsPrPĕ PePsPSC,CĤP°C†PμPiC†C-C—.

PŷP»C-Pr CĤPsP·PiP»CĬPSCfC,Pĕ
PrPsC†C-P»CHPSC-C†C,CH
P°PSC,PĕC,CĤPsPjP±PsC,PĕC±PSPsC—
C,PμCĤP°PiC-C—, CĬPeC‰Ps
P·P°C†C,PsC†CfPIP°PSPSCĬ PīCĤPμPīP°CĤP°C,Cf
P'C-PrPsCĤP° PjC-PeCĤPs PSPμ P±CfP»Ps
PīCĤPĕPīPĕPSPμPSPs PīPsPīPμCĤPμPrPSCĤPs.
Pj CĤP°P·C- PSP°CĬPIPSPsC†C,C-
C†PīP°PrPePsPiPsC— C†C...PĕP»CHPSPsC†C,C-
PīPμCĤPμPr P·P°C†C,PsC†CfPIP°PSPSCĬPj P±CfPrCH-
CĬPePĕC... PμP" Pμ P¶C-PSPeP°Pj
CĤPμPePsPjPμPSPrCfC"C,CHC†CĬ
PīPsCĤP°PrPĕC,PĕC†CĬ P·C-
C†PīPμC†C-P°P»C-C†C,PsPj.

P P°Pe, C†PĕC†C,PμPjPSPĕPNĕ C±PμCĤPIPSPSPĕPNĕ
PIPsPIC±P°Pe, PiPμPjPsP»C-C,PĕPePs-
CfCĤPμPjC-C±PSPĕPNĕ C†PĕPSPrCĤPsPj,
C...CĤPsPSC-C±PSPμ P·P°PīP°P»CHPSPμ
P·P°C...PIPsCĤCĤPIP°PSPSCĬ PePĕCĕPμC±PSPĕPeCf
(C...PIPsCĤPsP±P° PμCĤPsPSP° P°P±Ps
PIPĕCĤP°P·PePsPIPĕPNĕ PePsP»C-C,) C,P°
C†PμCĤPiPsPiPsPrC-P±PSPsPeP»C-C,PĕPSPSP°
P°PSPμPjC-CĬ.

PĤC†PsP±P»PĕPIPs Cf PIC-C†C- PīPsPSP°Pr 35
CĤPsPeC-PI

PkPμPjP°C" C"PrPĕPSPsC— PrCfPjPePĕ C‰PsPrPs PjPsP¶P»PĕPIPsPiPs PIPiP»PĕPICf
PIP°CĤPĕPePsP·PSPsPiPs CĤPsP·CĕPĕCĤPμPSPSCĬ PIPμPS C,P° PīPsPIPμCĤC...PSPμPIPsPiPs
C,CĤPsPjP±PsC,,P»PμP±C-C,Cf PSP°B CĤPsP·PIPĕC,PsPe C,P° PīCĤPsPiCĤPμC†CfPIP°PSPSCĬ
PIPμPSPsP·PSPsPiPs C,CĤPsPjP±PsP·Cf.

PkPμPsP±C...C-PrPSPs P·PIPμCĤPSCfC,Pĕ C†PIP°PiCf PSP° PiC-PrPIPĕC‰PμPSPĕPNĕ
CĤPĕP·PĕPe CĤPsP·PIPĕC,PeCf C,CĤPsPjP±PsPμPjP±PsP»C-C— Cf PīPμCĤC-PsPr
PIP°PiC-C,PSPsC†C,C-, PsC†PsP±P»PĕPIPs PīCĤPsC,CĬPiPsPj 6 C,PĕP¶PSC-PI PiC-C†P»CĬ
PīPsP»PsPiC-PI (C-PSC,,PsCĤPjP°C†C-CH C‰PsPrPs PīPμCĤC-PsPrCf PIP°PiC-C,PSPsC†C,C-
P°P±Ps PiPsPrCfPIP°PSPSCĬ PiCĤCfPrPrCĤ PrPĕPI. Cf CĤPsP·PrC-P»C-
B«P—P°C†C,PsC†CfPIP°PSPSCĬ Cf PīPμCĤC-PsPr PIP°PiC-C,PSPsC†C,C- P°P±Ps
PiPsPrCfPIP°PSPSCĬ PiCĤCfPrPrCĤB»).

РҮРөРјРіС,РѕРјРө Р’РҮР• (РҮР’Р’ С,Р° РҮР•Р•Рґ)

Р-С-РSPР°Рј СГР»С-Рr РіРѕСҢР°Р°РјРөС,Рө Сг СҢР°Р°С- РіРѕСҢРіРіРө
РSPР°РҢСРјРіРөР°Р°Р°РSPРөС... СГРөРјРіС,РѕРјС-РІ РSPРіРіР°Р°Р°РSPРѕ Р•РІРјСҢРSPСгС,РөСГСҢ
РrРѕ Р»С-РөР°СҢСҢ С,Р° РіРѕРІС-РrРѕРјРөС,Рө РіСҢРѕ С,Рј, С%Рѕ РіРѕРSPРө
Р•Р°СГС,РѕСГРѕРІСгСҢС,СҢ РґР’Рґ.

РҮРөРјРіС,РѕРјР°РјРө РҮР’Р’ РјРѕРҢСгС,СҢ Р±СгС,Рө: РѕРrРSPРѕР±С-СРSPРөРҢ РSPР°Р±СҢРө
РSPРіРө С,Р°/Р°Р±Рѕ СГС,СгРіРSPС- Р°Р±Рѕ РrС-Р»СРSPРө СгР•РrРѕРІРҢ РІРмРSPРө РSPР°
РSPР°С-; Р±С-Р»СҢ Р°Р±Рѕ РіС-РrРіРөС%РмРSPР° СРгС,Р»РөРІС-СГС,СҢ Сг РSPР°С-, С%Рѕ
РјРSPРҢ РІС-РrСРгРіР°С,РөСГСҢ С,С-Р»СРөРө РіСҢРө СГС,РѕСҢРSPС- Р°Р±Рѕ
С...РѕРrСҢР±С-, РІС-РrСРгС,С,СҢ РҢР°РҢСг РІ СгСҢР°РҢРмРSPС-РҢ РSPР°С-;
РіРѕСРмСҢРіРіРSPС-РSPСҢ Р°Р±Рѕ Р•РјС-РSPР° РөРѕСҢРSPСгС СРөС-СҢРө РSPР° РSPР°С-.

РҮРөРјРіС,РѕРјРаРјРө РҮР’Р’Рґ РјРѕРҢСгС,СҢ Р±СгС,Рө: СҢР°РіС,РѕРІР° Р•Р°РrРөСРөР°
РSPРмР•СҢ СГСГРіРSPР°РSPРәС— РмС,С-РѕР»РSPРіС- Р°Р±Рѕ РіСҢРөСГРөРѕСҢРмРSPРм
РrРөС...Р°РSPСҢ; СҢР°РіС,РѕРІРөРҢ РөР°СРөРмР»СҢ, РјРSPРҢР»РөРіРѕ Р•СҢРSPРіРіСҢ
СҢР°РіС,РѕРІРөРҢ Р±С-Р»СҢ Сг РіСҢСгРrРSPС-РҢ РөР»С-С,СгС-;
РіРмСҢРмРrРSPРмРіСҢРөС,РѕРмРSPРөРҢ СГС,Р°РSP Р°Р±Рѕ Р•Р°РіР°РјРSPСҢРSPСҢ;
СРөРіРөРrРөРм Р°Р±Рѕ РSPРмСҢРмРіСгР»СҢСҢРSPРм СГРмСҢСгРмР±С,С,СҢ.

Р’РмСҢРөС- Р• СгРөС... СГРөРјРіС,РѕРјС-РІ (РSPРіСҢРөРөР»Р»Р’Р’ Р’Р’Р’РөСРөР°,
РөР°СРөРмР»СҢ) С” РSPРгРіРіРмСгРөС,С-СРSPРөРј Р°Р±Рѕ РјРSPРҢСгС,СҢ Р±СгС,Рө
РSPРмРіСҢР°РіРөР»СҢРSPРә С-РSPС,РмСҢРіСҢРмС,РѕРІР°РSPС- СҢРө Р±С-Р»СҢС
РіРѕСРөРөСҢРмРSPС- Р°Р±Рѕ РјРмРSPС С,СҢРҢРөС- СҢРіРөС%Р° (РSPРіСҢРөРөР»Р»Р’Р’, СҢРө
С-РSPС,РмРөСгС- РrРөС...Р°Р»СРSPРөС... СРөР»СҢС...С-РІ).

РrРSPСС- РіСҢРSPСҢРіРі РІР°СГРөСгР»СҢСҢРSPРәС— РѕРөР»СҢР•С- РјРSPРҢСгС,СҢ
РІРөР»СҢР°С,Рө СҢР°РіС,РѕРІРөРҢ Р±С-Р»СҢ, РSPР°Р±СҢРө, РіРѕСГС,СҢРөРҢ
РҢРөРІС-С, С,Р° РSPРмР•РSPР°РSPРм РіРѕСГРөРSPС-РSPСҢ РөС-РSPСгС-РІРө.

РмСҢРө РѕРөР»СҢР•С— СГСгРrРөРSP РѕРөР РіРѕСР°С,РөРSPРSPСҢ
СГРөРјРіС,РѕРмР°,РөРөРSPС РјРSPРҢ Р±СгС,Рө РSPРмС-С,РөС-СГС,СҢ Р•СҢСгС, С%Рѕ
РSPРм СГСгРіСҢРSPРіРSPРrРҢСгС,СҢСГСҢ Р±РSPР»СҢРSPРөРј РІС-РrСРгС,С,СҢРјРө С-
СҢРөР° РјРSPРҢ РіСҢРSPРіСҢРмСГСгРіР°С,Рө РrРѕ РІС,СҢР°С,Рө Р•СҢСгС. РrРSPРSPРө
РІС,СҢРаС,Р° Р•СҢСгС СҢРSPРіРөРіР°С,СҢСГСҢ РјРҢРҢРм РјРөС,С,С”РіРѕ.

Р РөР•Рө СҢРSPР•РІРөС,РөСг РґРҮР•

Р—Р° РrР°РSPРөРјРө РмРіС-РrРмРјС-РѕР»РSPРіС-СРSPРөС... РrРѕСГР»С-РrРҢРмРSPСҢ
Р•Р°СГС,РѕСГСгРіРSPРә Р±СгРrСҢС-СҢРөРөС... РґР’Рґ Р°СГРSPСгС-СҢС”С,СҢСГСҢ С-Р•
РіС-РrРіРөС%РмРSPРөРј СҢРөР•РөРSPР РґРҮР• (С-РSPС,Р°СҢРөС, РјС-РѕРөР°СҢРrР°) Р°Р±Рѕ
СгРмСҢРмР±СҢРSPРіРөСгР»СҢСҢРSPРөС... РіРѕРrС-РҢ (С,СҢР°РSPРөС,РѕСҢРSPР°
С-СРөРмРјС-СРSPР° Р°С,Р°РөР (РҮРrРґ), С-РSPСгР»СҢС,). РґСҢС,РмСҢС-Р°Р»СРSPС-
С,СҢРSPРмРSPРмРSPР»С-СРSPС- СҢРіРөС%Ра РјРSPРҢСгС,СҢ РјР°С,Рө
Р»РмС,Р°Р»СҢРSPРөРҢ РSPРгР»С-РrРSPРө.

РР°РөС,РѕСҢРө СҢРөР•РөСг СҢРSPР•РІРөС,РөСг РґРҮР•

РмСҢРө Р•Р°СГС,РѕСГСгРіРSPРә РґР’Рґ СҢРөР•РөСҢРSPРәС,РөСг
Р°СҢС,РмСҢС-Р»СҢРSPРөС... С,СҢРSPРмРSPРмРSPР»С-СРSPРөС...
СгСГРөР»Р»РSPРмРSPС Р°Р±Рбо СгРмСҢРмР±СҢРSPРіРөСгРлСҢСҢРSPРөС... РіРѕРrС-РҢ

РѢС-РiСѢРμPSCѢ

Р—СѢРsСГ'С,Р°PSPSCЦ С±Р°СГ'С,РsС,РѢ
PIРѢPSPѢРePSPμPSPSCЦ Р°Р±Рs С,СЦP¶PеРsСГ'С,С-
РiРμСѢРμP±С-РiСр РjС-РiСѢРμPSC- РiС-Рr С±Р°СГ'
Р·Р°СГ'С,РsСГ'СрPIР°PSPSCЦ РљР“Рљ (РjРsР¶P»РѢPIC-
РiСѢРsРrСѢРsРjР°Р»СѢPSC- СГ'С,Р°PSPѢ РiРμСѢРμPr
СѢРsР·PIРѢС,РeРsРj
С±РμСѢРμP±СѢРsPIР°СГ'РeСрP»СЦСѢPSPѢС...
РiРsРrС-РNѢ) РjРsР¶CрC,СѢ СГ'С,Р°С,РѢ
РiСѢРѢС±РѢPSPsСѢ PSPμPiР°PNѢPSPsPiРs
РiСѢРѢPiРѢPSPμPSPSCЦ РiСѢРѢPNѢРsРjСр РљР“Рљ.
РiСрРeСѢРsPIРѢPNѢ РrС-Р°Р±РμC,,
PiС-РiРμСѢРiРsРjРsС±РѢСГ'С,РμC—PSPμPjС-СЦ, PIP°РrРѢ
РeР»Р°РiР°PSC-PI СГ'РμСѢС±СЦ,
С,,С-Р±СѢРѢP»СЦC±С-СЦ РiРμСѢРμPrСГ'РμСѢРrСѢ,
РrРѢСГ'P»С-РiРsРiСѢРsС,РμC—PSPμPjС-СЦ С,Р°
СГ'РѢСГ'С,РμPjPSPѢPNѢ С±РμСѢРiРsPSPѢPNѢ PIPsPIC±Р°Рe.

Р†PSCѢС- СГ'С,Р°PSPѢ,
РiРsPiБѢ™СЦP·Р°PSC- Р·
PSPμP±Р°P¶P°PSPѢРjРѢ
СѢРμP°РeС±С-СЦPjРѢ Р·
Р±РsРeСр СГ'СрРrРѢPS

РҮРѢРjРiС,РsРjРѢ РѢРҮР°

Р-С-PSPeР°Рj СГ'P»С-Рr РiРsСѢР°РrРѢС,РѢ Ср СѢР°Р·С- РiРsСЦPIРѢ
PSPѢP¶C±РμP·Р°Р·PSP°С±РμPSPѢС... СГ'РѢРjРiС,РsРjС-PI PSPμPiР°PNѢPSPs
Р·PIРμСѢРsСрC,РѢСГ'СЦ РrРs Р»С-РeР°СѢСЦ С,Р° РiРsPIC-РrРsРjРѢС,РѢ РiСѢРs С,Рμ, С%Ps
PIРsPSPѢ Р·Р°СГ'С,РsСГ'РsPICрCѢС,СѢ РљР“Рљ.

РҮРѢРjРiС,РsРjР°РjРѢ С±РμСѢРμP±СѢРsPIР°СГ'РeСрP»СЦСѢPSPsPiРs СѢРsР·P»Р°РrСр
РjРsР¶CрC,СѢ Р±СрC,РѢ: СѢР°РiС,РsPIРμ РsPSC-РjС-PSPSCЦ РsР±P»РѢС±СЦ,
СГ'P»Р°Р±РeС-СГ'С,СѢ Р°Р±Рs РsPSC-РjС-PSPSCЦ РeС-PSC±С-PIРsРe, РsСГ'РsР±P»РѢPIРs
РsРrPSPsР±С-С±PSPμ; СѢР°РiС,РsPIРμ РiРsСѢСрCєРμPSPSCЦ С...РsРrСѢР±РѢ,
Р·Р°РiР°РjРsСѢРsС±РμPSPSCЦ, PIC,СѢР°С,Р° СѢС-PIРsРsPIР°PiРѢ Р°Р±Рs
РeРsРsСѢРrРѢPSP°С±С-С—; СѢР°РiС,РsPIР° СГ'PiР»СрC,Р°PSC-СГ'С,СѢ СГ'PIC-РrРsРjРsСГ'С,С-,
РiРsСѢСрCєРμPSPSCЦ РjРsPIР»РμPSPSCЦ Р°Р±Рs СѢРsР·СрРjС-PSPSCЦ; СѢР°РiС,РsPIРμ
РiРsPiС-СѢСєРμPSPSCЦ Р·РsСѢСр PSP° РsРrPSPμ Р°Р±Рs РsР±РѢРrPIР° РsРeР°;
СѢР°РiС,РsPIРѢPNѢ, СГ'РѢP»СѢPSPѢPNѢ Р°Р±Рs С,СѢРѢPIР°P»РѢPNѢ РiРsР»РsPIРsPѢPNѢ
Р±С-Р»СѢ Р±РμP· PIPѢP·PSP°С±РμPSPsС— РiСѢРѢС±РѢPSPѢ; PIC,СѢР°С,Р°
СГ'PIC-РrРsРjРsСГ'С,С- Р°Р±Рs Р·РsРjР»С-PSPSCЦ С-Р· СГ'СрРrРsРjР°РjРѢ Р°Р±Рs Р±РμP·
PSPѢС....

РҮСѢР°PSP·РѢС,РsСѢPSPѢPNѢ С...Р°СѢР°РeС,РμСѢ СГ'РѢРjРiС,РsРjС-PI РjРsР¶Pμ
СГ'PIC-РrС±РѢС,РѢ РiСѢРs РҮР†РѢ.

РҮРѢРjРiС,РsРjР°РjРѢ С-PSC,,Р°СѢРeС,Ср РjС-РsРeР°СѢРrР° РjРsР¶CрC,СѢ Р±СрC,РѢ:
Р±С-Р»СѢ, РrРѢСГ'РeРsРjС,,РsСѢС,, PIC-РrС±СрC,С,СЦ СГ'С,РѢСГ'PSPμPSPSCЦ Р°Р±Рs
С,СЦP¶PеРsСГ'С,С- Ср PiСѢСрРrPSC-PNѢ РeР»С-С,С±С-, СѢСрC±С- Р°Р±Рs PSPѢP¶C±Рμ
PiСѢСрРrPSPѢPSPѢ; РrРѢСГ'РeРsРjС,,РsСѢС,PSPμ PIC-РrС±СрC,С,СЦ, С%Ps PIC-РrРrР°С” Ср
СГ'PiРѢPSCр, С%РμP»РμPiСр, РiРsСѢР»Рs, СѢСрРeСр, СєP»СрPSPsРe; PIC-РrС±СрC,С,СЦ
PiРμСѢРμPiРsPIРsPSPμPSPSCЦ СєP»СрPSPeР°, РiРsСѢСрCєРμPSPSCЦ С,СѢР°PIР»РμPSPSCЦ
Р°Р±Рs СЦPрCрC...Р°; РiРsСГ'РѢP»РμPSPμ РiРsС,РsPIРѢРrС-Р»РμPSPSCЦ, PSCрРrРsС,Р°,
Р±P»СѢPIР°PSPSCЦ Р°Р±Рs Р·Р°РiР°РjРsСѢРsС±РμPSPSCЦ; PSP°РrР·PIРѢС±Р°PNѢPSP°
СГ'P»Р°Р±РeС-СГ'С,СѢ, С,СѢРѢPIРsP¶PSPѢPNѢ СГ'С,Р°PS Р°Р±Рs Р·Р°РrРѢСєРeР°; СєPIРѢРrРeРμ
Р°Р±Рs PSPμСѢРμPiСрP»СЦСѢPSPμ СГ'РμСѢС±РμP±РѢС,С,СЦ.

Р—P»РsСЦPеС-СГ'PSC- PSPsPIРsСрC,PIРsСѢРμPSPSCЦ

Р РμP·СрP»СѢС,Р°С,РѢ РrРμСЦPеРѢС... РμPiС-РrРμPjС-РsР»РsPiС-С±PSPѢС...

PrPsCfP»C-PrP¶PµPSCн PIPeP°P·CfCнC,чн PSP° PrPsPrP°C,PePsPIPµ
PiC-PrPIPeC%PµPSPSC¶ CнPëP·PëPeCf CнPsP·PIPeC,PeCf CнP°PeCf C€PëPNëPePë PjP°C,PePë
PiCнPë PrPsPIPiPsC,CнPëPIP°P»PsPjCf P·P°CfC,PsCfCfPIP°PSPSC- PнPhPн (> 5 CнPsPeC-PI),
PiCнPsC,Pµ C†Pµ C,PIPµCнPrP¶PµPSPSC¶ P·P°P»PëC€P°C”C,чнCfC¶
CfCfPiPµCнPµC†P»PëPIPePj, PsCfPeC-P»чнPePë PsCfC,P°C,PsC†PSPs PSPµ
P·вн™ C¶CfPsPIP°PSPs, PSP°CfPeC-P»чнPePë CнPµP·CfP»чнC,P°C,Pë
PrPsCfP»C-PrP¶PµPSCн PICнP°C...PsPICfчнC,чн CfCfPiCfC,PSC- C„P°PeC,PsCнPë
CнPëP·PëPeCf, PSP°PiCнPëPeP»P°Pr CfC,P°C,PµPICf PiPsPIPµPrC-PSPeCf, C,P° C-PSC€C-
C„P°PeC,PsCнPë, PSP°PiCнPëPeP»P°Pr PiP°PiC-P»PsPjP°PIC-CнCfCfPSCf C-PSC„PµPeC†C-чн
P»чнPrPëPSPë.

PнPµC,P°P°PSP°P»C-P· PSP° PiC-PrCfC,P°PIC- 54 PµPiC-PrPµPjC-PsP»PsPiC-C†PSPëC...
PrPsCfP»C-PrP¶PµPSCн PIPeP°P·CfC” PSP° PSPµP·PSP°C†PSPµ PiC-PrPIPeC%PµPSPSC¶
PIC-PrPSPsCfPSPsPiPs CнPëP·PëPeCf (P’P = 1,24) CнPsP·PIPeC,PeCf CнP°PeCf
PjPsP»PsC†PSPsC— P·P°P»PsP·Pë Cf P¶C-PSPsPe, C¶PeC- P·P°CfC,PsCfPsPICfчнC,чн PнPhPн.
PiPµPNë PiC-PrPIPeC%PµPSPëPNë CнPëP·PëPe PiPsCfC,CfPiPsPIPs P·PSPëPeP°C”
PiCнPsC,C¶PiPsPj 10 CнPsPeC-PI PiC-CfP»C¶ P·P°PeC-PSC†PµPSPSC¶
P·P°CfC,PsCfCfPIP°PSPSC¶ PнPhPн. PhCfPeC-P»чнPePë CнP°Pe PjPsP»PsC†PSPsC—
P·P°P»PsP·Pë Cf P¶C-PSPsPe PIC-PePsPj PrPs 40 CнPsPeC-PI P·CfCfC,CнC-C†P°C”C,чнCfC¶
CнC-PrPePs, P·P±C-P»чнC€PµPSPSC¶ PeC-P»чнPePsCfC,C- PIPëPiP°PrPeC-PI
PrC-P°PiPSPsCfC,PëPePë CнP°PeCf PjPsP»PsC†PSPsC— P·P°P»PsP·Pë Cf P¶C-PSPsPe, C¶PeC-
P·P°CfC,PsCfPsPICfчнC,чн PSPëPSC- P°P±Ps PSPµC%PsPrP°PIPSPs
P·P°CfC,PsCfPsPICfPIP°P»Pë PнPhPн, PSPµP·PSP°C†PSPëPNë C%PsPrPs CнC-PIPSC¶
P·P°PiP°P»чнPSPsPiPs CнPëP·PëPeCf CнP°PeCf PjPsP»PsC†PSPsC— P·P°P»PsP·Pë.
P PµP·CfP»чнC,P°C,Pë C†PëC... PrPsCfP»C-PrP¶PµPSCн PSPµ PSP°PrP°чнC,чн
PrPsPeP°P·C-PI C-CfPSCfPIP°PSPSC¶ PiCнPëC†PëPSPSPsPiPs PIP°P°C”PjPsP·PIвн™ C¶P·PeCf.
PµC-PrPIPeC%PµPSPSC¶ CнPëP·PëPeCf PjPsP¶Pµ P±CfC,Pë P·CfPjPsPIP»PµPSPµ C¶Pe
P±C-P»чнC€ CнP°PSPSCнPsчн PrC-P°PiPSPsCfC,PëPePsчн CнP°PeCf PjPsP»PsC†PSPsC—
P·P°P»PsP·Pë Cf P¶C-PSPsPe, C¶PeC- P·P°CfC,PsCfPsPICfчнC,чн PнPhPн, C,P°Pe C-
P±C-PsP»PsPiC-C†PSPsчн PrC-C”чн PнPhPн P°P±Ps PiPsC”PrPSP°PSPSC¶Pj PsP±PsC...
C„P°PeC,PsCнC-PI. P’C-PrP·PSP°C†PµPSPs C,PµPSPPrPµPSC†C-чн, C%Ps CнP°Pe
PjPsP»PsC†PSPsC— P·P°P»PsP·Pë, PIPëC¶IP»PµPSPëPNë Cf P¶C-PSPsPe, C¶PeC- P±CfPrчн-
PePsP»Pë PiCнPëPNëPjP°P»Pë PнPhPн, PeP»C-PSC-C†PSPs PjPµPSC€ PIPëCнP°P¶PµPSPëPNë,
PSC-P¶ Cf C,PëC..., C...C,Ps PSC-PePsP»Pë PSPµ P·P°CfC,PsCfPsPICfPIP°PI PнPhPн.

Pj PiPsPsPrPëPSPsPePëC... PIPëPiP°PrPeP°C... Cf P¶C-PSPsPe, C¶PeC-
P·P°CfC,PsCfPsPICfчнC,чн PнPhPн, CfPiPsCfC,PµCнC-PiP°P»PëCfC¶
PrPsP±CнPsC¶PeC-CfPSC-, P° C%Pµ CнC-PrC€Pµ вн” P·P»PsC¶PeC-CfPSC- PiCfC...P»PëPSPë
PiPµC†C-PSPëPë, C%Ps PI PsPeCнPµPjPëC... PIPëPiP°PrPeP°C... PiCнPëP·PIPsPrPëP»Pë PrPs
PSPµP±PµP·PiPµC†PSPsC— PrP»C¶ P¶PeC,C,C¶ PIPSCfC,CнC-C€PSCнPsC†PµCнPµPIPSPsC—
PeCнPsPIPsC,PµC†C-. Pj CнP°P·C- PIPëPSPëPePSPµPSPSC¶ CfPeP°CнPi PSP°
CfPëP»чнPSPëPNë P±C-P»чн PI PµPiC-PiP°CfC,CнP°P»чнPSC-PNë PrC-P»C¶PSC†C-,
P·P±C-P»чнC€PµPSPSC¶ PiPµC†C-PSPëPë P°P±Ps PsP·PSP°PePë
PIPSCfC,CнC-C€PSCнPsC†PµCнPµPIPSPsC— PeCнPsPIPsC,PµC†C- PiCнPë
PrPëC„PµCнPµPSC†C-PNëPSC-PNë PrC-P°PiPSPsCfC,PëC†C- CfP»C-Pr PICнP°C...PsPICfPIP°C,Pë
PjPsP¶P»PëPIC-CfC,чн PSP°C¶PIPSPsCfC,C- PiCfC...P»PëPSPë PiPµC†C-PSPëPë PiCнPë
P·P°CfC,PsCfCfPIP°PSPSC- PнPhPн.

P—P°CfC,PsCfCfPIP°PSPSC¶ PнPhPн Cf PIPëCfPsPePëC... PrPsP·P°C... (50 PjPePi
PµC,PëPSC-P»PµCfC,CнP°PrC-PsP»Cf) P·PSPëP¶CfC” CнPëP·PëPe CнP°PeCf
PµPSPPrPsPjPµC,CнC-C¶ C,P° C¶C”C†PSPëPeC-PI. P—P°P»PëC€P°C”C,чнCfC¶

PiC-PrC,PIPμCḡPrPëC,Pë, C±Pë C†C- PrP°PSC- PjPsP¶CfC,CH C†C,PsC†CfPIP°C,PëC†Cḡ C-
PSPëP·CHPePsPrPsP·PsPIPëC... PḡPhPḡ.

P P°Pe PjPsP»PsC±PSPsC— P·P°P»PsP·Pë. (P—P°C†C,PμCḡPμP¶PμPSPSCḡ
PsPiCḡPëP»CḡPrPSPμPSC- P|PμPSC,CḡPsPj PsC†C-PSPePë C,P° PrPsC†P»C-PrP¶PμPSPSCḡ
P»C-PeP°CḡC†CHPePëC... P·P°C†PsP±C-PI (CDER) FDA).

P”CḡPsC†PiC-CḡPμPSPsPS; PμC,PëPSC-P»PμC†C,CḡP°PrC-PsP» PiCḡPsC,PëPiPsPeP°P·P°PSPëPḡ
P¶C-PSPeP°Pj, CḡPeC- PjP°CḡC,CH P·P°CḡP°P· P°P±Ps PjP°P»Pë PI PjPëPSC†P»PsPjC† CḡP°Pe
PjPsP»PsC±PSPsC— P·P°P»PsP·Pë, PsC†PeC-P»CHPePë CḡP°Pe PjPsP»PsC±PSPsC— P·P°P»PsP·Pë
PjPsP¶Pμ P±C†C,Pë PiPsCḡPjPsPSP°P»CHPSPs C†C†C,P»PëPIPëPj (PrPëPI. CḡPsP·PrC-P»
B«PμCḡPsC,PëPiPsPeP°P·P°PSPSCḡB»).

P·PiC-PrPμPjC-PsP»PsPiC-C±PSC- PrPsC†P»C-PrP¶PμPSPSCḡ PSPμ PIPëCḡPIPëP»Pë
PiPsC†P»C-PrPsPIPSPsPiPs P·PiBḡ™ CḡP·PeC† PjC-P¶ P·P°C†C,PsC†CfPIP°PSPSCḡPj
PePsPjP±C-PSPsPIP°PSPëC... PsCḡP°P»CHPSPëC... PePsPSC,CḡP°C†PμPiC,PëPIC-PI (PḡPhPḡ)
C,P° CḡPëP·PëPePsPj CḡP°PeC† PjPsP»PsC±PSPsC— P·P°P»PsP·Pë. P”PsC†P»C-PrP¶PμPSPSCḡ
PSPμ PiPsPeP°P·C†CḡC,CH P·PiBḡ™ CḡP·PeC† PjC-P¶ P·P°C†C,PsC†CfPIP°PSPSCḡPj
PḡPhPḡ (PSP° PrP°PSPëPḡ C±P°C† P°P±Ps PI PjPëPSC†P»PsPjC†) B C,P° CḡPëP·PëPePsPj
CḡP°PeC† PjPsP»PsC±PSPsC— P·P°P»PsP·Pë. PμCḡPsC,Pμ PrPμCḡPeC-
PrPsC†P»C-PrP¶PμPSPSCḡ PiPsPIC-PrPsPjP»CḡCḡC,CH PiCḡPs PSPμPIPμP»PëPePμ
PiC-PrPIPëCḡPμPSPSCḡ CḡPëP·PëPeC† CḡP°PeC† PjPsP»PsC±PSPsC— P·P°P»PsP·Pë
C†PμCḡPμPr C,PëC..., C...C,Ps P·P°CḡP°P· PiCḡPëPḡPjP°C” P°P±Ps
PSPμCḡPsPrP°PIPSPs PiCḡPëPḡPjP°P»Pë (< 6 PjC-C†CḡC†C-PI P· PjPsPjPμPSC,C†
PsC†C,P°PSPSCHPsPiPs P·P°C†C,PsC†CfPIP°PSPSCḡ), C- C,PëC..., C...C,Ps
CḡP°PSC-C€Pμ PiCḡPëPḡPjP°PI PḡPhPḡ (PrPëPI. CḡPsP·PrC-P» B«PμPsP±C-C±PSC-
CḡPμP°PeC†C-C—B», PiC-PrCḡPsP·PrC-P» B«PμPsC†C,PjP°CḡPePμC,PëPSPiPsPIC-
PrP°PSC-B»).

P†PSC€C- C†C,P°PSPë

PμCḡPsPiPμC†C,PëPSPsPIPëPḡ PePsPjPiPsPSPμPSC, PiCḡPμPiP°CḡP°C,C† P’C-PrPsCḡP°
PjC-PeCḡPs C” P°PSC,P°PiPsPSC-C†C,PsPj P°P»CHPrPsC†C,PμCḡPsPSC† C-P·
PeP°P»C-PḡP·P±PμCḡC-PiP°CḡC±PëPjPë PIP»P°C†C,PëPIPsC†C,CḡPjPë. Pj
P±C-P»CHC€PsC†C,C- PIPëPiP°PrPeC-PI P·P°C†C,PsC†CfPIP°PSPSCḡ PSPμ
PsC†C-PeC†C”C,CHC†Cḡ PiC-PrPIPëCḡPμPSPSCḡ CḡC-PIPSCḡ PeP°P»C-Cḡ. Pj
PiCḡPsC†PμC†C- PeP»C-PSC-C±PSPëC... PrPsC†P»C-PrP¶PμPSCḡ C† PrPμCḡPePëC...
PiP°C†C-C”PSC,C-PI C-P· P»PμPiPePsCḡ C,P° PiPsPjC-CḡPSPsCḡ PSPëCḡPePsIPsCḡ
PSPμPrPsC†C,P°C,PSC-C†C,Cḡ C,P° PsPrPSPsC±P°C†PSPëPj P·P°C†C,PsC†CfPIP°PSPSCḡPj
PeP°P»C-PḡP·P±PμCḡC-PiP°CḡC±PëC... P»C-PeP°CḡC†CHPePëC... P·P°C†PsP±C-PI
CḡC-PIPμPSCḡ PeP°P»C-Cḡ PI C†PëCḡPsPIP°C,C†C- PeCḡPsPIC- PrPμCḡPs, P°P»Pμ PSPμ
C†C†C,C,C”PIPs, PiC-PrPIPëCḡC†PIP°PIC†Cḡ PiC-Pr C±P°C† P·P°C†C,PsC†CfPIP°PSPSCḡ
PrCḡPsC†PiC-CḡPμPSPsPSC†. PḡPsPjC† CḡPμPePsPjPμPSPrC†C”C,CHC†Cḡ PePsPSC,CḡPsP»CH
CḡC-PIPSCḡ PeP°P»C-Cḡ PiC-Pr C±P°C† PiPμCḡC€PsPiPs C†PëPeP»C† P»C-PeC†PIP°PSPSCḡ
PiP°C†C-C”PSC,PeP°Pj C-P· PSPëCḡPePsIPsCḡ PSPμPrPsC†C,P°C,PSC-C†C,Cḡ.
P’PeP°P·P°PSPëPj PiP°C†C-C”PSC,PeP°Pj C,P°PePsP¶ CḡPμPePsPjPμPSPrPsPIP°PSPs PiPμCḡPμPr
PiPsC±P°C,PePsPj P·P°C†C,PsC†CfPIP°PSPSCḡ PiCḡPμPiP°CḡP°C,C† C†C,CḡPëPjC†PIP°C,Pë
CḡC-PIPμPSCḡ PeP°P»C-Cḡ C†PëCḡPsPIP°C,PePë PeCḡPsPIC- PSPμ PIPëCḡPμ
PIPμCḡC...PSCḡPsC— PjPμP¶C- PSPsCḡPjPë, PsC†PsP±P»PëPIPs PiCḡPë
PsPrPSPsC±P°C†PSPsPjC† P·P°C†C,PsC†CfPIP°PSPSC- PeP°P»C-PḡP·P±PμCḡC-PiP°CḡC±PëC...
P»C-PeP°CḡC†CHPePëC... P·P°C†PsP±C-PI (PrPëPI. CḡPsP·PrC-P» B«P·P·P°C”PjPsPrC-Cḡ P·

C-PSC€PëPjPë P»C-PeP°CґCґCHPePëPjPë P·P°CґPsP±P°PjPë C,P° C-PSC€C- PIPëPrPë
PIP·P°C”PjPsPrC-PNëB»).

P-C-PSPePë P· PiC-PiPµCґC, CґPëPiP»C-C†PµCґPëPrPµPjC-C”Cґ P°P±Ps CґC-PjPµPNëPSPëPj
P°PSP°PjPSPµP·PsPj C%PsPrPs C†CHPsPiPs PiPsCґCґC€PµPSPSCґ CґC,P°PSPsPIP»CґC,CH
PiCґCґPiCґ CґPëP·PëPeCґ CґPsP·PIPëC,PeCґ PiP°PSPeCґPµP°C,PëC,Cґ PiCґPë
P·P°CґC,PsCґCґPIP°PSPSC- PᄡPᄡPᄡ.

PґPsC†P° PiPsPIC-PrPsPjP»CґP»PsCґCґ PiCґPs PSPµP·PSP°C†PSPµ PiC-PrPIPëC%PµPSPSCґ
P°CґC,PµCґC-P°P»CHPSPsPiPs C,PëCґPeCґ Cґ P±P°PiP°C,CHPsC... PґC-PSPsPe, CґPeC-
PiCґPëPNëPjP°P»Pë PᄡPᄡPᄡ, PeP»C-PSC-C†PSPs P·PSP°C†CґC%Pµ PiC-PrPIPëC%PµPSPSCґ
P°CґC,PµCґC-P°P»CHPSPsPiPs C,PëCґPeCґ CґPiPsCґC,PµCґC-PiP°C”C,CHCґCґ Cґ
PiPsPsPrPëPSPsPePëC... PIPëPiP°PrPeP°C... PќPµPiP°PNëPSPµ PiCґPëPiPëPSPµPSPSCґ
PiCґPëPNëPsPjCґ PᄡPᄡPᄡ PSPµPsP±C...C-PrPSPµ P»PëC€Pµ Cґ C†PëC... PiPsPsPrPëPSPsPePëC...
PIPëPiP°PrPeP°C... Pj CґP°P·C- C, CґPëPiP°P»PsC— P°CґC,PµCґC-P°P»CHPSPsC—
PiC-PiPµCґC,PµPSP·C-C— P°P±Ps PSPµPjPsPґP»PëPiPsCґC,C- PePsPSC,CґPsP»CґPIP°C,Pë
PiPsPeP°P·PSPëPePë P°CґC,PµCґC-P°P»CHPSPsPiPs C,PëCґPeCґ P·P° PrPsPiPsPjPsPiPsCґ
P°PSC,PëPiC-PiPµCґC,PµPSP·PëPIPSPëC... P·P°CґPsP±C-PI, PґC-PSPeP°Pj CґPeC-
PiCґPëPNëPjP°CґC,CH PᄡPᄡPᄡ, CґP»C-Pr PiCґPëPiPëPSPëC,Pë C—C...
P·P°CґC,PsCґCґPIP°PSPSCґ. PґPeC%Ps C†Pµ PrPsC†C-P»CHPSPs,
P·P°CґC,PsCґCґPIP°PSPSCґ PᄡPᄡPᄡ PjPsPґPSP° PIC-PrPSPsPIPëC,Pë PiC-CґP»Cґ
PrPsCґCґPiPSPµPSPSCґ PSPsCґPjPsC,PsPSC-C— P·P° PrPsPiPsPjPsPiPsCґ
P°PSC,PëPiC-PiPµCґC,PµPSP·PëPIPSPëC— C,PµCґP°PiC-C—.

PµPsPIC-PrPsPjP»CґP»PsCґCґ PiCґPs PIPëPSPëPePSPµPSPSCґ P°P±Ps
P·P°PiPsCґC,CґPµPSPSCґ P·P°P·PSP°C†PµPSPëC... PSPëPґC†Pµ P·P°C...PIPsCґCґPIP°PSCґ Cґ
PiPµCґC-PsPr PIP°PiC-C,PSPsCґC,C- C,P° PiCґPë P·P°CґC,PsCґCґPIP°PSPSC- PᄡPᄡPᄡ, P°P»Pµ
C—C... PIP·P°C”PjPsP·PiBґ™ CґP·PsPe C-P· P·P°CґC,PsCґCґPIP°PSPSCґPj
PµCґC,CґPsPiPµPSC-PI/PiCґPsPiPµCґC,PëPSC-PI PsCґC,P°C,PsC†PSPs PSPµ
P·Bґ™ CґCґPsPIP°PSPëPNë: PґPsPIC,CґPSPëC†Cґ C,P°/P°P±Ps CґPiPµCґP±C-Pґ,
PiPsPiBґ™ CґP·P°PSPëPNë C-P· C...PsP»PµCґC,P°P·PsPj, CґC,PIPsCґPµPSPSCґ PґPsPIC†PSPëC...
PeP°PjPµPSC-PI, PiPsCґC,,C-CґC-Cґ, CґPëCґC,PµPjPSPëPNë C†PµCґPIPpsPSPëPNë PIPsPIC†P°Pe,
PiPµPjPsP»C-C,PëPePs-CґCґPµPjC-C†PSPëPNë CґPëPSPrCґPsPj, C...PsCґPµCґ
PґC-PrPµPSC...P°PjP°, PiPµCґPiPµCґ PIP°PiC-C,PSPëC..., PIC,CґP°C,P° CґP»CґC...Cґ,
PiPsPiBґ™ CґP·P°PSP° P· PsC,PsCґPeP»PµCґPsP·PsPj.

Pj PґC-PSPsPe P·C- CґPiP°PrPePsPIPëPj P°PSPiC-PsPSPµPICґPsC,PëC†PSPëPj
PSP°P±CґCґPePsPj PµPeP·PsPiPµPSPSC- PµCґC,CґPsPiPµPSPë PjPsPґCґC,CH
C-PSPrCґPeCґPIP°C,Pë P°P±Ps PiPsCґPëP»CґPIP°C,Pë CґPëPjPiC,PsPjPë
P°PSPiC-PsPSPµPICґPsC,PëC†PSPsPiPs PSP°P±CґCґPeCґ.

P”PsCґC,CґC- P°P±Ps C...CґPsPSC-C†PSC- CґPsP·P»P°PrPë C,,CґPSPeC†C-C— PiPµC†C-PSPePë
PjPsPґCґC,CH PiPsC,CґPµP±CґPIP°C,Pë PiCґPëPiPëPSPµPSPSCґ P·P°CґC,PsCґCґPIP°PSPSCґ
PᄡPᄡPᄡ, PiPsPePë PiPsPeP°P·PSPëPePë C,,CґPSPeC†C-C— PiPµC†C-PSPePë PSPµ
PiPsPiPµCґPSCґC,CHCґCґ Cґ PjPµPґC- PSPsCґPjPë C,P° PiCґPëC†PëPSPSPëPNë P·PiCґP·PsPe
C-P· PᄡPᄡPᄡ P±CґPrPµ PIPëPeP»CґC†PµPSPëPNë.

PµCґPë CґPµC†PëPrPëPIC- C...PsP»PµCґC,P°C,PëC†PSPsC— PґPsPIC,CґPSPëC†C- C,P°/P°P±Ps
CґPiPµCґP±PµPґCґ, PiPsPiBґ™ CґP·P°PSPsPiPs P· C...PsP»PµCґC,P°P·PsPj, C%Ps
CґP°PSC-C€Pµ PIPëPSPëPeP°P»Pë Cґ PiPµCґC-PsPr PIP°PiC-C,PSPsCґC,C- P°P±Ps
PiPsPiPµCґPµPrPSCґPsPiPs PiCґPëPNëPjP°PSPSCґ CґC,P°C,PµPIPëC... PiPsCґPjPsPSC-PI,
P·P°CґC,PsCґCґPIP°PSPSCґ PᄡPᄡPᄡ CґP»C-Pr PiCґPëPiPëPSPëC,Pë.

PIPsC#P° PьPhPь PjPsP¶CfC,CH PIPiP»PëPIP°C,Pë PSP° PiPµC¶PëC„PµC¶PëC#PSCf
C-PSCfCfP»C-PSPsC¶PµP·PëCfC,PµPSC,PSC-CfC,CH C,P° C,PsP»PµC¶P°PSC,PSC-CfC,CH PrPs
PiP»C¶PePsP·Pë, PSPµPjP°C” PrP°PSPëC... C%PsPrPs PiPsC,C¶PµP±Pë P·PjC-PSC¶PIP°C,Pë
C,PµC¶P°PiPµPIC,PëC#PSPëP№ C¶PµP¶PëPj P¶C-PSPeP°Pj P· PrC-P°P±PµC,PsPj, C¶PeC-
PiC¶PëP№PjP°C¶C,CH PSPëP·CHPePsPrPs·PsPIP°PSC- PьPhPь (< 0,05 PjPi
PµC,PëPSC-P»PµCfC,C¶P°PrC-PsP»Cf). PµC¶PsC,Pµ P¶C-PSPsPe, C¶PeC-
CfC,C¶P°P¶PrP°C¶C,CH PSP° C†CfPeC¶PsPIPëP№ PrC-P°P±PµC,, CfP»C-Pr
C¶PµC,PµP»CHPSPs PsP±CfC,PµP¶CfPIP°C,Pë PiC¶PsC,C¶PiPsPj
P·P°CfC,PsCfCfPIP°PSPSC¶ PьPhPь, PsCfPsP±P»PëPIPs PSP° PiPsC#P°C,PeCf
P»C-PeCfPIP°PSPSC¶.

P’PëPiP°PrPePë P·P°PiPsCfC,C¶PµPSPSC¶ PµPSPPrPsPiPµPSPSPsC— PrPµPiC¶PµCfC-C—,
PµPiC-P»PµPiCfC-C—, C...PIPsC¶PsP±Pë PьC¶PsPSP° C,P° PIPëC¶P°P·PePsPIPsPiPs
PePsP»C-C,Cf C,P°PePsP¶ CfPiPsCfC,PµC¶C-PiP°P»PëCfC¶ PiC-Pr C#P°Cf
P·P°CfC,PsCfCfPIP°PSPSC¶ PьPhPь.

P†PSPsPrC- PjPsP¶Pµ PIPëPSPëPeP°C,Pë C...P»PsP°P·PjP°, PsCfPsP±P»PëPIPs Cf P¶C-PSPsPe
C-P· C...P»PsP°P·PjPsC¶ PIP°PiC-C,PSPëC... PI P°PSP°PjPSPµP·C-. P-C-PSPeP°Pj,
CfC...PëP»CHPSPëPj PrPs PIPëPSPëPePSPµPSPSC¶ C...P»PsP°P·PjPë, CfP»C-Pr CfPSPëPeP°C,Pë
PrC-C— PiC¶C¶PjPëC... CfPsPSC¶C#PSPëC... PiC¶PsPjPµPSC-PI P°P±Ps
CfP»CHC,C¶P°C„C-PsP»PµC,PsPIPsPiPs PsPiC¶PsPjC-PSC¶PIP°PSPSC¶ PiC-Pr C#P°Cf
P·P°CfC,PsCfCfPIP°PSPSC¶ PьPhPь.

1 C,P°P±P»PµC,PeP° CfPIC-C,P»Ps-C¶PsP¶PµPIPsPiPs PePsP»CHPsC¶Cf PiC¶PµPiP°C¶P°C,Cf
PjC-CfC,PëC,CH 46 PjPi P»P°PeC,PsP·Pë, 1 C,P°P±P»PµC,PeP° P±C-P»PsPiPs PePsP»CHPsC¶Cf
PjC-CfC,PëC,CH 22 PjPi P»P°PeC,PsP·Pë. PµC¶Pë PSP°C¶PIPSsCfC,C- C¶C-PrPeC-CfPSPëC...
CfPiP°PrPePsPIPëC... CfC,P°PSC-PI PSPµPiPµC¶PµPSPsCfPëPjPsCfC,C- PiP°P»P°PeC,PsP·Pë,
PrPµC„C-C†PëC,Cf P»P°PeC,P°P·Pë P»P°PiPiP° P°P±Ps PjP°P»CHP°P±CfPsC¶P±C†C-C—
PiP»C¶PePsP·Pë-PiP°P»P°PeC,PsP·Pë, Cf C¶P°P·C- PiPµC¶PµP±CfPIP°PSPSC¶ PSP°
P±PµP·P»P°PeC,PsP·PSC-P№ PrC-C”C,C- CfP»C-Pr PIC¶P°C...PsPICfPIP°C,Pë
P·P°P·PSP°C#PµPSCf PeC-P»CHPeC-CfC,CH P»P°PeC,PsP·Pë.

PьPsPSCfCfP»CHC,P°C†C-C—/PjPµPrPëC#PSPµ PsP±CfC,PµP¶PµPSPSC¶

PµPµC¶PµPr PiPsC#P°C,PePsPj P°P±Ps PIC-PrPSPsPIP»PµPSPSC¶Pj PiC¶PëP№PsPjCf
PiC¶PµPiP°C¶P°C,Cf P’C-PrPsC¶P° PjC-PeC¶Ps C¶PµPePsPjPµPSPPrCfC”C,CHCfC¶
P·C-P±C¶P°C,Pë PiPsPIPSëP№ PjPµPrPëC#PSPëP№ P°PSP°PjPSPµP· (PIPeP»C¶C#P°C¶Pë
CfC-PjPµP№PSPëP№ P°PSP°PjPSPµP·), PiC¶PsP№C,Pë PiPsPIPSµ PjPµPrPëC#PSPµ
PsP±CfC,PµP¶PµPSPSC¶ C,P° PIPëPeP»C¶C#PëC,Pë PIP°PiC-C,PSC-CfC,CH.
PµPµPsP±C...C-PrPSPs PIPëPjC-C¶C¶C,Pë P°C¶C,PµC¶C-P°P»CHPSPëP№ C,PëCfPe C,P°
PiC¶PsPIPµCfC,Pë PjPµPrPëC#PSPµ PsP±CfC,PµP¶PµPSPSC¶, PIC¶P°C...PsPICfC¶C#Pë
PiC¶PsC,PëPiPsPeP°P·P°PSPSC¶ (PrPëPI. C¶PsP·PrC-P» B«PµC¶PsC,PëPiPsPeP°P·P°PSPSC¶B»)
C,P° PsCfPsP±P»PëPIPsCfC,C- P·P°CfC,PsCfCfPIP°PSPSC¶ (PrPëPI. C¶PsP·PrC-P»
B«PhCfPsP±P»PëPIPsCfC,C- P·P°CfC,PsCfCfPIP°PSPSC¶B»). P’P»C-Pr P·PIPµC¶PSCfC,Pë
CfPIP°PiCf P¶C-PSPePë PSP° C-PSC„PsC¶PjP°C†C-C¶ C%PsPrPs PIPµPSPsP·PSPsPiPs C,P°
P°C¶C,PµC¶C-P°P»CHPSPsPiPs C,C¶PsPjP±PsP·Cf, Cf C,PsPjCf C#PëCfP»C- PSP° C¶PëP·PëPe,
PiPsPiB¶™ C¶P·P°PSPëP№ P·C- P·P°CfC,PsCfCfPIP°PSPSC¶Pj PiC¶PµPiP°C¶P°C,Cf
P’C-PrPsC¶P° PjC-PeC¶Ps, PiPsC¶C-PIPS¶PSPs P· C,P°PePëPj PiC¶Pë
P·P°CfC,PsCfCfPIP°PSPSC- C-PSCëPëC... PьP”Pь, C%PsPrPs CfPëPjPiC,PsPjC-PI P’P’P· C,P°
P¶P’P·, PIC-PrPsPjPëC... C„P°PeC,PsC¶C-PI C¶PëP·PëPeCf C,P° PrC-P№, C¶PeC-
PSPµPsP±C...C-PrPSPs P·PrC-P№CfPSPëC,Pë PiC¶Pë PiC-PrPsP·C¶C- PSP° C,C¶PsPjP±PsP·.

PJ PrP_uCI_uPePëC... P¶C-PSPsPe PjPsP¶P_u PSP_u PSP°CÍC,P°C,Pë PeC¶PsPIPsC,P_uC‡P°
 PIC-PrPjC-PSPe PiC-Pr C‡P°CÍ PíP_uC¶P_uC¶PIPë PI PíC¶PëPN_uPsPjC- PíC¶P_uPíP°C¶P°C,Cr. PJ
 C¶P°P·C- PíC¶PëPN_uPsPjCr P_uPhP_u PIC-PrPíPsPIC-PrPSPs PrPs PíPeP°P·C-PIPsPe
 C¶PsP·PrC-P»Cr B«P¶PíPsCÍC-P± P·P°CÍC,P_uCÍCrPIP°PSPSCI C,P° PrPsP·PëB»
 PIP°PiC-C,PSC-CÍC,CH PjP°P»PsPN_uPjPsPIC-C¶PSP°. P_uC¶PsC,P_u CI_uPeC%_uPs PíC¶PëPN_uPsPj
 P_uPhP_u PIC-PrP±CÍPIP°PICÍC¶ PSP_uC¶P_uPíCíP»C¶C¶PSPs PrPs PIC-PrCÍCrC,PSPsCÍC,C-
 PíP_uC¶C€PsC— PeC¶PsPIPsC,P_uC‡C- PIC-PrPjC-PSPe P°P±Ps CI_uPeC%_uPs PeC¶PsPIPsC,P_uC‡C-

PIC-PrPjC-PSPë PIC-PrCfCfC,PSC- PïCfjPsC,CfPiPsPj PrPIPsC... C†PëPeP»C-PI, PïPµCfjPµPr PïCfjPsPrPsPIP¶PµPSPSCfj P·P°CfC,PscfCfPïP°PSPSCfj PµPhPµ PSPµPsP±C...C-PrPSPs PIPëPeP»CfC†PëC,Pë PIP°PiC-C,PSC-CfC,CH.

P—P°CfC,PscfCzPIP°PSPSCfj Cz PïPµCfjC-PsPr PIP°PiC-C,PSPscfC,C- P°P±Ps PïPsPrCzPIP°PSPSCfj PïCfjCzPrPrCf.

P·P°PiC-C,PSC-CfC,CH. PµCfjPµPïP°CfjP°C, PïCfjPsC,PëPïPsPeP°P·P°PSPëPNë PrPs P·P°CfC,PscfCfPïP°PSPSCfj C† PïPµCfjC-PsPr PIP°PiC-C,PSPscfC,C-.

Pj CfjP°P·C- PIPëPSPëPePSPµPSPSCfj PIP°PiC-C,PSPscfC,C- PïC-Pr C†P°Cf P·P°CfC,PscfCfPïP°PSPSCfj PïCfjPµPïP°CfjP°C,C† P·C-PrPsCfjP° PjC-PeCfjPs PNëPsPiPs PïCfjPëPNëPsPj PSPµPsP±C...C-PrPSPs PïCfjPëPïPëPSPëC,Pë PSPµPïP°PNëPSPs. PµCfjPsC,Pµ CfjPµP·C†P»CHC,P°C,Pë PµPïC-PrPµPjC-PsP»PsPiC-C†PSPëC... PrPsCfP»C-PrP¶PµPSCfj PSPµ PIPëP°P·C†CfC,CH PSP° PïC-PrPIPëC%PµPSPSCfj CfjPëP·PëPeC† PïPsCfjPIPë PICfjPsPrP¶PµPSPëC... PIP°Pr C† PrC-C,PµPNë, PjP°C,PµCfjC- CfjPePëC... PïCfjPëPNëPjP°P»Pë PµPhPµ PrPs PIP°PiC-C,PSPscfC,C-, C,P°Pe C†P°PjPs, CfjPe C- PSP° C-C†PSCfPïP°PSPSCfj C,PµCfjP°C,PsPiPµPSPSPsC— PrC-C— PïCfjPë PSPµPSP°PIPjPëC†PSPsPjC† PïCfjPëPNëPsPjC- PµPhPµ PïCfjPsC,CfPiPsPj PIP°PiC-C,PSPscfC,C-.

P°PscfP»C-PrP¶PµPSPSCfj PSP° C,PIP°CfjPëPSP°C... PïPsPeP°P·P°P»Pë PSP°CfjPIPSC-CfC,CH PSPµP±P°P¶P°PSPëC... PµC,,PµPeC,C-PI PïCfjPsC,CfPiPsPj PIP°PiC-C,PSPscfC,C- C,P° PïPµCfjC-PsPrC† PïPsPrC†PIP°PSPSCfj PïCfjC†PrPrCf (PrPëPI. CfjPsP·PrC-P» B«P°P°CfjPjP°PePsP»PsPiC-C†PSC- PIP»P°CfC,PëPIPsCfC,C-B»). PkP° PscfPSPsPIC- C†PëC... PrPsCfP»C-PrP¶PµPSCfj PSP° C,PIP°CfjPëPSP°C... PSPµ PjPsP¶PSP° PIPëPeP»CfC†P°C,Pë PSPµP±P°P¶P°PSC- PµC,,PµPeC,Pë PIPSP°C†P»C-PrPsPe PïPsCfjPjPsPSP°P»CHPSPsC— PrC-C— PrC-CfC†PëC... CfjPµC†PsPIPëPS. PhPrPSP°Pe P·P°PiP°P»CHPSPëPNë PrPsCfPIC-Pr P·P°CfC,PscfCfPïP°PSPSCfj PµPhPµ C† PïPµCfjC-PsPr PIP°PiC-C,PSPscfC,C- PSPµ C†PIC-PrC†PëC,CH PïCfjPs C-C†PSCfCfC†PëPNë PSPµP±P°P¶P°PSPëPNë PIPïP»PëPI C† P»CfPrPëPSPë.

PkP°CfjPIPSC- PrP°PSC- C%PsPrPs PïCfjPëPNëPsPjC† PïCfjPµPïP°CfjP°C,C† C† PïPµCfjC-PsPr PIP°PiC-C,PSPscfC,C- P·P°PSP°PrC,Ps PsP±PjPµP¶PµPSC- PrP»Cfj C,PsPiPs, C%PsP± P·CfjPsP±PëC,Pë PIPëC†PSPsPIPePë C%PsPrPs PSPµPïP°C,PëPIPsPsPiPs PIPïP»PëPIC† PïCfjPµPïP°CfjP°C,C† P·C-PrPsCfjP° PjC-PeCfjPs PSP° PïPµCfjPµP±C-Pi PIP°PiC-C,PSPscfC,C-, P·PrPsCfjPsPibf™ Cfj PïP»PsPrP° C,P° PSPsPIPsPSP°CfjPsPrP¶PµPSPsPiPs. P°Psc,PµPïPµCfj PSPµPjP°C° P¶PsPrPSPëC... PIC-PrPïPsPIC-PrPSPëC... PµPïC-PrPµPjC-PsP»PsPiC-C†PSPëC... PrP°PSPëC....

PµCfjPë PIC-PrPSPsPIP»PµPSPSC- P·P°CfC,PscfCfPïP°PSPSCfj PïCfjPµPïP°CfjP°C,C† P·C-PrPsCfjP° PjC-PeCfjPs C†P»C-Pr PïCfjP°C...PsPIC†PIP°C,Pë PïC-PrPIPëC%PµPSPSCfj CfjPëP·PëPeC† CfjPsP·PIPëC,PeC† P·P°P· C† PïC-C†P»CfjPïPsP»PsPiPsPIPsPjC† PïPµCfjC-PsPrC- (PrPëPI. CfjPsP·PrC-P»Pë B«PhC†PsP±P»PëPIPsCfC,C- P·P°CfC,PscfCfPïP°PSPSCfjB» C,P° B«P°PïPsCfC-P± P·P°CfC,PscfCfPïP°PSPSCfj C,P° PrPsP·PëB»).

PµPµCfjC-PsPr PïPsPrC†PIP°PSPSCfj PïCfjC†PrPrCf. PµPhPµ PjPsP¶C†C,CH PIPïP»PëPIP°C,Pë PSP° PïPsPrC†PIP°PSPSCfj PïCfjC†PrPrCf, PscfPeC-P»CHPePë PïC-Pr C—C... PIPïP»PëPIPsPj PjPsP¶Pµ P·PjPµPSC€C†PIP°C,PëC†Cfj PeC-P»CHPeC-C†C,CH PïCfjC†PrPSPsPiPs PjPsP»PsPeP°, P° C,P°PePsP¶ P·PjC-PSCfHIP°C,PëC†Cfj PNëPsPiPs C†PeP»P°Pr. P—PIP°P¶P°CfC†Pë PSP° C†Pµ, PµPhPµ PSPµ

$$PuPsC\sharp P^{\circ}C,PsPe\ P\cdot P^{\circ}C\acute{I}C,PsC\acute{I}C\acute{z}PIP^{\circ}PSPSC\sqcup\ P\ddot{I}C\overline{H}P\mu P\ddot{I}P^{\circ}C\overline{H}P^{\circ}C,C\acute{z}\ P' C-PrPsC\overline{H}P^{\circ}\ PjC-PeC\overline{H}Ps$$

- P“PsCḡPjPsPSP°P»CHḡPSPëC... PePsPSC,CḡP°C†PμPīC,PëPIC-PI Cr PīPsPīPμCḡPμPrPSC-PNë PīPμCḡC-PsPr (PjPëPSCrP»PëPNë PjC-CḡCḡC†CHḡ) PSPμ P·P°CḡC,PsCḡPsPICrPIP°P»Pë

PμCḡPëPNëPjP°PSPSCḡ C,P°P±P»PμC,PsPe CḡP»C-Pr CḡPsP·PīPsC†PëPSP°C,Pë Cr 1-PNë PrPμPSCḡ PīCḡPëCḡPsPrPSPsPiPs C†PëPeP»Cr (C,PsP±C,Ps Cr 1-PNë PrPμPSCḡ PjPμPSCḡC,CḡCḡP°P»CHḡPSPsC— PeCḡPsPIPsC,PμC†C-).

- PμPμCḡPμC...C-Pr P· C-PSC€PsPiPs PḡPhPḡ, PIP°PiC-PSP°P»CHḡPSPsPiPs PeC-P»CHḡC†Cḡ P°P±Ps C,CḡP°PSCḡPrPμCḡPjP°P»CHḡPSPsPiPs PīP»P°CḡC,PëCḡCḡ

P·P°PḡP°PSPs CḡPsP·PīPsC†P°C,Pë PīCḡPëPNëPjP°PSPSCḡ C,P°P±P»PμC,PsPe PīCḡPμPīP°CḡP°C,Cr P·C-PrPsCḡP° PjC-PeCḡPs PSP°CḡC,CrPīPSPsPiPs PrPSCḡ PīC-CḡP»Cḡ PīCḡPëPNëPjP°PSPSCḡ PsCḡC,P°PSPSCHḡPsC— PīPsCḡPjPsPSPsPIPjC-CḡPSPsC— C,P°P±P»PμC,PePë PīPsPīPμCḡPμPrPSCḡPsPiPs PḡPhPḡ, P°P»Pμ PSPμ PīC-P·PSC-C€Pμ PSP°CḡC,CrPīPSPsPiPs PrPSCḡ PīC-CḡP»Cḡ PīPμCḡPμCḡPIPë Cr PīCḡPëPNëPjP°PSPSC- C,P°P±P»PμC,PsPe P°P±Ps PīC-CḡP»Cḡ PīCḡPëPNëPjP°PSPSCḡ C,P°P±P»PμC,PsPe PīP»P°C†PμP±Ps PīPsPīPμCḡPμPrPSCḡPsPiPs PḡPhPḡ. Pj CḡP°P·C- PIPëPePsCḡPëCḡC,P°PSPSCḡ PePsPSC,CḡP°C†PμPīC,PëPIPsPsPiPs PIP°PiC-PSP°P»CHḡPSPsPiPs PeC-P»CHḡC†Cḡ P°P±Ps C,CḡP°PSCḡPrPμCḡPjP°P»CHḡPSPsPiPs PīP»P°CḡC,PëCḡCḡ CḡP»C-Pr CḡPsP·PīPsC†P°C,Pë PīCḡPëPNëPjP°C,Pë PīCḡPμPīP°CḡP°C, P·C-PrPsCḡP° PjC-PeCḡPs Cr PrPμPSCḡ PIPëPrP°P»PμPSPSCḡ P·P°CḡPs±Cr, P°P»Pμ PSPμ PīC-P·PSC-C€Pμ PrPSCḡ, PePsP»Pë PSPμPsP±C...C-PrPSPμ PSP°CḡC,CrPīPSPμ P·P°CḡC,PsCḡCḡPIP°PSPSCḡ C†PëC... PīCḡPμPīP°CḡP°C,C-PI.

- PμPμCḡPμC...C-Pr C-P· PjPμC,PsPrCr, C%Ps P±P°P·CḡC”C,CHḡCḡCḡ PSP° P·P°CḡC,PsCḡCḡPIP°PSPSC- P»PëC€Pμ PīCḡPsPiPμCḡC,PsPiPμPSCḡ (B«PjC-PSC-- PīC-P»C-B», C-PSḡḡ™ C”PeC†C-C—, C-PjPīP»P°PSC,Pë) P°P±Ps PIPSCrC,CḡC-C€PSCḡPsPjP°C,PePsPIPsC— CḡPëCḡC,PμPjPë P· PīCḡPsPiPμCḡC,PsPiPμPSPsPj

PḡPsPḡPSP° CḡPsP·PīPsC†P°C,Pë PīCḡPëPNëPjP°PSPSCḡ PīCḡPμPīP°CḡP°C,Cr P·C-PrPsCḡP° PjC-PeCḡPs Cr P±CrPrCHḡ-CḡPePëPNë PrPμPSCḡ PīC-CḡP»Cḡ PīCḡPëPīPëPSPμPSPSCḡ PīCḡPëPNëPjP°PSPSCḡ B«PjC-PSC--PīC-P»C-B» (Cr PIPëPīP°PrPeCr C-PjPīP»P°PSC,P° P°P±Ps PIPSCrC,CḡC-C€PSCḡPsPjP°C,PePsPIPsC— CḡPëCḡC,PμPjPë ḡḡ“ Cr PrPμPSCḡ C—C... PIPëPrP°P»PμPSPSCḡ, Cr PIPëPīP°PrPeCr C-PSḡḡ™ C”PeC†C-C— ḡḡ“ P·P°PjC-CḡC,CHḡ PSP°CḡC,CrPīPSPsC— C-PSḡḡ™ C”PeC†C-C—). PhPrPSP°Pe Cr PICḡC-C... PIPëPīP°PrPeP°C... CḡPμPePsPjPμPSPrCrC”C,CHḡCḡCḡ PrPsPrP°C,PePsPIPs PIPëPePsCḡPëCḡC,PsPICrPIP°C,Pë P±P°Cḡḡḡ™ C”CḡPSPëPNë PjPμC,PsPr PePsPSC,CḡP°C†PμPīC†C-C— PīCḡPsC,CḡPiPsPj PīPμCḡC€PëC... 7 PrPSC-PI PīCḡPëPNëPjP°PSPSCḡ PīCḡPμPīP°CḡP°C,Cr.

- PμC-CḡP»Cḡ P°P±PsCḡC,Cr Cr PīPμCḡC€PsPjCr C,CḡPëPjPμCḡC,CḡC- PIP°PiC-C,PSPsCḡC,C-

PḡPsPḡPSP° CḡPsP·PīPsC†PëPSP°C,Pë PīCḡPëPNëPsPj PīCḡPμPīP°CḡP°C,Cr P·C-PrPsCḡP° PjC-PeCḡPs PsPrCḡP°P·Cr Pḡ. Pj C,P°PePsPjCr PIPëPīP°PrPeCr PSPμPjP°C” PSPμPsP±C...C-PrPSPsCḡC,C- PIPëPePsCḡPëCḡC,PsPICrPIP°C,Pë PrPsPrP°C,PePsPIC- P·P°CḡPs±Pë PePsPSC,CḡP°C†PμPīC†C-C—.

- PμC-CḡP»Cḡ PīPsP»PsPiC-PI P°P±Ps P°P±PsCḡC,Cr PI PrCḡCḡPiPsPjCr C,CḡPëPjPμCḡC,CḡC-

P PμPePsPjPμPSPrCrC”C,CHḡCḡCḡ CḡPsP·PīPsC†PëPSP°C,Pë PīCḡPëPNëPjP°PSPSCḡ

B. P''P_μPSCH 1-7

P©PsP± P·P°C,CḡPëPjP°C,Pë PiPµCḡC-PsPr PSP°CÍ'C,P°PSPSCḡ PeCḡPsPIPsC,PµC‡C-
PIC-PrPjC-PSPë, CÍP»C-Pr PiCḡPsPrPsPIP¶CÍrPIP°C,Pë PiCḡPëPNëPjP°C,Pë C,P°P±P»PµC,PePë
PiCḡPµPiP°CḡP°C,CÍ P'C-PrPsCḡP° PjC-PeCḡPs P· PSPsPIPsC— CÍPiP°PePsPIPePë C- PSPµ
PiCḡPëPNëPjP°C,Pë C,P°P±P»PµC,PePë PiP»P°C‡PµP±Ps P· PiPsC,PsC‡PSPsC— CÍPiP°PePsPIPePë.
PiPeC%Ps C" P±P°P¶P°PSPSCḡ, C,PµCḡPjC-PS PiCḡPëPNëPjP°PSPSCḡ PjPsP¶PSP°
PiCḡPsPrPsPIP¶PëC,Pë P°P¶ PrPs P·P°PeC-PSC‡PµPSPSCḡ P°PeC,PëPIPSPëC...
C,P°P±P»PµC,PsPe C-P· PrCḡCÍrPiPsC— CÍPiP°PePsPIPePë. PµCḡPë C‡CHPsPjCÍ PjPsP¶Pµ
CÍPiPsCÍ'C,PµCḡC-PiP°C,PëCÍ'Cḡ PiCḡPsCḡPëPIPSP° PeCḡPsPIPsC,PµC‡P° P°P±Ps
PeCḡPsPIPsPjP°P·P°PSPSCḡ. P—P°P·PiPëC‡P°PNë PiCḡPëPNëPjP°PSPSCḡ PiCḡPµPiP°CḡP°C,CÍ

P'C-PrPsCḡP° PjC-PeCḡPs PIC-PrPSPsPIP»CḡCḡC,CH P'c-CḡP»Cḡ P'cḡPëPNëPjP°PSPSCḡ C,P°P±P»PμC,PsPe P'P»P°C†PμP±Ps.

P©PsP± P·PjC-CḡC,PëC,Pë C†P°Cḡ PSP°CḡC,P°PSPSCḡ PeCḡPsPIPsC,PμC†C- PIC-PrPjC-PSPë PSP° C-PSCëPëPNë PrPμPSCḡ C,PëPḡPSCḡ, CḡPμPePsPjPμPSPPrCḡC",CḡCḡCḡ CḡPePsCḡPsC,PëC,Pë P'PμCḡPμCḡPICḡ Cḡ P'cḡPëPNëPjP°PSPSC- C,P°P±P»PμC,PsPe P'P»P°C†PμP±Ps PSP° CḡC,C-P»CHPePë PrPSC-PI, PSP° CḡPeC-P»CHPePë P±P°PḡP°PSPs. PŸP»C-Pr P·P°P·PSP°C†PëC,Pë, C%Ps C†PëPj PePsCḡPsC,CëPsCḡ P±CḡPrPμ P'PμCḡPμCḡPIP°, C,PëPj C†P°CḡC,C-CëPμ CḡP'PsCḡC,PμCḡC-PiP°C",CḡCḡCḡ PIC-PrCḡCḡC,PSC-CḡC,CH PeCḡPsPIPsC,PμC†C- PIC-PrPjC-PSPë C,P° P'PsCḡPIP° P'cḡPsCḡPëPIPSPsC— PeCḡPsPIPsC,PμC†C- P°P±Ps PeCḡPsPIPsPjP°P·P°PSPSCḡ P'cḡPsC,ḡP'PsPj P'cḡPëPNëPjP°PSPSCḡ C,P°P±P»PμC,PsPe C-P· PrCḡCḡPiPsC— CḡP'P°PePsPIPePë (CḡPe C- Cḡ PIPëP'P°PrPeCḡ P·P°C,CḡPëPjPePë PSP°CḡC,P°PSPSCḡ PjPμPSCḡC,CḡCḡP°C†C-C— PeCḡPsPIPsC,PμC†C- PIC-PrPjC-PSPë).

P"C-C,Pë.

PμCḡPμP'P°CḡP°C, P'PsPeP°P·P°PSPëPNë PrP»Cḡ P·P°CḡC,PsCḡCḡPIP°PSPSCḡ P·P° P'cḡPëP·PSP°C†PμPSPSCḡPj P»C-PeP°CḡCḡ C,C-P»CHPePë P'c-CḡP»Cḡ PSP°CḡC,P°PSPSCḡ CḡC,P°P»PëC... PjPμPSCḡC,CḡCḡP°C†C-PNë.

PμPμCḡPμPrPsP·CḡPIP°PSPSCḡ.

P"PsC,PμP'PμCḡ PSPμPjP°C" PḡPsPrPSPëC... PrP°PSPëC... PeP»C-PSC-C†PSPëC... PrPsCḡP»C-PrPḡPμPSCḡ C%PsPrPs P'PμCḡPμPrPsP·CḡPIP°PSPSCḡ C,P°P±P»PμC,PsPe P'cḡPμP'P°CḡP°C,Cḡ P'C-PrPsCḡP° PjC-PeCḡPs. PḡP° P'c-PrCḡC,P°PIC- P·P°P'P°P»CHPSPsPiPs PrPsCḡPIC-PrCḡ P·P°CḡC,PsCḡCḡPIP°PSPSCḡ PḡPhPḡ P'cḡPë P'PμCḡPμPrPsP·CḡPIP°PSPSC- PjPsPḡPμ CḡP'PsCḡC,PμCḡC-PiP°C,PëCḡCḡ PSCḡPrPsC,P°, P±P»CHPIP°PSPSCḡ C,P° PeCḡPsPIPsC,PμC†P° PIC-PrPjC-PSPë. PḡCḡPsPIPsC,PμC†P° PIC-PrPjC-PSPë PjPsPḡPμ CḡP'PsCḡC,PμCḡC-PiP°C,PëCḡCḡ Cḡ PrC-PIC†P°C, PSP°PIC-C,CH PrPs PSP°CḡC,P°PSPSCḡ PjPμPSP°CḡC...Pμ Cḡ PIPëP'P°PrPeCḡ PSPμPSP°PIPjPëCḡPSPsPiPs/PIPëP'P°PrPePsPIPsPiPs P·P°CḡC,PsCḡCḡPIP°PSPSCḡ P»C-PeP°CḡCḡCHPePsPiPs P·P°CḡPsP±Cḡ. PŸP'PμC†C-P°P»CHPSPsPiPs P°PSC,PëPrPsC,Cḡ PSPμ C-CḡPSCḡC", P»C-PeCḡPIP°PSPSCḡ P'PsPIPëPSPSPμ P±CḡC,Pë CḡPëPjP'c,PsPjP°C,PëC†PSPëPj.

PμPsP±C-C†PSC- CḡPμP°PeC†C-C—.

P©PsPrPs CḡPμCḡPNëPsP·PSPëC... P'PsP±C-C†PSPëC... CḡPμP°PeC†C-PNë Cḡ P'P°C†C-C"PSC,PsPe, CḡPeC- P·P°CḡC,PsCḡPsPICḡCḡC,CH PḡPhPḡ, PrPëPI. C,P°PePsPḡ CḡPsP·PrC-P» B«PhCḡPsP±P»PëPIPsCḡC,C- P·P°CḡC,PsCḡCḡPIP°PSPSCḡB». PḡPëPḡC†PμP·P°P·PSP°C†PμPSC- P'PsP±C-C†PSC- CḡPμP°PeC†C-C— CḡP'PsCḡC,PμCḡC-PiP°P»PëCḡCḡ P'c-Pr C†P°Cḡ P·P°CḡC,PsCḡCḡPIP°PSPSCḡ P'cḡPμP'P°CḡP°C,Cḡ P'C-PrPsCḡP° PjC-PeCḡPs (PrPëPI. C,P°P±P»PëC†Cḡ 3).

$$P \dot{y} P^{\circ} P \pm P \gg P \ddot{e} C \dagger C \downarrow 3$$
[illegible]

P— P±PsPeCf CḡPμPiCḡPsPrCfPeC, PēPIPSpS— CḡPēCfC, PμPjPē C, P° PjPsP»PsC±PSPēC... P·P°P»PsP·	P°PsP»CḡC±C—CfC, Cḡ PjPsP»PsC±PSPēC... P·P°P»PsP·, PjPμC, CḡPsCḡP°PiC—Cḡ*, P°PjPμPSPsCḡPμCḡ	P°P°PiC—PSP°P»CḡPSPēPNē PeP°PSPPrḡPrPsP·, C, P°P·PsPIPēPNē P±C—P»Cḡ, P·P±C—P»CḡCēPμPSPSCḡ PjPsP»PsC±PSPēC... P·P°P»PsP·, C, C—P±CḡPsP·PSPs—PeC—CfC, PsP·PSP° PjP°CfC, PsPIP°C, C—Cḡ, PjP°C, PePsPIC—/ PIP°PiC—PSP°P»CḡPSC— PeCḡPsPIPSC, PμC±C—*, PIPēPrC—P»PμPSPSCḡ P·C— CfC, P°C, PμPIPēC... PsCḡPiP°PSC—PI, PiCḡPēPiP»PēPIPē, PIP°PiC—PSC—C,, PiPsCḡCfCēPμPSPSCḡ PjPμPSCfC, CḡCfP°P»CḡPSPsPiPs CfPēPeP»Cf, PrPēCḡPjPμPSPsCḡPμCḡ, PiC—PiPsPjPμPSPsCḡPμCḡ, PjPμPSPsCḡP°PiC—Cḡ, PIP°PiC—PSP°P»CḡPSP° CfCfC...C—CfC, Cḡ, CfCfPjPSC—PIPSēPNē PjP°P·PsPe PμP°PiP°PSC—PePsP»P°Cf, P·PSPēPμPμPSPSCḡ P»C—P±C—PrPs	P°PēCḡPiP°CḡPμCfPSC—Cḡ, PiCfP»CḡPiPsPIP°PiC—PSC—C,, PiPsCfC, PePsC—C, P°P»CḡPSP° PeCḡPsPIPSC, PμC±P° PeCḡPsPIPSC, PμC±P° PiC—PrPjC—PSPē, PeC—CfC, P° PjPsP»PsC±PSPsC— P·P°P»PsP·Pē, PiC—PiPμCḡPiP»P°P·C—Cḡ PjPsP»PsC±PSPsC— P·P°P»PsP·Pē, PSPsPIPSCfC, PIPsCḡPμPSPSCḡ Cf PjPsP»PsC±PSC—PNē P·P°P»PsP·C—, PiPsP»C—Pi CēPēPNēPePē PjP°C, PePē, P°C, CḡPsC,, C—Cḡ PμPSPPrḡPjPμC, CḡC—Cḡ, PeC—CfC, P° CḡC°C±PSPēPeP°, P·P±C—P»CḡCēPμPSPSCḡ PjP°C, PePē	
P—P°PiP°P»CḡPSC— CḡPsP·P»P°PrPē		PḡCfC, PμPSC—Cḡ, PiC—PrPIPēC%PμPSPēPNē PiPsC, PsPIPēPrC—P»PμPSPSCḡ, PSP°P±CḡCḡPe (PμPμPSPμCḡP°P»C—P·PsPIP°PSPēPNē PSP°P±CḡCḡPe, PiPμCḡPēC,, PμCḡPēC±PSPēPNē PSP°P±CḡCḡPe, PSP°P±CḡCḡPe PsP±P»PēC±CḡCḡ)	PḡPμP·PrCfPμP°PSPSCḡ	
P°PsCfP»C—PrPμPμPSPSCḡ		P—P±C—P»CḡCēPμPSPSCḡ PjP°CfPē C, C—P»P°	P—PjPμPSCēPμPSPSCḡ PjP°CfPē C, C—P»P°	

*PSPμCḡPμPiCfP»CḡCḡPSC— PeCḡPsPIPSC, PμC±C— P·P°P·PIPēC±P°PNē
P·PSPēPeP°CḡC, Cḡ PiCḡPē PiCḡPsPrPsPIPμPμPSPSC— C, PμCḡP°PiC—C—

PhPiPēCḡ PsPeCḡPμPjPēC... PiPsP±C—C±PSPēC... CḡPμP°PeC†C—PNē

Pj PμC—PSPsPe, CḡPeC— PiCḡPēPNēPjP°P»Pē PḡP“Pḡ, CḡPiPsCfC, PμCḡC—PiP°PICḡCḡ
PiC—PrPIPēC%PμPSPēPNē CḡPēP·PēPe CḡPsP·PIPēC, PeCḡ PIPμPSPsP·PSPēC... P°P±Ps
P°CḡC, PμCḡC—P°P»CḡPSPēC... C, CḡPsPjP±PsC, PēC±PSPēC... C, P°
C, CḡPsPjP±PsPμPjP±PsP»C—C±PSPēC... CḡPIPēC%, Cr C, PsPjCr C±PēCḡP»C—
C—PSC,, P°CḡPeC, Cr PjC—PsPeP°CḡPrP°, C—PSCḡCfP»CḡC, Cr, PḡP†Pḡ,
PIPμPSPsP·PSPsPiPs C, CḡPsPjP±PsP·Cr C, P° PḡP·P>Pḡ, CḡPeC— PrPμC, P°P»CḡPSC—CēPμ
PsPiPēCḡP°PSC— Cr CḡPsP·PrC—P»C— B«PhCḡPsP±P»PēPIPsCfC, C—
P·P°CfC, PsCḡCfPIP°PSPSCḡB».

PḡPēPμC±PμP·P°P·PSP°C±PμPSC— CḡPμCḡPNēPsP·PSC— PiPsP±C—C±PSC—
CḡPμP°PeC†C—C— CḡPiPsCfC, PμCḡC—PiP°P»PēCḡCḡ Cr PμC—PSPsPe, CḡPeC—
P·P°CfC, PsCḡPsPICḡCḡC, Cḡ PḡPhPḡ, C%Ps C, P°PePsPμ P±CfP»Pē PsPiPēCḡP°PSC— Cr
CḡPsP·PrC—P»C— B«PhCḡPsP±P»PēPIPsCfC, C— P·P°CfC, PsCḡCfPIP°PSPSCḡB»:

- PIPμPSPsP·PSC— C, CḡPsPjP±PsPμPjP±PsP»C—C±PSC— CḡPsP·P»P°PrPē;
- P°CḡC, PμCḡC—P°P»CḡPSC— C, CḡPsPjP±PsPμPjP±PsP»C—C±PSC— CḡPsP·P»P°PrPē;
- P°CḡC, PμCḡC—P°P»CḡPSP° PiC—PiPμCḡC, PμPSP·C—Cḡ;
- PiCfC...P»PēPSPē PiPμC±C—PSPēPē;
- CḡPsP·PIPēC, PsPe P°P±Ps P·P°PiPsCfC, CḡPμPSPSCḡ P·P°C...PIPsCḡCḡPIP°PSCḡ, PrP»Cḡ
CḡPePēC... P·Piḡḡ™ CḡP·PsPe C—P· PiCḡPēPNēPsPjPsPj PḡPhPḡ PSPμ
P·ḡḡ™ CḡCḡPsPIP°PSPēPNē PsCfC, P°C, PsC±PSPs: C...PIPsCḡPsP±P° PḡCḡPsPSP°,
PSPμCḡPiPμC†PēC,, C—C±PSPēPNē PIPēCḡP°P·PePsPIPēPNē PePsP»C—C,,
PμPiC—P»PμPiCḡC—Cḡ, PjC—PsPjP° PjP°C, PePē, PiPsCḡC,, C—CḡC—Cḡ, CḡPēCḡC, PμPjPSPēPNē
C±PμCḡPIPSPSPēPNē PIPsPIC±P°Pe, PiPμCḡPiPμCḡ PIP°PiC—C, PSPēC..., C...PsCḡPμCḡ
PḡC—PrPμPSC...P°PjP°, PiPμPjPsP»C—C, PēPePs—CfCḡPμPjC—C±PSPēPNē CḡPēPSPrCḡPsPj,

- C...PsP»PμCfC,P°C,PëC±PSP° P¶PsPIC,C¶PSPëC†C¶;
- C...P»PsP°P·PjP°;
 - PiPsCfC,C¶C- P°P±Ps C...C¶PsPSC-C±PSC- C¶PsP·P»P°PrPë C,,CfPSPeC†C-C— PïPμC±C-PSPePë, C%Ps PjPsP¶CfC,CH PïPsC,C¶PμP±CfPIP°C,Pë PïC¶PëPïPëPSPμPSPSC¶ P·P°CfC,PsCfCfPIP°PSPSC¶ PλPhPλ, PrPsPePë PïPsPeP°P·PSPëPePë C,,CfPSPeC†C-C— PïPμC±C-PSPePë PSPμ PïPsPIPμC¶PSCfC,CHCfC¶ PrPs PSPsC¶PjPë;
 - Cf P¶C-PSPsPe P·C- CfPïP°PrPePsPIPsC¶ CfC...PëP»CHPSC-CfC,C¶ PrPs P°PSPiC-PsPSPμPIC¶PsC,PëC±PSPsPiPs PSP°P±C¶C¶PeCf PμPeP·PsPiPμPSPSC- PμCfC,C¶PsPiPμPSPë PjPsP¶CfC,CH CfPïC¶PëC±PëPSPëC,Pë P°P±Ps PïPsCfPëP»C¶PIP°C,Pë CfPëPjPïC,PsPjPë P°PSPiC-PsPSPμPIC¶PsC,PëC±PSPsPiPs PSP°P±C¶C¶PeCf.

P§P°CfC,PsC,P° PrC-P°PiPSPsCfC,CfPIP°PSPSC¶ C¶P°PeCf PjPsP»PsC±PSPsC— P·P°P»PsP·Pë PrPμC%Ps PïC-PrPIPëC%CfC”C,CHCfC¶ CfPμC¶PμPr P¶C-PSPsPe, C¶PeC- P·P°CfC,PsCfPsPICfCHC,CH PλPhPλ. PhCfPeC-P»CHPePë C¶P°Pe PjPsP»PsC±PSPsC— P·P°P»PsP·Pë Cf P¶C-PSPsPe PIC-PePsPj PrPs 40 C¶PsPeC-PI P·CfCfC,C¶C-C±P°C”C,CHCfC¶ C¶C-PrPePs, P·P±C-P»CHC¶PμPSPSC¶ PeC-P»CHPePsCfC,C- PIPëPïP°PrPeC-PI PrC-P°PiPSPsCfC,CfPIP°PSPSC¶ C¶P°PeCf PjPsP»PsC±PSPsC— P·P°P»PsP·Pë Cf P¶C-PSPsPe, C¶PeC- P·P°CfC,PsCfPsPICfCHC,CH PSPëPSC- P°P±Ps PSPμC%PsPrP°PIPSPs P·P°CfC,PsCfPsPICfPIP°P»Pë PλPhPλ, PSPμP·PSP°C±PSPμ C%PsPrPs C¶C-PIPSC¶ P·P°PiP°P»CHPSPsPiPs C¶PëP·PëPeCf C¶P°PeCf PjPsP»PsC±PSPsC— P·P°P»PsP·Pë. P’P·P°C”PjPsP·PIB¶™ C¶P·PsPe C-P· P·P°CfC,PsCfCfPIP°PSPSC¶Pj PλPhPλ PSPμPIC-PrPsPjPëP№. P”PëPI. C,P°PePsP¶ C¶PsP·PrC-P»Pë B«P¶C¶PsC,PëPïPsPeP°P·P°PSPSC¶B» C,P° B«PhCfPsP±P»PëPIPsCfC,C- P·P°CfC,PsCfCfPIP°PSPSC¶B».

P’P·P°C”PjPsPrC-C—

PμC¶PsC¶PëPIPSC- PeC¶PsPIPsC,PμC±C- C,P°/P°P±Ps P·PSPëP¶PμPSPSC¶ PePsPSC,C¶P°C†PμPïC,PëPIPSPsC— PrC-C— PjPsP¶Pμ PIPëPSPëPePSCfC,Pë PIPSP°CfP»C-PrPsPe PIP·P°C”PjPsPrC-C— C-PSCëPëC... P»C-PeP°C¶CfCHPePëC... P·P°CfPs±C-PI (C-PSPrCfPeC,PsC¶C-PI C,,PμC¶PjPμPSC,C-PI) P· PsC¶P°P»CHPSPëPjPë PePsPSC,C¶P°C†PμPïC,PëPIP°PjPë (PrPëPI. C¶PsP·PrC-P» B«P’P·P°C”PjPsPrC-C¶ P· C-PSCëPëPjPë P»C-PeP°C¶CfCHPePëPjPë P·P°CfPs±P°PjPë C,P° C-PSCëC- PIPëPrPë PIP·P°C”PjPsPrC-P№B»).

PμPsCfC,PjP°C¶PePμC,PëPSPiPsPIC- PrP°PSC-. (P—P°CfC,PμC¶PμP¶PμPSPSC¶ PsPïC¶PëP»C¶PrPSPμPSC- PïPμPSC,C¶PsPj PsC†C-PSPePë C,P° PrPsCfP»C-PrP¶PμPSPSC¶ P»C-PeP°C¶CfCHPePëC... P·P°CfPs±C-PI (CDER) FDA).

PμB¶™ C¶C,CH PrPsCfP»C-PrP¶PμPSC¶, Cf C¶PePëC... PïPsC¶C-PIPSC¶PIP°P»Pë C¶PëP·PëPe PIPëPSPëPePSPμPSPSC¶ C¶P°PeCf PjPsP»PsC±PSPsC— P·P°P»PsP·Pë PjC-P¶ C,PëPjPë, C...C,Ps PePsP»Pë-PSPμP±CfPrCH P·P°CfC,PsCfPsPICfPIP°PI (PSP° PrP°PSPëP№ C±P°Cf C±Pë PI PjPëPSCfP»PsPjCf) PλPhPλ, C- C,PëPjPë, C...C,Ps PSC-PePsP»Pë PSPμ P·P°CfC,PsCfPsPICfPIP°PI PλPhPλ, PïPsPIC-PrPsPjP»C¶P»Pë PïC¶Ps PIC-PrCfCfC,PSC-CfC,CH P·PIB¶™ C¶P·PeCf PjC-P¶ P·P°CfC,PsCfCfPIP°PSPSC¶Pj PλPhPλ C,P° C¶PëP·PëPePsPj PIPëPSPëPePSPμPSPSC¶ C¶P°PeCf PjPsP»PsC±PSPsC— P·P°P»PsP·Pë, P· PsC†C-PSPeP°PjPë PμC,,PμPeC,Cf PIC-Pr 0,90 PrPs 1,12.

Pj C,C¶CHPsC... PrPsCfP»C-PrP¶PμPSPSC¶C... PïPsC¶C-PIPSC¶PIP°P»Pë C¶PëP·PëPe PIPëPSPëPePSPμPSPSC¶ C¶P°PeCf PjPsP»PsC±PSPsC— P·P°P»PsP·Pë PjC-P¶ C,PëPjPë, C...C,Ps P·P°C¶P°P· PïC¶PëP№PjP°C” C- C,PëPjPë, C...C,Ps PSPμC%PsPrP°PIPSPs PïC¶PëP№PjP°PI PλPhPλ (< 6 PjC-CfC¶C†C-PI P· PjPsPjPμPSC,Cf PsCfC,P°PSPSCHPsPiPs

P·P°CÍC,PsCÍCÍPIP°PSPSCÍ), C- C,PëPjPë, C...C,Ps PSC-PëPsP»Pë C—C... PSPµ
P·P°CÍC,PsCÍPsPICÍPIP°PI. P' PsPrPSPsPjCÍ P· C†PëC... PrPsCÍP»C-PrP¶PµPSCĤ
PİPsPIC-PrPsPjP»CÍP»PsCÍCÍ PİCĤPs PIC-PrCÍCÍC,PSC-CÍC,CH P·PIĤ™ CÍP·PëCÍ PjC-P¶
CĤPëP·PëPePsPj PIPëPSPëPePSPµPSPSCÍ CĤP°PëCÍ PjPsP»PsC†PSPsC— P·P°P»PsP·Pë C,P°
P·P°CÍC,PsCÍCÍPIP°PSPSCÍPj PĤPĤPĤ. P"PIP° C-PSCëPëC... PrPsCÍP»C-PrP¶PµPSPSCÍ
PIPëCÍPIPëP»Pë PİC-PrPIPëC%PµPSPëPNë PIC-PrPSPsCÍPSPëPNë CĤPëP·PëPe 1,19-1,33 PİCĤPë
PİPsC,PsC†PSPsPjCÍ P°P±Ps PSPµC%PsPrP°PIPSCHPsPjCÍ P·P°CÍC,PsCÍCÍPIP°PSPSC-.
PĤP±PëPrPIP° C†C- PrPsCÍP»C-PrP¶PµPSPSCÍ PIPëCÍPIPëP»Pë PİC-PrPIPëC%PµPSPëPNë
CĤPëP·PëPe PIPëPSPëPePSPµPSPSCÍ CĤP°PëCÍ PjPsP»PsC†PSPsC— P·P°P»PsP·Pë PİCĤPë
C,CĤPëPIP°P»PsPjCÍ P·P°CÍC,PsCÍCÍPIP°PSPSC-, PİCĤPëC†PsPjCÍ PIC-PrPSPsCÍPSPëPNë
CĤPëP·PëPe PePsP»PëPIP°C"C,CHCÍCÍ PIC-Pr 1,03 PİCĤPë P·P°CÍC,PsCÍCÍPIP°PSPSC- PĤPĤPĤ
PİCĤPsC,CÍPiPsPj PjPµPSCëPµ PsPrPSPsPiPs CĤPsPëCÍ PrPs PİCĤPëP±P»PëP·PSPs 1,4 PİCĤPë
P·P°CÍC,PsCÍCÍPIP°PSPSC- PĤPĤPĤ P±C-P»CHCëPµ PSC-P¶ 8-10 CĤPsPëC-PI.

*PµPsPIC-PrPsPjP»PµPSPSCÍ PİCĤPs PİC-PrPsP·CĤCĤPIP°PSC- PİPsP±C-C†PSC-
CĤPµP°PëC†C-C—*

PµPsPIC-PrPsPjP»PµPSPSCÍ PİCĤPs PİC-PrPsP·CĤCĤPIP°PSC- PİPsP±C-C†PSC-
CĤPµP°PëC†C-C— CÍ PİPµCĤC-PsPr PİPsCÍC,PjP°CĤPePµC,PëPSPiPsPiPsPiPs
CÍPİPsCÍC,PµCĤPµP¶PµPSPSCÍ C" PrCÍP¶Pµ PIP°P¶P»PëPIPëPjPë. PİPµ PrP°C"
PjPsP¶P»PëPIC-CÍC,CH P·PrC-PNëCÍPSCĤPIP°C,Pë PePsPSC,CĤPsP»CH P·P°
CÍPİC-PIPIC-PrPSPsCëPµPSPSCÍPj PePsCĤPëCÍC,CH/CĤPëP·PëPe PrP»CÍ
P»C-PeP°CĤCÍCHPePëC... P·P°CÍPsP±C-PI. PĤPµPrPëC†PSC- PİCĤP°C†C-PIPSPëPePë
PİPsPIPëPSPSC- PİPsPIC-PrPsPjP»CÍC,Pë PİCĤPs PİC-PrPsP·CĤCĤPIP°PSC- PİPsP±C-C†PSC-
CĤPµP°PëC†C-C—.

PŸPµCĤPjC-PS PİCĤPëPrP°C,PSPsCÍC,C-. 3 CĤPsPePë.

PIPjPsPIPë P·P±PµCĤC-PİP°PSPSCÍ.

P—P±PµCĤC-PİP°C,Pë CÍ PSPµPrPsCÍC,CÍPİPSPsPjCÍ PrP»CÍ PrC-C,PµPNë PjC-CÍC†C- PİCĤPë
C,PµPjPİPµCĤP°C,CÍCĤC- PSPµ PIPëC%Pµ 25 B°PŸ.

PIPİP°PePsPIPeP°.

PµPs 28 C,P°P±P»PµC,PsPe CÍ P±P»C-CÍC,PµCĤC- (21 C,P°P±P»PµC,PeP° CĤPsP¶PµPIPsPiPs
PePsP»CHPsCĤCÍ C,P° 7 C,P°P±P»PµC,PsPe P±C-P»PsPiPs PePsP»CHPsCĤCÍ), PİPs 1 P°P±Ps 3
P±P»C-CÍC,PµCĤPë PI PeP°CĤC,PsPSPSC-PNë PePsCĤPsP±C†C-.

PĤP°C,PµPiPsCĤC-CÍ PIC-PrPİCÍCÍPeCÍ.

P—P° CĤPµC†PµPİC,PsPj.

P’PëCḡPsP±PSPëPε.

P>P°P±PsCḡP°C,PsCḡC-PsCÍ P>PμPsPS PαP°CḡPjP°, PŸ.Pḡ.

**PḡC-CÍC†PμP·PSP°C...PsPrP¶PμPSPSCḡ PIPëCḡPsP±PSPëPεP° C,P° P°PrCḡPμCÍP°
PïCḡPsPIP°PrP¶PμPSPSCḡ P№PsPiPs PrC-CḡP»CḤPSPsCÍC,C-.**

PŸ/P>P° P’P°P»P»C-PSP° CÍ/PS, PμPsP»C-PiPsPSPs P†PSPTrP°CÍC,CḡC-P°P»
PḡP°PIP°C,PμPrP¶PμCḡP°, P’C-P»P»P°PεC-P»P°PjP±CḡPμ, 24193 P>PμPsPS,
P†CÍPïP°PSC-CḡB B B B B B B B B B B B B