

Р†РќРЎРЎР РЈРљР|Р†РЇ

PrP»CII PjPµPrPëC‡PSPsPiPs P·P°CíC,PsCíCíPIP°PSPSCI
P»C-PëP°CíCíCíPëPsPiPs P·P°CíPsP±Cí

P" PJPᄡPᄢPŸPŷPᄢPᄢ^{B®}

(DUPHASTON^{B®})

$$P\check{Y}P\in P\gg P^{\circ}P_{\Gamma}:$$
$$PrC-CHC\#P^{\circ}CHP\mu C\#PsPIP\ddot{e}PSP^{\circ}:Pr\ddot{e}PrCHPsPiP\mu C\dot{I}C,P\mu CHPsPS;$$

1 C,P°P±P»PµC,PeP° PjC-ClC,PëC,CH PrPëPrCḡPsPiPµClC,PµCḡPsPSCr 10 PjPi;

PrPsPiPsPjC-P¶PSC- C¶PµC±PsPIPëPSPë: C¶IPrC¶Ps C,P°P±P»PµC,PePë в¶ P»P°PeC,PsP·P°, PjPsPSPsPiC-PrC¶P°C,; PiC-PiC¶PsPjPµP»PsP·P°; PeC¶PsC...PjP°P»CH PeCrPeCrC¶CrPrP·C¶IPSPëPNë; PeC¶PµPjPSC-CH PrC-PsPeCrPëPr PePsP»PsC—PrPSPëPNë P±PµP·PIPsPrPSPëPNë; PjP°PiPSC-CH CrC,PµP°C¶P°C,;B

$PsP\pm PsP \gg PsPSPeP^\circ$: $PjP^\circ PeC\bar{H}PsPiPsP \gg 400$, $PiC-P\bar{i}C\bar{H}PsPjP\mu P \gg PsP\cdot P^\circ$, $C, P\bar{e}C, P^\circ PSCr$, $PrC-PsPeC\bar{I}P\bar{e}Pr$ ($P\cdot 171$).

**P>C-PeP°CTĜĆĤĤPeP° C,,PsCTĜPjP°. PŷP°P±P»PμC,PεPĕ, PIPeCTĜPĕC,C-
PİP»C-PIPePsPIPScĤ PsP±PsP»PsPSPePsCĤ.**

*Ph*Cl*ʼ*PSPsPIPSC- C,,C-P·PëPePs-C...C-PjC-C‡PSC- PIP»P°ClʼC,PëPIPsClʼC,C-: PeCḤCrPiP»P°, PrPIPsPsPïCrPeP»P°, PIPeCḤPëC,P° PiP»C-PIPePsPIPsCḤ PsP±PsP»PsPSPePsCḤ, P±C-P»P° C,P°P±P»PμC,PeP° P·C- ClʼPePsC€PμPSPëPj PeCḤP°CʼPj, P· P»C-PSC-CʼCḤ PrP»CḤ CḤPsP·P»PsPjCr C,P° PjP°CḤPeCrPIP°PSPSCḤPj B«155B» P· PsPrPSPsPiPsB P±PsPeCr PïPs PsP±PëPrPIP° P±PsPePë PIC-Pr P»C-PSC-C— PrP»CḤ CḤPsP·P»PsPjCr. PʼʼC-P°PjPμC,CḤ BḤ 7 PjPj.

$P \rightarrow C - PSC - Cl$ $PrP \rightarrow Cl$ $C_7H_5P_5P \cdot P \rightarrow PsPjCr$ $PiC_7H_5P_5P \cdot PSP^\circ C \pm P_{\mu}PSP^\circ$ $C, C - P \rightarrow CH_5PeP_5$ $PrP \rightarrow Cl$
 $PiP_5P \rightarrow P_{\mu}PiC_6P_{\mu}PSPSCl$ $PePsPIC, P^\circ PSPSCl$ $C - PSP_{\mu}$ $C_7H_5P_5P \cdot PrC - P \rightarrow ClC''$ $C, P^\circ P \pm P \rightarrow P_{\mu}C, PeCr$
 PSP° $C_7H_5C - PIPSC - PrPsP \cdot P_5$.

PpP°CḡPjP°PePsC,PpCḡP°PīPμPIC,PēC‡PSP° PiCḡCíPīP°. P°PsCḡPjPsPSPē
CíC,P°C,PμPIPēC... P·P°P»PsP· C- PīCḡPμPīP°CḡP°C,Pē, CḡPeC- P·P°CíC,PsCíPμPICíCḡC,CH
PīCḡPē PīP°C,PsP»PsPiC-C— CíC,P°C,PμPIPsC— CíPēCíC,PμPjPē. P°PμCíC,P°PiPμPSPē.
PμPsC...C-PrPSC- PīCḡPμPiPSP°PrC-C°PSCí. PḡPsPr PḡPḡPḡ G03D B01.

$\text{P}\mu\text{C}\eta\text{PsPIP}\mu\text{PrP}\mu\text{PSPs}$ $\text{C}\eta\text{P}^\circ\text{PSPrPsPjC-P}\cdot\text{PsPIP}^\circ\text{PSP}\mu$, $\text{PIC-PrPeC}\eta\text{P}\ddot{\text{e}}\text{C},\text{P}\mu$,
 $\text{P}\pm\text{P}^\circ\text{PiP}^\circ\text{C},\text{PsC}\dagger\text{P}\mu\text{PSC},\text{C}\eta\text{PsPIP}\mu$ $\text{PrPsC}\ddot{\text{I}}\text{P}\gg\text{C-PrP}\P\mu\text{PSPSC}\ddot{\text{I}}\text{P}\cdot\text{P}^\circ$ $\text{C}\acute{\text{r}}\text{C}\ddagger\text{P}^\circ\text{C}\ddot{\text{I}}\text{C},\text{C}\eta$ $\text{PrPIPsC}\dots$
 $\text{P}\ddot{\text{I}}\text{P}^\circ\text{C}\eta\text{P}^\circ\text{P}\gg\text{P}\mu\text{P}\gg\text{C}\eta\text{PSP}\ddot{\text{e}}\text{C}\dots$ $\text{PiC}\eta\text{C}\acute{\text{r}}\text{P}\ddot{\text{I}}$ $\text{PrP}\gg\text{C}\ddot{\text{I}}$ $\text{P}\ddot{\text{I}}\text{PsC}\eta\text{C-PIPSC}\ddot{\text{I}}\text{PSPSC}\ddot{\text{I}}$
 $\text{P}\mu\text{C},,\text{P}\mu\text{PeC},\text{P}\ddot{\text{e}}\text{PIPSPsC}\ddot{\text{I}}\text{C},\text{C-},$ $\text{P}\pm\text{P}\mu\text{P}\cdot\text{P}\ddot{\text{I}}\text{P}\mu\text{PeP}\ddot{\text{e}}$ C- $\text{P}\ddot{\text{I}}\text{P}\mu\text{C}\eta\text{P}\mu\text{PSPsC}\ddot{\text{I}}\text{P}\ddot{\text{e}}\text{PjPsC}\ddot{\text{I}}\text{C},\text{C-}$
 $\text{PrP}\ddot{\text{e}}\text{PrC}\eta\text{PsPiP}\mu\text{C}\ddot{\text{I}}\text{C},\text{P}\mu\text{C}\eta\text{PsPSC}\acute{\text{r}}$ $\text{PrP}\gg\text{C}\ddot{\text{I}}$ $\text{P}\ddot{\text{I}}\text{P}\mu\text{C}\eta\text{PsC}\eta\text{P}^\circ\text{P}\gg\text{C}\eta\text{PSPsPiPs}$
 $\text{P}\cdot\text{P}^\circ\text{C}\ddot{\text{I}}\text{C},\text{PsC}\ddot{\text{I}}\text{C}\acute{\text{r}}\text{PIP}^\circ\text{PSPSC}\ddot{\text{I}}$ PI $\text{PrPsP}\cdot\text{C-}$ 30 PjPi PSP° $\text{PrPsP}\pm\text{C}\acute{\text{r}}$ C,P°
 $\text{C-PSC},\text{C}\eta\text{P}^\circ\text{PIP}^\circ\text{PiC-PSPP}^\circ\text{P}\gg\text{C}\eta\text{PSPsPiPs}$ $\text{P}\ddot{\text{I}}\text{C}\eta\text{PsPiP}\mu\text{C}\ddot{\text{I}}\text{C},\text{P}\mu\text{C}\eta\text{PsPSC}\acute{\text{r}}$ PI
 $\text{P}\gg\text{C-PeP}^\circ\text{C}\eta\text{C}\acute{\text{r}}\text{C}\eta\text{PeC-PN}\ddot{\text{e}}$ $\text{C},,\text{PsC}\eta\text{PjC-}$ 8% $\text{PiP}\mu\text{P}\gg\text{C}\eta$ $(\text{P}\eta\text{C}\eta\text{P}\ddot{\text{e}}\text{PSPsPS})$ PI $\text{PrPsP}\cdot\text{C-}$ 90 PjPi PSP°
 $\text{PrPsP}\pm\text{C}\acute{\text{r}}$ $\text{PrP}\gg\text{C}\ddot{\text{I}}$ $\text{P}\ddot{\text{I}}\text{C-PrC},\text{C}\eta\text{P}\ddot{\text{e}}\text{PjPeP}\ddot{\text{e}}$ $\text{P}\gg\text{C}\eta\text{C},\text{P}\mu\text{C-PSPsPIPsC-}$ $\text{C},,\text{P}^\circ\text{P}\cdot\text{P}\ddot{\text{e}}$ $\text{P}\ddot{\text{I}}\text{C}\eta\text{P}\ddot{\text{e}}$

P·P°CíC,PsCíCíPíP°PSPSC- C,PµC...PSPsP»PsPiC-PN° P·P°PíP»C-PrPSPµPSPSCí in vitro (LOTUS P†P†).

*PµP»C-PSC-C†PSC- PrPsCíP»C-PrP¶PµPSPSCí LOTUS P† C- LOTUS P†P†
PíC-PrC,PIPµC¶PrPëP»Pë PSPëP¶C†PµP·P°P·PSP°C†PµPSPµ.*

P“PsP»PsPIPSCí PjPµC,Cí PrPsCíP»C-PrP¶PµPSCí бґ” PrPsPeP°P· PSPµ PjPµPSCëPsC—
PµC,,PµPeC,PëPIPSPsCíC,C- PíPµC¶PsC¶P°P»CHPSPsPiPs PrPëPrC¶PsPiPµCíC,PµC¶PsPSCí PI
PíPsC¶C-PIPSCíPSPSC- P· C-PSC,C¶P°PIP°PiC-PSP°P»CHPSPëPj
PjC-PeC¶PsPSC-P·PsPIP°PSPëPj PíC¶PsPiPµCíC,PµC¶PsPSPsPj P· C,PsC†PePë P·PsC¶Cí
PSP°C¶PIPSPsCíC,C- CíPµC¶C†PµPIPëC... CíPePsC¶PsC†PµPSCí Cí PíP»PsPrP° PSP° 12-PjCí
C,PëP¶PSC- PíPµCíC,P°C†C-C— (10-PN° C,PëP¶PrPµPSCí PIP°PiC-C,PSPsCíC,C-) бґ” P±CíP»Ps
PrPsCíC¶PiPSCíC,Ps.

PJ PrPsCíP»C-PrP¶CíPíP°PSC-PN° PíPsPíCíP»CíC†C-C— PíP°C†C-C”PSC,C-PI C†P°CíC,PsC,P°
PSP°CíC,P°PSPSCí PIP°PiC-C,PSPsCíC,C-, PíC-PrC,PIPµC¶PrP¶PµPSPsC— PSP° 12-PjCí
C,PëP¶PSC- PíPµCíC,P°C†C-C— (10-PN° C,PëP¶PrPµPSCí PIP°PiC-C,PSPsCíC,C-),
CíC,P°PSPsPiPëP»P° 37,6 % C- 33,1 % (LOTUS P†) C,P° 36,7 % C- 34,7 % (LOTUS II).
P C-P·PSPëC†C¶PI C†P°CíC,PsC,C- PSP°CíC,P°PSPSCí PIP°PiC-C,PSPsCíC,C- PjC-P¶
PrPIPsPjP° PíC¶CíPíP°PjPë CíC,P°PSPsPiPëP»P° 4,7 (95 % P”P†, -1,2; 10,6) (LOTUS P†) C,P° 2,0
(95 % P”P†, -4,0; 8,0) (LOTUS II).

PJ PIPëP±C-C¶C†C- CíCíP±бґ™ C”PeC,C-PI PrPsCíP»C-PrP¶PµPSPSCí PrP»C¶ PsC†C-PSPëPë
P· P±PµP·PíPµPePë (1029 CíCíP±бґ™ C”PeC,C-PI (LOTUS P†) C- 1030 CíCíP±бґ™ C”PeC,C-PI
(LOTUS P†P†), C¶PeC- PsC,C¶PëPjP°P»Pë PíC¶PëPSP°PN°PjPSC- PsPrPSCí PrPsP·Cí
PrPsCíP»C-PrP¶CíPíP°PSPsPiPs PíC¶PµPíP°C¶P°C,Cí) PIPëPíP°PrPePë PSPµP±P°P¶P°PSPëC...
C¶PIPëC%, C%Ps PIPëPSPëPeP»Pë PíC-Pr C†P°Cí C,PµC¶P°PiC-C— (TEAE), PíC¶Ps C¶PeC-
PíPsPIC-PrPsPjP»C¶P»PsCíC¶ PSP°PN°C†P°CíC,C-CëPµ, P±CíP»Pë C-PrPµPSC,PëC†PSPëPjPë PI
PsP±PsC... PrPsCíP»C-PrP¶CíPíP°PSPëC... PíC¶CíPíP°C....

PJ P·PIбґ™ C¶P·PeCí P· C...P°C¶P°PeC,PµC¶PsPj PrPsCíP»C-PrP¶CíPíP°PSPsPiPs
PíPsPeP°P·P°PSPSCí C,P° PrPsCíP»C-PrP¶CíPíP°PSPsC— PíPsPíCíP»CíC†C-C—
PíP°C†C-C”PSC,C-PI PíPµPIPSP° PeC-P»CHPeC-CíC,CH C¶P°PSPSC-C...
P°P±PsC¶C,C-PI/PIPëPePëPrPSC-PI C” PsC†C-PeCíPíP°PSPsC¶, PsCíPsP±P»PëPIPs PrPs 12-PiPs
C,PëP¶PSCí PíPµCíC,P°C†C-C— (10-PiPs C,PëP¶PSCí PIP°PiC-C,PSPsCíC,C-),
PsCíPeC-P»CHPePë PíC¶PsPiPSPsP·PsPIP°PSPëPN° PíPsPeP°P·PSPëPe C†P°CíC,PsC,Pë
PSP°CíC,P°PSPSCí PIP°PiC-C,PSPsCíC,C- Cí C†PµPN° PíPµC¶C-PsPr CíC,P°PSPsPiPëC,CH
P±P»PëP·CHPePs 35 %.

PµC¶PsC,,C-P»CH P±PµP·PíPµPePë, C%Ps CíPíPsCíC,PµC¶C-PíP°PICíC¶ PI PsP±PsC...
PrPsCíP»C-PrP¶PµPSPSCíC... LOTUS, PIC-PrPíPsPIC-PrP°PI PsC†C-PeCíPíP°PSPsPjCí,
PIC¶P°C...PsPICíC¶C†Pë PICíC,P°PSPsPiP»PµPSPëPN° PíC¶PsC,,C-P»CH P±PµP·PíPµPePë
PrPëPrC¶PsPiPµCíC,PµC¶PsPSCí, P° C,P°PePsP¶ PrPsCíP»C-PrP¶CíPíP°PSCí
PíPsPíCíP»CíC†C-C¶ PíP°C†C-C”PSC,C-PI C- PrPsCíP»C-PrP¶CíPíP°PSPµ PíPsPeP°P·P°PSPSCí.

PαP°C¶PjP°PePsPeC-PSPµC,PëPeP°.

PһP±CíPsC¶P±C†C-C¶

PµC-CíP»C¶ PíPµC¶PsC¶P°P»CHPSPsPiPs PíC¶PëPN°PsPjCí PrPëPrC¶PsPiPµCíC,PµC¶PsPSCí
Cí C,,PsC¶PjC- C,P°P±P»PµC,PsPe, PíPeC¶PëC,PëC... PíP»C-PIPePsPiPsC¶
PsP±PsP»PsPSPePsC¶, PIC-PS CëPIPëPrPePs P°P±CíPsC¶P±CíC”C,CHCíC¶.

P'PëPIPuPrPuPSPSCI

РμCḡPsC, PëPīPsPeP°P·P°PSPSCḡ.

- PḡPμPrC-P°PiPSPsCḡC, PsPIP°PSP° PIP°PiC-PSP°P»CHḡPSP° PeCḡPsPIPsC, PμC‡P°;
- PSP°CḡPIPSC- CḡPμCḡPNḡPsP·PSC- P·P°C...PIPsCḡCḡPIP°PSPSCḡ PīPμC‡C-PSPePë P°P±Ps PSP°CḡPIPSC-CḡC, CHḡ CḡPμCḡPNḡPsP·PSPëC... P·P°C...PIPsCḡCḡPIP°PSCḡ PīPμC‡C-PSPePë Cḡ PjPëPSCḡP»PsPjCḡ, CḡPeC%Ps PīPsPeP°P·PSPëPePë C,,CḡPSPeC‡C-C— PīPμC‡C-PSPePë PSPμ PSPsCḡPjP°P»C-P·CḡPIP°P»PëCḡCḡ;
- CḡP»C-Pr PICḡP°C...PsPICḡPIP°C, Pë PīCḡPsC, PëPīPsPeP°P·P°PSPSCḡ PrP»Cḡ PμCḡC, CḡPsPiPμPSC-PI, CḡPeC%Ps C—C... P·P°CḡC, PsCḡPsPICḡPIP°C, Pë Cḡ PePsPjP±C-PSP°C‡C-C— P· PīCḡPsPiPμCḡC, P°PiPμPSP°PjPë, C, P°PePëPjPë CḡPe PrPëPrCḡPsPiPμCḡC, PμCḡPsPS;
- PICḡC, P°PSPsPIP»PμPSP° PiC-PīPμCḡC‡CḡC, P»PëPIC-CḡC, CHḡ PrPs P°PeC, PëPIPSPsC— CḡPμC‡PsPIPëPSPë P°P±Ps PrPs P±CḡPrCHḡ-CḡPePsPiPs C-PSC€PsPiPs PePsPjPīPsPSPμPSC, P° PīCḡPμPīP°CḡP°C, Cḡ;
- PICḡC, P°PSPsPIP»PμPSC- P°P±Ps PīC-PrPsP·CḡCḡPIP°PSC- PīCḡPsPiPμCḡC, P°PiPμPSP·P°P»PμPḡPSC- PSPsPIPsCḡC, PIPsCḡPμPSPSCḡ;
- PjPμPSC-PSPiC-PsPjP° P°P±Ps PjPμPSC-PSPiC-PsPjP° PI P°PSP°PjPSPμP·C-.

P>C-PeCḡPIP°PSPSCḡ P· PjPμC, PsCḡ PīC-PrC, CḡPëPjPePë P»CḡC, PμC—PSPsPIPsC— C,,P°P·Pë PīCḡPë P·P°CḡC, PsCḡCḡPIP°PSPSC- PrPsPīPsPjC-PḡPSPëC... CḡPμPīCḡPsPrCḡPeC, PëPIPSPëC... C, PμC...PSPsP»PsPiC-PNḡ (P" P Pḡ) CḡP»C-Pr PīCḡPëPīPëPSPëC, Pë, CḡPeC%Ps PrC-P°PiPSPsCḡC, PsPIP°PSPëPNḡ P°P±PsCḡC,/PIPëPePëPrPμPSCḡ.

P°P·P°C" PjPsPrC-Cḡ P· C-PSC€PëPjPë P»C-PeP°CḡCḡCHḡPePëPjPë P·P°CḡPsP±P°PjPë C, P° C-PSC€C- PIPëPrPë PIP·P°C" PjPsPrC-PNḡ.

P" P°PSC- PrPsCḡP»C-PrPḡPμPSCḡ C-n vitro CḡPIC-PrC‡P°C, CHḡ, C%Ps PsCḡPSPsPIPSPëPNḡ C€P»CḡC... PjPμC, P°P±PsP»C-P·PjCḡ, P·P°PIPrCḡPePë CḡPePsPjCḡ CḡC, PIPsCḡCḡC" C, CHḡCḡCḡ PīPsP»PsPIPSPëPNḡ C,,P°CḡPjP°PePsP»PsPiC-C‡PSPs P°PeC, PëPIPSPëPNḡ PjPμC, P°P±PsP»C-C, 20α-PrPëPiC-PrCḡPsPrPëPrCḡPsPiPμCḡC, PμCḡPsPS (P"P"P"), PeP°C, P°P»C-P·CḡC" C, CHḡCḡCḡ P°P»CHḡPrPsPePμC, PsCḡPμPrCḡPeC, P°P·PsCḡ 1Pḡ (AKR 1C) Cḡ C‡PëC, PsP·PsP»C- P»CḡPrPëPSPë. PḡP°CḡC-PIPSC- C-P· C‡PëC, PsP·PsP»CHḡPSPëPj PjPμC, P°P±PsP»C-P·PjPsPj PjPμC, P°P±PsP»C-C‡PSC- PīPμCḡPμC, PIPsCḡPμPSPSCḡ P·PrC-PNḡCḡPSCḡCḡC, CHḡCḡCḡ C-P·PsC,,PμCḡPjPμPSC, P°PjPë C‡PëC, PsC...CḡPsPjCḡ P 450 (CYP), PjP°PNḡPḡPμ PIPëPSCḡC, PePsPIPs C-P·PsC,,PμCḡPjPμPSC, PsPj CYP3Pḡ4, C%Ps CḡPīCḡPëC‡PëPSCḡC" CḡC, PIPsCḡPμPSPSCḡ PrPμPeC-P»CHḡPePsC... PSPμP·PSP°C‡PSPëC... PjPμC, P°P±PsP»C-C, C-PI. P"PsP»PsPIPSPëPNḡ P°PeC, PëPIPSPëPNḡ PjPμC, P°P±PsP»C-C, P"P"P" C" CḡCḡP±CḡC, CḡP°C, PsPj PrP»Cḡ PjPμC, P°P±PsP»C-C‡PSPsPiPs PīPμCḡPμC, PIPsCḡPμPSPSCḡ P·P° PrPsPīPsPjPsPiPsCḡ CYP3Pḡ4. PḡPsPjCḡ PjPμC, P°P±PsP»C-P·Pj PrPëPrCḡPsPiPμCḡC, PμCḡPsPSCḡ C- P"P"P" PjPsPḡPμ PīCḡPëCḡPePsCḡCḡPIP°C, PëCḡCḡ PīCḡPë PsPrPSPsC‡P°CḡPSPsPjCḡ PīCḡPëPNḡPsPjC- CḡPμC‡PsPIPëPS, C%Ps C-PSPḡCḡPeCḡCḡC, CHḡ C,,PμCḡPjPμPSC, Pë C‡PëC, PsC...CḡPsPjCḡ P 450, C, P°PePëC... CḡPe P°PSC, PëPePsPSPICḡP»CHḡCḡP°PSC, Pë (PSP°PīCḡPëPeP»P°Pr

C,,PμPSPsP±P°CḡP±C-C,P°P», C,,PμPSC-C,PsC—PS, PēP°CḡP±P°PjP°P·PμPīC-PS),
PīCḡPsC,PēPjC-PēCḡPsP±PSC- PīCḡPμPīP°CḡP°C,Pē (PSP°PīCḡPēPēP»P°Pr
CḡPēC,,P°PjPīC-C†PēPS, CḡPēC,,P°P±C†C,PēPS, PSPμPIC-CḡP°PīC-PS, PμC,,P°PIC-CḡPμPSC†)
C,P° C,,C-C,PsPīCḡPμPīP°CḡP°C,Pē, C%Ps PjC-C†C,C†C,CH P·PIC-CḡPsP±C-PNē (*Hypericum perforatum*), CēP°PIP»C-Cḡ P°P±Ps PīC-PSPePīPs P±C-P»PsP±P°.

P PēC,PsPSP°PIC-Cḡ C,P° PSPμP»C,,C-PSP°PIC-Cḡ PIC-PrPsPjC- C†Pe C†PēP»CHPSC-
C-PSPiC-P±C-C,PsCḡPē C,,PμCḡPjPμPSC,C-PI C†PēC,PsC...CḡPsPjC†,
PrPμPjPsPSC†C,CḡC†CḡC,CH C,,PμCḡPjPμPSC,PsC-PSPrC†PeC†CḡC†C-
PIP»P°C†C,PēPIPsC†C,C- PīCḡPē PsPrPSPsC†P°C†PSPsPjC† P·P°C†C,PsC†C†PIP°PSPSC- P·C-
C†C,PμCḡPsC—PrPSPēPjPē PīPsCḡPjPsPSP°PjPē. PḡP»C-PSC-C†PSPs PīC-PrPIPēC%PμPSPēPNē
PjPμC,P°P±PsP»C-P·Pj PrPēPrCḡPsPīPμC†C,PμCḡPsPSC† PjPsP¶Pμ PīCḡPēP·PIPμC†C,Pē PrPs
P·PSPēP¶PμPSPSC† PμC,,PμPeC,C†.

P°PsC†P»C-PrP¶PμPSPSC† C-n vitro PīPsPeP°P·P°P»Pē, C%Ps PrPēPrCḡPsPīPμC†C,PμCḡPsPS
C,P° P°P°P° C† PeP»C-PSC-C†PSPs P·PSP°C†C†C%PēC... PePsPSC†PμPSC,CḡP°C†C-C†C... PSPμ
PīCḡPēPīPSC-C†C†CḡC,CH C,P° PSPμ C-PSPrC†PeC†CḡC,CH C,,PμCḡPjPμPSC,Pē
C†PēC,PsC...CḡPsPjC† P 450, C%Ps P±PμCḡC†C,CH C†C†P°C†C,CH C† PjPμC,P°P±PsP»C-P·PjC-
P»C-PēP°CḡC†CHPePēC... PīCḡPμPīP°CḡP°C,C-PI.

PhC†PsP±P»PēPIPsC†C,C- P·P°C†C,PsC†C†PIP°PSPSC†.

PμPμCḡPμPr PīPsC†P°C,PePsPj P·P°C†C,PsC†C†PIP°PSPSC† PrPēPrCḡPsPīPμC†C,PμCḡPsPSC†
PrP»C† P»C-PēC†PIP°PSPSC† PīP°C,PsP»PsPīC-C†PSPsC— PeCḡPsPIPsC,PμC†C- C†P»C-Pr
PIPēPeP»CḡC†PēC,Pē PsCḡPīP°PSC-C†PSC† PīCḡPēC†PēPSC† PeCḡPsPIPsC,PμC†C-.

Pj PīPμCḡCēC- PjC-C†C†C†C- P»C-PēC†PIP°PSPSC† PjPsP¶C†C,CH PIPēPSPēPeP°C,Pē
PīCḡPsCḡPēPIPsC- PeCḡPsPIPsC,PμC†C- P°P±Ps PeCḡPsPīPḡ™ C†PSPēC†C,C-
PIPēPrC-P»PμPSPSC†. PīPeC%Ps PīCḡPsCḡPēPIPsP° PeCḡPsPIPsC,PμC†P° P°P±Ps
PeCḡPsPīPḡ™ C†PSPēC†C,C- PIPēPrC-P»PμPSPSC† PīCḡPsPrPsPIP¶C†CḡC,CH
PIPēPSPēPeP°C,Pē C†PμCḡPμP· PrPμC†PePēPNē C†P°C† P»C-PēC†PIP°PSPSC† P°P±Ps
PīCḡPsPrPsPIP¶C†CḡC,CHC†C† PīC-C†P»C† P·P°PeC-PSC†PμPSPSC† P»C-PēC†PIP°PSPSC†,
C†P»C-Pr PIC†C,P°PSPsPIPsC,Pē PīCḡPēC†PēPSC†, PI C,PsPjC† C†PēC†P»C-, C† PIPēPīP°PrPeC†
PSPμPsP±C...C-PrPSPsC†C,C-, PIPēPeP»CḡC†PēC,Pē P·P»PsC†PeC-C†PSPμ
PSPsPIPsC†C,PIPsCḡPμPSPSC† PμPSPPrPsPjPμC,CḡC-C† CēP»C†C...PsPj
PīCḡPsPIPsPμPrPμPSPSC† P±C-PsPīC†C-C— PμPSPPrPsPjPμC,CḡC-C†.

PīPeC%Ps P±C†PrCH-C†PePμ P· PSPēP¶C†PμPSP°PIPμPrPμPSPēC... PīPsCḡC†CēPμPSCḡ
PIC-PrP±C†PIP°C,C,CHC†C† PIPīPμCḡCēPμ P°P±Ps PīPsPīC-CḡCēC†C,C,CHC†C† PīC-Pr
C†P°C† P·P°C†C,PsC†C†PIP°PSPSC† PīCḡPμPīP°CḡP°C,C†, PjP°C" P±C†C,Pē
CḡPsP·PīP»C†PSC†C,Ps PīPēC,P°PSPSC† PīCḡPs PīCḡPēPīPēPSPμPSPSC† P»C-PēC†PIP°PSPSC†:

- PSP°PrP·PIPēC†P°PNēPSPs C†PēP»CHPSPēPNē PīPsP»PsPIPsPēPNē P±C-P»CH,
PjC-PīCḡPμPSCḡ P°P±Ps C†PēPjPīC,PsPjPē, C†PeC- PjPsP¶C†C,CH PIPēP°P·C†PIP°C,Pē PSP°
C-CēPμPjC-Cḡ PīPsP»PsPIPsPēPīPs PjPsP·PeC†;
- P·PSP°C†PSPμ PīC-PrPIPēC%PμPSPSC† P°CḡC,PμCḡC-P°P»CHPSPsPīPs C,PēC†PeC†;
- PīPsC†PIP° PIPμPSPsP·PSPsC— C,CḡPsPjP±PsPμPjP±PsP»C-C—.

Pj CḡP°P·C- P·PIPēC†PSPsPīPs P°P±Ps P·P°PīCḡPsP·P»PēPIPsPīPs PIPēPePēPrPSC†

PSP_μPsP±C...C-PrPSPs PIPëP·PSP°C±PëC, Pë C- PìP_μC₇P_μPIC-C₇C₁C, Pë PìC-Pr C±P°Cí
P»C-PeCíPIP°PSPSC₁ P¶PëC, C, C”P·PrP°C, PSC-CíC, C₇ PìP»PsPrP°, C%₀PsP±
PìP_μC₇P_μPePsPSP°C, PëCíC₁C, C%₀Ps PIP°PìC-C, PSC-CíC, C₇ C, C₇PëPIP°C” C- P_μPjP±C₇C-PsPS
P¶PëPIPëPN₀.

PŸC, P°PSPë, C%₀Ps PìPsC, C₇P_μP±CíC₇C, C₇ PSP°PìP»C₁PrCí

P’C-PrPsPjPs, C%₀Ps PSP° PSP°CíC, CíPìPSC- C₇C-PrPeC-CíPSC- CíC, P°PSPë PjPsP¶CíC, C₇
PIPìP»PëPIP°C, Pë CíC, P°C, P_μPIC- PìPsC₇PjPsPSPë, C- C, PsPjCí PìC-Pr C±P°Cí
PIP°PìC-C, PPS₁CíC, C- P°P±Ps PìC₇Pë P·P°CíC, PsCíCíPIP°PSPSC- CíC, P°C, P_μPIPëC...
PìPsC₇PjPsPSC-PI PjPsP¶P_μ P·B₇TM C₁PIPëC, PëCíC₁C P°P±Ps PìPsPìC-C₇CëPëC, PëCíC₁C:
C...PsP»P_μCíC, P°C, PëC±PSP° P¶PsPIC, C₁PPSPëC±C₁C, PìP_μC₇PìP_μCí PIP°PìC-C, PSPëC...,
C, C₁PP¶PePëPN₀ CíPIP_μC₇P±C-P¶, PsC, PsCíPëP»P_μC₇PsP°, PìPsC₇C, C-C₇C-C₁C,
PrP_μPìC₇P_μCíC-C₁C, P° P°PSPsPjP°P»C₇HPSC- PìPsPeP°P·PSPëPePë C, CíPSPeC±C-C—
PìP_μC±C-PSPePë, CíPìC₇PëC±PëPSP_μPSC- PìPsCíC, C₇PëPj P°P±Ps C...C₇PsPSC-C±PSPëPj
PìP_μC±C-PSPePsPIPëPj P·P°C...PIP₁C₇C₇PIP°PSPSC₁Pj. PìPeC%₀Ps P±CíPrC₇C-C₁PePëPN₀ C-P·
C±PëC... CíC, P°PSC-PI PìC₇PëCíCíC, PSC-PN₀ P°P±Ps P·B₇TM C₁PIP»C₁PICíC₁C C₇P°PSC-CëP_μ,
C, P°/P°P±Ps PìPsPìC-C₇CëCíPIP°PICíC₁C Cí PìP_μC₇C-PsPr PIP°PìC-C, PPS₁CíC, C- P°P±Ps
PìPsPìP_μC₇P_μPrPSC₇PsPìPs P»C-PeCíPIP°PSPSC₁ PìPsC₇PjPsPSP°PjPë, PìP°C±C-C”PSC,
PìPsPIPëPSP_μPS P·PSP°C...PsPrPëC, PëCíC₁C PìC-Pr C₇P_μC, P_μP»C₇HPSPëPj PSP°PìP»C₁PrPsPj.
P₁P_μPsP±C...C-PrPSPs PIC₇P°C...PsPICíPIP°C, Pë, C%₀Ps C±C- CíC, P°PSPë PjPsP¶CíC, C₇
C₇P_μC±PëPrPëPICíPIP°C, Pë P°P±Ps PìPsPìC-C₇CëPëC, PëCíC₁C PìC-Pr C±P°Cí C, P_μC₇P°PìC-C—
PrPëPrC₇PsPìP_μCíC, P_μC₇PsPSPsPj, C, PsPjCí CíP»C-Pr C₇PsP·PìP»C₁PSCíC, Pë
PìC₇PëPìPëPSP_μPSPSC₁C, P_μC₇P°PìC-C— Cí C, P°PePëC... PIPëPìP°PrPeP°C....

P_μP°C±C-C”PSC, PeP°Pj P· PrP_μPìC₇P_μCíC-C”C₇ PI P°PSP°PjPSP_μP·C- CíP»C-Pr
P·PSP°C...PsPrPëC, PëCíC₁C PìC-Pr C₇P_μC, P_μP»C₇HPSPëPj PSP°PìP»C₁PrPsPj. PìPeC%₀Ps
C, C₁PP¶PeP° PrP_μPìC₇P_μCíC-C₁C C₇P_μC±PëPrPëPICíC”, P»C-PeCíPIP°PSPSC₁
PrPëPrC₇PsPìP_μCíC, P_μC₇PsPSPsPj CíP»C-Pr PìC₇PëPìPëPSPëC, Pë.

P₁P°CíC, CíPìPSC- P·P°CíC, P_μC₇P_μP¶P_μPSPSC₁C CíC, PsCíCíC₇C, C₇CíC₁C
P·P°CíC, PsCíCíPIP°PSPSC₁ PìC₇P_μPìP°C₇P°C, Cí P”CíC, P°CíC, PsPS^{B®} P·P°
PìPsPeP°P·P°PSPSC₁Pj B«PrP»C₁ PìPsPìP_μC₇P_μPrP¶P_μPSPSC₁
PìC-PìP_μC₇PìP»P°P·C-C— P_μPSP₁PsPjP_μC, C₇C-C₁C Cí PìP_μC₇C-PsPr
PjP_μPSPsPìP°CíP·PëB»

P”PëPI. C, P°PePsP¶ P·P°CíC, P_μC₇P_μP¶P_μPSPSC₁ PI C-PSCíC, C₇CíPeC±C-C₁C... PrP»C₁
PjP_μPrPëC±PSPsPìPs P·P°CíC, PsCíCíPIP°PSPSC₁ PìC₇P_μPìP°C₇P°C, C-PI
P_μCíC, C₇PsPìP_μPSC-PI.

P”P»C₁C P»C-PeCíPIP°PSPSC₁ PìPsCíC, PjP_μPSPsPìP°CíP·P°P»C₇HPSPëC... CíPëPjPìC, PsPjC-PI
P·P°PjC-CíPSCí PìPsC₇PjPsPSP°P»C₇HPSCí C, P_μC₇P°PìC-C₇ CíP»C-Pr
P·P°CíC, PsCíP₁PICíPIP°C, Pë PIPëPSC₁C, PePsPIPs Cí PIPëPìP°PrPeP°C..., PePsP»Pë
CíPëPjPìC, PsPjPë PSP_μPìP°C, PëPIPSPs PIPìP»PëPIP°C₇C, C₇ PSP° C₁PeC-CíC, C₇ P¶PëC, C, C₁C.
P’ CíCíC-C... PIPëPìP°PrPeP°C... PSP_μPsP±C...C-PrPSPs C₇P_μC, P_μP»C₇HPSPs
PsC±C-PSC₇PIP°C, Pë PePsC₇PëCíC, C₇ C, P° C₇PëP·PëPe P·P°PjC-CíPSPsC—
PìPsC₇PjPsPSP°P»C₇HPSPsC— C, P_μC₇P°PìC-C— PSP_μ PjP_μPSCëP_μ PsPrPSPsPìPs C₇P°P·Cí PSP°
C₇C-Pe. P—P°PjC-CíPSCí PìPsC₇PjPsPSP°P»C₇HPSCí C, P_μC₇P°PìC-C₇ CíP»C-Pr
PìC₇PsPrPsPIP¶CíPIP°C, Pë P»PëCëP_μ PI C, PsPjCí PIPëPìP°PrPeCí, C₁PeC%₀Ps PePsC₇PëCíC, C₇
PìP_μC₇P_μPIP°P¶P°C” C₇PëP·PëPe.

P”PsPeP°P·Pë CíC, PsCíP₁PIPSPs C₇PëP·PëPeC-PI, PìPsPìB₇TM C₁P·P°PSPëC... C-P·

P·P°PjC-Cl'PSPsCñ PiPsCñPjPsPSP°P»CHbPSPsCñ C,PµCñP°PiC-C''Cñ PrP»Cñ
P»C-PeCrPIP°PSPSCñ PiPµCñPµPrC±P°Cl'PSPsC— PjPµPSPsPiP°CrP·Pë, C''
PsP±PjPµPñPµPSPëPjPë. P—P°PIPrCñPePë PSPëP·CHbPePsPjCr CñC-PIPSCñ
P°P±Cl'PsP»CñC, PSPsPiPs CñPëP·PëPeCr Cr PñC-PSPsPe PjPsP»PsPrCëPsPiPs PIC-PeCr
P±P°P»P°PSCl' PjC-Pñ PePsCñPëCl'C, Cñ C,P° CñPëP·PëPePsPj Cr C†C-PNë PiCñCrPiC- PjPsPñPµ
P±CrC,Pë P±C-P»CHbCë Cl'PiCñPëCñC,P»PëPIPePj, PSC-Pñ Cr PñC-PSPsPe Cl'C,P°CñCëPsPiPs
PIC-PeCr.

PñPµPrPëC±PSPµ PsP±Cl'C,PµPñPµPSPSCñ/PiPsPrP°P»CHbCëPµ P»C-PeP°CñCl'CHbPePµ
Cl'PiPsCl'C,PµCñPµPñPµPSPSCñ

PµPµCñPµPr PiPsC±P°C,PePsPj P·P°PjC-Cl'PSPsC— PiPsCñPjPsPSP°P»CHbPSPsC—
C,PµCñP°PiC-C— P°P±Ps PiCñPë C—C— PIC-PrPSPsPiP»PµPSPSC- PiC-Cl'P»Cñ
PiPµCñPµCñPIPë PSPµPsP±C...C-PrPSPs P·C-P±CñP°C,Pë PiPsPiPSPëPNë PsCl'PsP±PëCl'C,PëPNë
C,P° Cl'C-PjPµPNëPSPëPNë P°PSP°PjPSPµP·. P'CñP°C...PsPICrCñC±Pë PrP°PSC- P°PSP°PjPSPµP·Cr,
P° C,P°PePsPñ PiCñPsC,PëPiPsPeP°P·P°PSPSCñ C- P·P°Cl'C,PµCñPµPñPµPSPSCñ PrPs
PiCñPëPNëPsPjCr PiCñPµPiP°CñP°C, Cr, Cl'P»C-Pr PiCñPsPiPµCl'C,Pë PsP±bñ™C''PeC,PëPIPSµ
PsP±Cl'C,PµPñPµPSPSCñ PiP°C†C-C''PSC,PePë (PIPeP»CñC±P°CñC±Pë PsP±Cl'C,PµPñPµPSPSCñ
C,P°P·PsPiPëC... PsCñPiP°PSC-PI C- PsPiP»CñPr PjPsP»PsC±PSPëC... P·P°P»PsP·). PµC-Pr C±P°Cl'
P»C-PeCrPIP°PSPSCñ CñPµPePsPjPµPSPrCrC''C,CHbCl'Cñ PiCñPsPiPsPrPëC,Pë
PiPµCñC-PsPrPëC±PSC- PsPiP»CñPrPë, C±P°Cl'C,PsC,P° C- C...P°CñP°PeC,PµCñ CñPePëC...
P·P°P»PµPñP°C,CHb PIC-Pr C-PSPrPëPIC-PrCrP°P»CHbPSPëC... PsCl'PsP±P»PëPIPsCl'C,PµPNë
PiP°C†C-C''PSC,PePë. P-C-PSPsPe Cl'P»C-Pr PiPsC-PSC,,PsCñPjCrPiP°C,Pë, PiCñPs CñPeC-
P·PjC-PSPë Cr PjPsP»PsC±PSPëC... P·P°P»PsP·P°C... PIPsPSPë PjP°CñC,CHb
PiPsPIC-PrPsPjP»CñC,Pë P»C-PeP°CñPµPIC- P°P±Ps PjPµPrCl'PµCl'C,CñC- (PrPëPI. PSPëPñC±Pµ
P P°Pe PjPsP»PsC±PSPsC— P·P°P»PsP·Pë). PñP±Cl'C,PµPñPµPSPSCñ PjPsP»PsC±PSPëC...
P·P°P»PsP·, PIPeP»CñC±P°CñC±Pë PIC-PrPiPsPIC-PrPSC- PjPµC,PsPrPë
PIC-P·CrP°P»C-P·P°C†C-C—, PSP°PiCñPëPeP»P°Pr, PjP°PjPsPiCñP°C,,C-Cñ, Cl'P»C-Pr
PiCñPsPiPsPrPëC,Pë P·PiC-PrPSPs P· PrC-CñC±PsCñ PiCñP°PeC,PëPePsCñ
Cl'PeCñPëPSC-PSPiCr P· CrCñP°C...CrPiP°PSPSCñPj C-PSPrPëPIC-PrCrP°P»CHbPSPëC...
PeP»C-PSC-C±PSPëC... PiPsC,CñPµP± PiP°C†C-C''PSC,PePë.

P''C-PiPµCñPiP»P°P·C-Cñ C,P° PeP°CñC†PëPSPsPjP° PµPSPrPsPjPµC,CñC-Cñ

Pj PñC-PSPsPe P· C-PSC,P°PeC,PSPsCñ PjP°C,PePsCñ CñPëP·PëPe PIPëPSPëPePSPµPSPSCñ
PiC-PiPµCñPiP»P°P·C-C— C,P° PeP°CñC†PëPSPsPjPë PµPSPrPsPjPµC,CñC-Cñ
PiC-PrPIPëC%CrC''C,CHbCl'Cñ PiCñPë C,CñPëPiP°P»C-PNë PjPsPSPsC,PµCñP°PiC-C—
PµCl'C,CñPsPiPµPSP°PjPë. P—P°P»PµPñPSPs PIC-Pr C,CñPëPiP°P»PsCl'C,C-
P»C-PeCrPIP°PSPSCñ C,P° PrPsP·Pë PµCl'C,CñPsPiPµPSCr, CñPëP·PëPe PjPsPñPµ P±CrC,Pë
PIC-Pr 2 PrPs 12 CñP°P·C-PI PIPëC%PëPNë, PSC-Pñ Cr PñC-PSPsPe, CñPeC- PSPµ
PiCñPëPNëPjP°CñC,CHb PµCl'C,CñPsPiPµPS. PµC-Cl'P»Cñ PiCñPëPiPëPSPµPSPSCñ
C,PµCñP°PiC-C— PµCl'C,CñPsPiPµPSP°PjPë C†PµPNë CñPëP·PëPe P·P±PµCñC-PiP°C''C,CHbCl'Cñ
C%PsPSP°PNëPjPµPSCëPµ CrPiCñPsPrPsPiPñ 10 CñPsPeC-PI. P''PsPrP°PIP°PSPSCñ
PiCñPsPiPµCl'C,P°PiPµPSC-PI, C,P°PePëC... CñPe PrPëPrCñPsPiPµCl'C,PµCñPsPS,
C†PëPeP»C-C±PSPs PiCñPsC,CñPiPsPj C%PsPSP°PNëPjPµPSCëPµ 12 PrPSC-PI PSP°
PjC-Cl'Cl'C†CHb/28-PrPµPSPSPëPNë C†PëPeP» P°P±Ps Cr PIPëPiP»CñPrC- PiPsCl'C,C-PNëPSPsC—
PePsPjP±C-PSPsPiP°PSPsC— PµCl'C,CñPsPiPµPS-PiCñPsPiPµCl'C,P°PiPµPSPsPiPsC—
C,PµCñP°PiC-C— Cr PñC-PSPsPe P·C- P·P±PµCñPµPñPµPSPsCñ PjP°C,PePsCñ PjPsPñPµ
P·P°PiPsP±C-PiC,Pë PSP°PrPjC-CñPSPsPjCr CñPëP·PëPeCr, P°Cl'PsC†C-PNëPsPiP°PSPsPjCr C-P·
P·P°PjC-Cl'PSPsCñ PiPsCñPjPsPSP°P»CHbPSPsCñ C,PµCñP°PiC-C''Cñ P»PëCëPµ
PµCl'C,CñPsPiPµPSP°PjPë.

РμCḡPsCḡPēPIPSC- PeCḡPsPIPsC, PμC†C- C, P° PeCḡPsPIBḡ™ CḡPSPēCḡC, C-
PIPēPrC-P»PμPSPSCḡ PjPsPḡCḡC, Cḡ PIPēPSPēPeP°C, Pē PiCḡPsC, CḡPiPsPj PiPμCḡCēPēC...
PjC-CḡCḡC†C-PI P»C-PeCḡPIP°PSPSCḡ. PīPeC%Ps PiCḡPsCḡPēPIPSC- PeCḡPsPIPsC, PμC†C-
P°P±Ps PeCḡPsPIBḡ™ CḡPSC- PIPēPrC-P»PμPSPSCḡ PIPēPSPēPeP°CḡC, Cḡ PiC-CḡP»Cḡ
PiCḡPēP·PSP°C†PμPSPSCḡ C, PμCḡP°PiC-C- PiCḡPsC, CḡPiPsPj PrPμCḡPePsPiPs C†P°CḡCḡ,
P°P±Ps CḡPeC%Ps PIPsPSPē C, CḡPēPIP°CḡC, Cḡ C- PiC-CḡP»Cḡ P·P°PeC-PSC†PμPSPSCḡ
P»C-PeCḡPIP°PSPSCḡ, PiPsPeP°P·P°PSPμ PiPsPrP°P»CḡCēPμ PsP±CḡC, PμPḡPμPSPSCḡ. PiPμ
PjPsPḡPμ PsP·PSP°C†P°C, Pē, C%Ps PSPμPsP±C...C-PrPSPs PiCḡPsPIPμCḡC, Pē P±C-PsPiCḡC-Cḡ
PμPSPPrPsPjPμC, CḡC-Cḡ, C%PsP± PIPēPeP»CḡC†PēC, Pē P·P»PsCḡPeC-CḡPSC-CḡC, Cḡ.

P P°Pe PjPsP»PsC†PSPsC— P·P°P»PsP·Pē

PjCḡC- PSP°CḡPIPSC- PrP°PSC- PIPeP°P·CḡCḡC, Cḡ PSP° PiC-PrPIPēC%PμPSPēPNḡ CḡPēP·PēPe
CḡP°PeCḡ PjPsP»PsC†PSPsC— P·P°P»PsP·Pē Cḡ PḡC-PSPsPe, CḡPeC- PiCḡPēPNḡPjP°CḡC, Cḡ
PePsPjP±C-PSPsPIP°PSCḡ PμCḡC, CḡPsPiPμPS-PiCḡPsPiPμCḡC, P°PiPμPSPsPICḡ C, PμCḡP°PiC-Cḡ
P°P±Ps P·P°PjC-CḡPSCḡ PiPsCḡPjPsPSP°P»CḡPSCḡ C, PμCḡP°PiC-Cḡ P»PēCēPμ
PμCḡC, CḡPsPiPμPSP°PjPē. PiPμPNḡ CḡPēP·PēPe P·P°P»PμPḡPēC, Cḡ PIC-Pr
C, CḡPēPIP°P»PsCḡC, C- P·P°CḡC, PsCḡCḡPIP°PSPSCḡ P·P°PjC-CḡPSPsC—
PiPsCḡPjPsPSP°P»CḡPSPsC— C, PμCḡP°PiC-C—.

PμPsPjP±C-PSPsPIP°PSP° PμCḡC, CḡPsPiPμPS-PiCḡPsPiPμCḡC, P°PiPμPSPsPIP° C, PμCḡP°PiC-Cḡ:
CḡP°PSPPrPsPjC-P·PsPIP°PSPμ PiP»P°C†PμP±Ps-PePsPSC, CḡPsP»CḡPsPIP°PSPμ
PrPsCḡP»C-PrPḡPμPSPSCḡ WomenBḡ™s Health Initiative (WHI) C, P° PjPμC, P°P°PSP°P»C-P·
PiCḡPsCḡPiPμPeC, PēPIPSPēC... PμPiC-PrPμPjC-PsP»PsPiC-C†PSPēC... PrPsCḡP»C-PrPḡPμPSCḡ
PiPsPeP°P·P°P»Pē PiC-PrPIPēC%PμPSPēPNḡ CḡPēP·PēPe CḡP°PeCḡ PjPsP»PsC†PSPsC—
P·P°P»PsP·Pē Cḡ PḡC-PSPsPe, CḡPeC- PiCḡPēPNḡPjP°CḡC, Cḡ PμCḡC, CḡPsPiPμPS-
PiCḡPsPiPμCḡC, P°PiPμPSPsPICḡ P·P°PjC-CḡPSCḡ PiPsCḡPjPsPSP°P»CḡPSCḡ C, PμCḡP°PiC-Cḡ,
C%Ps PiCḡPsCḡPIP»CḡC”C, CḡCḡCḡCḡ PiCḡPēP±P»PēP·PSPs C†PμCḡPμP· 3 (PIC-Pr 1 PrPs 4)
CḡPsPePē. P PμP·CḡP»CḡC, P°C, Pē CēPēCḡPsPePsPiPs PjPμC, P°P°PSP°P»C-P·Cḡ
PiPsPeP°P·P°P»Pē, C%Ps PiC-CḡP»Cḡ PiCḡPēPiPēPSPμPSPSCḡ P»C-PeCḡPIP°PSPSCḡ C†PμPNḡ
PiC-PrPIPēC%PμPSPēPNḡ CḡPēP·PēPe P·PjPμPSCēCḡC”C, CḡCḡCḡCḡ P· C†P°CḡPsPj C- C%Ps
C†P°Cḡ, PSPμPsP±C...C-PrPSPēPNḡ PrP»Cḡ PiPsPIPμCḡPSPμPSPSCḡ PrPs P±P°P·PsPIPsPiPs
CḡC-PIPSCḡ CḡPēP·PēPeCḡ, P·P°P»PμPḡPēC, Cḡ PIC-Pr C, CḡPēPIP°P»PsCḡC, C-
PiPsPiPμCḡPμPrPSCḡPsPiPs P·P°CḡC, PsCḡCḡPIP°PSPSCḡ P·P°PjC-CḡPSPsC—
PiPsCḡPjPsPSP°P»CḡPSPsC— C, PμCḡP°PiC-C—. PīPeC%Ps C, P°PeP° C, PμCḡP°PiC-Cḡ
C, CḡPēPIP°P»P° PIPiCḡPsPrPsPIPḡ P±C-P»CḡCē PSC-Pḡ 5 CḡPsPeC-PI, C†PμPNḡ CḡPēP·PēPe
PjPsPḡPμ C-CḡPSCḡPIP°C, Pē PiCḡPsC, CḡPiPsPj 10 CḡPsPeC-PI P°P±Ps P±C-P»CḡCēPμ.

P—P°PjC-CḡPSP° PiPsCḡPjPsPSP°P»CḡPSP° C, PμCḡP°PiC-Cḡ, P·PsPeCḡPμPjP°
PμCḡC, CḡPsPiPμPS-PiCḡPsPiPμCḡC, P°PiPμPSPsPIP° PePsPjP±C-PSPsPIP°PSP° C, PμCḡP°PiC-Cḡ,
PiC-PrPIPēC%CḡC” C%C-P»CḡPSC-CḡC, Cḡ PjP°PjPsPiCḡP°C, C-C†PSPēC...
P·PsP±CḡP°PḡPμPSCḡ, C%Ps PjPsPḡPμ PSPμPiP°C, PēPIPSPs PIPiP»PēPSCḡC, Pē PSP°
CḡP°PrC-PsP»PsPiC-C†PSPμ PIPēCḡPIP»PμPSPSCḡ CḡP°PeCḡ PjPsP»PsC†PSPsC—
P·P°P»PsP·Pē.B

P P°Pe CḡC”C†PSPēPeC-PI

P P°Pe CḡC”C†PSPēPeC-PI PIPēPSPēPeP°C” P·PSP°C†PSPs CḡC-PrCēPμ P·P° CḡP°Pe
PjPsP»PsC†PSPsC— P·P°P»PsP·Pē. P·PiC-PrPμPjC-PsP»PsPiC-C†PSC- PrP°PSC-,
PsC, CḡPēPjP°PSC- PI CḡPμP·CḡP»CḡC, P°C, C- CēPēCḡPsPePsPiPs PjPμC, P°P°PSP°P»C-P·Cḡ,
PiPsPeP°P·P°P»Pē PrPμC%Ps PiC-PrPIPēC%PμPSPēPNḡ CḡPēP·PēPe Cḡ PḡC-PSPsPe, CḡPeC-
P·P°CḡC, PsCḡPsPICḡCḡC, Cḡ PjPsPSPsC, PμCḡP°PiC-Cḡ PμCḡC, CḡPsPiPμPSPsPj P°P±Ps

PePsPjP±C-PSP°C†C-Cḡ PμCḡC,CḡPsPiPμPSCḡ P· PīCḡPsPiPμCḡC,P°PiPμPSPsPj CḡPe
P·P°PjC-CḡPSCḡ PiPsCḡPjPsPSP°P»CHḡPSCḡ C,PμCḡP°PiC-Cḡ; C†PμPNḡ CḡPḡP·PḡPe
PīCḡPsCḡPIP»CḡC”C,CHḡCḡCḡ PīCḡPsC,CḡPiPsPj 5 CḡPsPeC-PI P·P°CḡC,PsCḡCḡPIP°PSPSCḡ
C,P° P·PjPμPSCḡCḡC”C,CHḡCḡCḡ P· C†P°CḡPsPj PīC-CḡP»Cḡ PīCḡPḡPīPḡPSPμPSPSCḡ
C,PμCḡP°PiC-C—. P”PμCḡPeC- C-PSCḡC- PrPsCḡP»C-PrPḡPμPSPSCḡ, Cḡ C,PsPjCḡ C†PḡCḡP»C-
WHI, PīPsPeP°P·P°P»Pḡ, C°Ps P·P°CḡC,PsCḡCḡPIP°PSPSCḡ PePsPjP±C-PSPsPIP°PSPsC—
P·P°PjC-CḡPSPsC— PiPsCḡPjPsPSP°P»CHḡPSPsC— C,PμCḡP°PiC-C— PjPsPḡPμ P±CḡC,Pḡ
PīPsPiḡḡ™ CḡP·P°PSPμ P· C,P°PePḡPj CḡP°PjPḡPj P°P±Ps PrPμC°Ps PSPḡPḡC†PḡPj
CḡPḡP·PḡPePsPj (PrPḡPI. B«PμPsP±C-C†PSC- CḡPμP°PeC†C-C—B»).

P’PμPSPsP·PSP° C,CḡPsPjP±PsPμPjP±PsP»C-Cḡ

P—P°PjC-CḡPSP° PiPsCḡPjPsPSP°P»CHḡPSP° C,PμCḡP°PiC-Cḡ PīPsPiḡḡ™ CḡP·P°PSP° P· 1,3-3-
CḡP°P·PsPIPḡPj PīC-PrPIPḡC°PμPSPSCḡPj CḡPḡP·PḡPeCḡ PIPμPSPsP·PSPsC—
C,CḡPsPjP±PsPμPjP±PsP»C-C—, C,PsP±C,Ps C,CḡPsPjP±PsP·Cḡ PiP»PḡP±PsPePḡC... PIPμPS
P°P±Ps P»PμPiPμPSPμPIPSC— PμPjP±PsP»C-C—. P’PḡPSPḡPePSPμPSPSCḡ C,P°PePsC—
PīPsPrC-C— P±C-P»CHḡCḡ C-PjPsPIC-CḡPSPμ PSP° PīPμCḡCḡPsPjCḡ CḡPsC†C-
P·P°PjC-CḡPSPsC— PiPsCḡPjPsPSP°P»CHḡPSPsC— C,PμCḡP°PiC-C—, PSC-Pḡ PīC-P·PSC-CḡPμ.

PμP°C†C-C”PSC,Pḡ P· PIC-PrPsPjPḡPjPḡ C,CḡPsPjP±PsC,,C-P»C-C†PSPḡPjPḡ CḡC,P°PSP°PjPḡ
PjP°CḡC,CHḡ PīC-PrPIPḡC°PμPSPḡPNḡ CḡPḡP·PḡPe CḡPsP·PIPḡC,PeCḡ PIPμPSPsP·PSPsC—
C,CḡPsPjP±PsPμPjP±PsP»C-C—, C- P·P°PjC-CḡPSP° PiPsCḡPjPsPSP°P»CHḡPSP° C,PμCḡP°PiC-Cḡ
PjPsPḡPμ C°Pμ PīC-PrPIPḡC°PḡC,Pḡ C†PμPNḡ CḡPḡP·PḡPe. PḡPsPjCḡ P·P°PjC-CḡPSP°
PiPsCḡPjPsPSP°P»CHḡPSP° C,PμCḡP°PiC-Cḡ PīCḡPsC,PḡPiPsPeP°P·P°PSP° C†C-PNḡ PīCḡCḡPīC-
PīP°C†C-C”PSC,PsPe.

P—P°PiP°P»CHḡPSPsPIPḡP·PSP°PSPḡPjPḡ C,,P°PeC,PsCḡP°PjPḡ CḡPḡP·PḡPeCḡ PIPμPSPsP·PSPsC—
C,CḡPsPjP±PsPμPjP±PsP»C-C— C” P·P°CḡC,PsCḡCḡPIP°PSPSCḡ PμCḡC,CḡPsPiPμPSC-PI,
P»C-C,PSC-PNḡ PIC-Pe, PIPμP»PḡPeC- C...C-CḡCḡCḡPiC-C†PSC- PIC,CḡCḡC†P°PSPSCḡ,
C,CḡPḡPIP°P»P° C-PjPjPsP±C-P»C-P·P°C†C-Cḡ, PsPḡPḡCḡC-PSPSCḡ (P†PḡPḡ > 30 PePi/Pj²),
PIP°PiC-C,PSC-CḡC,CHḡ/PīC-CḡP»CḡCḡPsPrPsPIPḡPNḡ PīPμCḡC-PsPr, CḡPḡCḡC,PμPjPSPḡPNḡ
C†PμCḡPIPSPḡPNḡ PIPsPIC†P°Pe (PḡPḡP’) C,P° CḡP°Pe. PḡPμPjP°C” C”PrPḡPSPsC— PrCḡPjPePḡ
CḡC,PsCḡPsPIPSPs PjPsPḡP»PḡPIPSC— CḡPsP»C- PIP°CḡPḡPePsP·PSPsPiPs
CḡPsP·CḡPḡCḡPμPSPSCḡ PIPμPS Cḡ PIPḡPSPḡPePSPμPSPSC- PIPμPSPsP·PSPsC—
C,CḡPsPjP±PsPμPjP±PsP»C-C—.

PīPe C- Cḡ PICḡC-C... PīC-CḡP»CḡPsPīPμCḡP°C†C-PNḡPSPḡC... PīP°C†C-C”PSC,C-PI,
PīCḡPsC,,C-P»P°PeC,PḡC†PSC- P·P°C...PsPrPḡ PSPμPsP±C...C-PrPSPs CḡPsP·PiP»CḡPSCḡC,Pḡ
PrP»Cḡ P·P°PīPsP±C-PiP°PSPSCḡ PIPμPSPsP·PSPsC— C,CḡPsPjP±PsPμPjP±PsP»C-C—
PīC-CḡP»Cḡ C...C-CḡCḡCḡPiC-C†PSPsPiPs PIC,CḡCḡC†P°PSPSCḡ. PīPeC°Ps PīP»P°PSPsPIPμ
PsPīPμCḡP°C,PḡPIPSPμ PIC,CḡCḡC†P°PSPSCḡ PīPsC,CḡPμP±CḡC” PīPsPrP°P»CHḡCḡPsC—
C,CḡPḡPIP°P»PsC— C-PjPjPsP±C-P»C-P·P°C†C-C—, CḡPμPePsPjPμPSPPrPsPIP°PSPs
C,PḡPjC†P°CḡPsIPs PīCḡPḡPīPḡPSPḡC,Pḡ P·P°PjC-CḡPSCḡ PiPsCḡPjPsPSP°P»CHḡPSCḡ
C,PμCḡP°PiC-Cḡ P·P° 4-6 C,PḡPḡPSC-PI PrPs PsPīPμCḡP°C†C-C—. PμPsPePḡ PḡC-PSPeP° PSPμ
PSP°P±CḡPrPμ PīPsPIPSPsC— CḡCḡC...P»PḡPIPSCḡC-, PIC-PrPSPsPIP»CHḡPIP°C,Pḡ
P»C-PeCḡPIP°PSPSCḡ PSPμ CḡP»C-Pr.

P-C-PSPeP°Pj P±PμP· PsCḡPsP±PḡCḡC,PsPiPs P°PSP°PjPSPμP·Cḡ PIPμPSPsP·PSPsC—
C,CḡPsPjP±PsPμPjP±PsP»C-C—, P°P»Pμ PīCḡPḡ PSP°CḡPIPSPsCḡC,C- PI P°PSP°PjPSPμP·C- Cḡ
CḡPsPrPḡC†C-PI PīPμCḡCḡPsPiPs CḡC,CḡPiPμPSCḡ C,CḡPsPjP±PsP·Cḡ Cḡ PjPsP»PsPrPsPjCḡ
PIC-C†C- PjPsPḡPSP° P·P°PīCḡPsPīPsPSCḡPIP°C,Pḡ CḡPeCḡPḡPSC-PSPi PīC-CḡP»Cḡ
CḡPμC,PμP»CHḡPSPsPiPs PsP±PiPsPIPSCḡPμPSPSCḡ PNḡPsPiPs PsP±PjPμPḡPμPSCḡ (P»PḡCḡPμ

C†P°C†C,PëPSP° C,CḡPsPjP±PsC,,C-P»C-C†PSPëC... PrPμC,,PμPeC,C-PI PjPsP¶Pμ
PIPëC¶IPIP»C¶C,PëC†C¶ P†CḡPë C†PëCḡPëPSC-PSPiC†). P†PëC%Ps PIPëC¶IPIP»PμPSPëPNë
C,CḡPsPjP±PsC,,C-P»C-C†PSPëPNë PrPμC,,PμPeC, P†PsPIBḡ™ C¶P·P°PSPëPNë C-P·
C,CḡPsPjP±PsP·PsPj C† C†P»PμPSC-PI CḡPsPrPëPSPë P°P±Ps PrPμC,,PμPeC,
P†PsPIBḡ™ C¶P·P°PSPëPNë C-P· C†PμCḡPNëPsP·PSPsCḡ P°PSPsPjP°P»C-C"ḡCḡ
(PSP°P†CḡPëPeP»P°Pr PSPμPrPsC†C,P°C,PSC-C†C,Cḡ P°PSC,PëC,CḡPsPjP±C-PSC†,
P†CḡPsC,PμC—PSC† S P°P±Ps P†CḡPsC,PμC—PSC† PḢ, P°P±Ps PePsPjP±C-PSP°C†C-C¶
PrPμC,,PμPeC,C-PI), P·P°PjC-C†PSP° P†PsCḡPjPsPSP°P»CḡPSP° C,PμCḡP°P†C-C¶
P†CḡPsC,PëP†PsPeP°P·P°PSP°.

PJ P¶C-PSPsPe, C¶PeC- PIP¶Pμ PsC,CḡPëPjC†CḡC,Cḡ P†PsC†C,C-PNëPSC†
P°PSC,PëPePsP°P†C†P»C¶PSC,PSC† C,PμCḡP°P†C-Cḡ, C†P»C-Pr CḡPμC,PμP»CḡPSPs
P·PIP°P¶PëC,Pë PePsCḡPëC†C,Cḡ C,P° CḡPëP·PëPe P·P°PjC-C†PSPsC—
P†PsCḡPjPsPSP°P»CḡPSPsC— C,PμCḡP°P†C-C—.

P†PëC%Ps PIPμPSPsP·PSP° C,CḡPsPjP±PsPμPjP±PsP»C-C¶ CḡPsP·PIPëPIP°C"ḡC,CḡC†C¶
P†C-C†P»C¶ P†PsC†P°C,PeC† C,PμCḡP°P†C-C—, P†CḡPëPNëPsPj P†CḡPμP†P°CḡP°C,C† C†P»C-Pr
P†CḡPëP†PëPSPëC,Pë. PμP°C†C-C"ḡPSC,PsPe C†P»C-Pr P†PsC-PSC,,PsCḡPjC†PIP°C,Pë, C%Ps C—Pj
C†P»C-Pr PSPμP†P°PNëPSPs P·PIPμCḡPSC†C,PëC†C¶ PrPs P»C-PëP°CḡC¶ P†CḡPë
PIPëPSPëPePSPμPSPSC- P†PsC,PμPSC†C-PNëPSPëC... C,CḡPsPjP±PsPμPjP±PsP»C-C†PSPëC...
C†PëPjP†C,PsPjC-PI (PSP°P†CḡPëPeP»P°Pr P±PsP»CḡC†PëPNë PSP°P±CḡC¶Pë PSPsP†Pë,
CḡP°P†C,PsP†PëPNë P±C-P»Cḡ C† P†CḡC†PrC¶C..., P·P°PrPëCëPeP°).

P†CëPμPjC-C†PSP° C...PIPsCḡPsP±P° C†PμCḡC†C¶

PJ CḡP°PSPPrPsPjC-P·PsPIP°PSPëC... PePsPSC,CḡPsP»CḡPsPIP°PSPëC...
PrPsC†P»C-PrP¶PμPSPSC¶C... PSPμ PIPëC¶IPIP»PμPSPs PrPsPeP°P·C-PI P·P°C...PëC†C,C† PIC-Pr
C-PSC,,P°CḡPeC,C† PjC-PsPeP°CḡPrP° C† P¶C-PSPsPe P· P°P±Ps P±PμP· C-CëPμPjC-C†PSPsC—
C...PIPsCḡPsP±Pë C†PμCḡC†C¶, C¶PeC- PsC,CḡPëPjC†CḡC,Cḡ PePsPjP±C-PSPsPIP°PSC†
PμC†C,CḡPsP†PμPS-P†CḡPsP†PμC†C,P°P†PμPSPsPIC† C,PμCḡP°P†C-Cḡ P°P±Ps P·P°PjC-C†PSC†
P†PsCḡPjPsPSP°P»CḡPSC† C,PμCḡP°P†C-Cḡ P»PëCëPμ PμC†C,CḡPsP†PμPSP°PjPë.

PμPsPjP±C-PSPsPIP°PSP° PμC†C,CḡPsP†PμPS-P†CḡPsP†PμC†C,P°P†PμPSPsPIP° C,PμCḡP°P†C-C¶:
PIC-PrPSPsC†PSPëPNë CḡPëP·PëPe PIPëPSPëPePSPμPSPSC¶ C-CëPμPjC-C†PSPsC—
C...PIPsCḡPsP±Pë C†PμCḡC†C¶ P†C-Pr C†P°C† P·P°PjC-C†PSPsC—
P†PsCḡPjPsPSP°P»CḡPSPsC— C,PμCḡP°P†C-C— PSPμP·PSP°C†PSPs P†C-PrPIPëC%PμPSPëPNë.
PḡC†PeC-P»CḡPePë P±P°P·PsPIPëPNë P°P±C†PsP»CḡC,PSPëPNë CḡPëP·PëPe
C-CëPμPjC-C†PSPsC— C...PIPsCḡPsP±Pë C†PμCḡC†C¶ P·PSP°C†PSPsCḡ PjC-CḡPsCḡ
P·P°P»PμP¶PëC,Cḡ PIC-Pr PIC-PëC†, PeC-P»CḡPeC-C†C,Cḡ PrPsPrP°C,PePsPIPëC...
PIPëP†P°PrPeC-PI C-CëPμPjC-C†PSPsC— C...PIPsCḡPsP±Pë C†PμCḡC†C¶ C†PμCḡPμP·
P·P°C†C,PsC†C†PIP°PSPSC¶ PμC†C,CḡPsP†PμPSC-PI-P†CḡPsP†PμC†C,P°P†PμPSC-PI PrC†P¶Pμ
PjP°P»P° C† P·PrPsCḡPsPIPëC... P¶C-PSPsPe PSP° PjPsPjPμPSC, PSP°C†C,P°PSPSC¶
PjPμPSPsP†P°C†P·Pë, P°P»Pμ P±C†PrPμ P·CḡPsC†C,P°C,Pë C†B C†C,P°CḡCëPsPjC† PIC-C†C-.

P†CëPμPjC-C†PSPëPNë C-PSC†C†P»CḡC,

PμPsPjP±C-PSPsPIP°PSP° PμC†C,CḡPsP†PμPS-P†CḡPsP†PμC†C,P°P†PμPSPsPIP° C,PμCḡP°P†C-C¶
C,P° PjPsPSPsC,PμCḡP°P†C-C¶ PμC†C,CḡPsP†PμPSP°PjPë P°C†PsC†C-PNëPsPIP°PSP° P· 1-1,5-
CḡP°P·PsPIPëPj P†C-PrPIPëC%PμPSPSC¶Pj CḡPëP·PëPeC† C-CëPμPjC-C†PSPsP†Ps
C-PSC†C†P»CḡC,C†. P·C-PrPSPsC†PSPëPNë CḡPëP·PëPe PSPμ P·PjC-PSCḡC"ḡC,CḡC†C¶ P·
PIC-PëPsPj P°P±Ps C†P°C†PsPj P· PjPsPjPμPSC,C† PSP°C†C,P°PSPSC¶ PjPμPSPsP†P°C†P·Pë.
PμCḡPsC,Pμ, PsC†PeC-P»CḡPePë P±P°P·PsPIPëPNë CḡPëP·PëPe C-PSC†C†P»CḡC,C†

P·PSP°C‡PSPsCḤ PjC-CḤPsCḤ P·P°P»PμP¶PëC,CH PIC-Pr PIC-PeCṛ, P·P°PiP°P»CHbPSPëPNḡ
CḤPëP·PëPe C-PSCṽCṛP»CHbC,Cṛ Cṛ P¶C-PSPsPe, C¶PeC- PiCḤPëPNḡPjP°CḤC,CH
P·P°PjC-CṽPSCṛ PiPsCḤPjPsPSP°P»CHbPSCṛ C,PμCḤP°PiC-CḤ, P·P±C-P»CHbCḤCṛC”C,CHbCṽC¶ P·
PIC-PePsPj.

PḤPμPSC-PSPiC-PsPjP°

PμPsPIC-PrPsPjP»C¶P»PsCṽC¶ PiCḤPs PIPëPSPëPePSPμPSPSC¶ PjPμPSC-PSPiC-PsPj
(PiPsPsPrPëPSPsPePëC... C,P° PjPSPsP¶PëPSPSPëC...) PiCḤPë P·P°CṽC,PSCṽCṛPIP°PSPSC-
PePsPjP±C-PSPsPIP°PSPsC— C,PμCḤP°PiC-C—
PμCṽC,CḤP°PrC-PsP»PsPj/PrPëPrCḤPsPiPμCṽC,PμCḤPsPSPsPj. PμP°C†C-C”PSC,Pë
PiPsPIPëPSPSC- PiPμCḤPμP±CṽPIP°C,Pë PiC-Pr PSP°PiP»C¶PrPsPj PrP»C¶
PIPëC¶PIP»PμPSPSC¶ PsP·PSP°Pe C,P° CṽPëPjPiC,PsPjC-PI PjPμPSC-PSPiC-PsPj
PIC-PrPiPsPIC-PrPSPs PrPs PeP»C-PSC-C‡PSPsC— PiCḤP°PeC,PëPePë. PiPeC%Ps Cṛ
PiP°C†C-C”PSC,P° PrC-P°PiPSPsCṽC,PsPIP°PSPs PjPμPSC-PSPiC-PsPjCṛ, P±CṽPrCHb-C¶PePμ
P»C-PeCṽPIP°PSPSC¶ PrPëPrCḤPsPiPμCṽC,PμCḤPsPSPsPj PSPμPsP±C...C-PrPSPs
PiCḤPëPiPëPSPëC,Pë (PrPëPI. CḤPsP·PrC-P» B«PμCḤPsC,PëPiPsPeP°P·P°PSPSC¶B»).

PμC-CṽP»C¶ PiCḤPëPiPëPSPμPSPSC¶ P»C-PeCṽPIP°PSPSC¶ CṽPiPsCṽC,PμCḤC-PiP°P»PsCṽC¶
P·PjPμPSC¶PμPSPSC¶ PiCṽC...P»PëPSPë.

P”PsPiPsPjC-P¶PSC- CḤPμC‡PsPIPëPSPë

PiPμPNḡ P»C-PeP°CḤCṽCHbPePëPNḡ P·P°CṽC-P± PjC-CṽC,PëC,CH P»P°PeC,PsP·Pë
PjPsPSPsPiC-PrCḤP°C,. PμP°C†C-C”PSC,P°Pj P· CḤC-PrPeC-CṽPSPëPjPë CṽPiP°PrPePsPIPëPjPë
C,,PsCḤPjP°PjPë PSPμPiPμCḤPμPSPsCṽPëPjPsCṽC,C- PiP°P»P°PeC,PsP·Pë,
PSPμPrPsCṽC,P°C,PSC-CṽC,CḤ P»P°PeC,P°P·Pë P°P±Ps CṽPëPSPṽCḤPsPjPsPj PiP»CḤPePsP·Ps-
PiP°P»P°PeC,PsP·PSPsC— PjP°P»CHbP°P±CṽPsCḤP±C†C-C— PSPμ CṽP»C-Pr
P·P°CṽC,PSCṽPsPICṽPIP°C,Pë C†PμPNḡ PiCḤPμPiP°CḤP°C,.

*P—P°CṽC,PSCṽCṽPIP°PSPSC¶ Cṽ PiPμCḤC-PsPr PIP°PiC-C,PSPsCṽC,C- P°P±Ps
PiPsPrCṽPIP°PSPSC¶ PiCḤCṽPrPrCḤ.*

P’P°PiC-C,PSC-CṽC,CHb

P—P° CḤPsP·CḤP°C...CṽPSPeP°PjPë P±C-P»CHbCḤPμ 9 PjC-P»CHbPNḡPsPSC-PI PIP°PiC-C,PSPëC...
P¶C-PSPsPe PiCḤPëPNḡPjP°P»Pë PrPëPrCḤPsPiPμCṽC,PμCḤPsPS. P”PsC,PμPiPμCḤ PSPμ
PIPëC¶PIP»PμPSPs PrPsPeP°P·C-PI CḤPeC-PrP»PëPiPsPiPs PIPiP»PëPICṛ
PrPëPrCḤPsPiPμCṽC,PμCḤPsPSCṛ PiCḤPë P·P°CṽC,PSCṽCṛPIP°PSPSC- Cṽ PiPμCḤC-PsPr
PIP°PiC-C,PSPsCṽC,C-.

PJ P»C-C,PμCḤP°C,CṽCḤC- PsPiPëCṽP°PSPμ PrPsCṽP»C-PrP¶PμPSPSC¶, C¶PePμ
PiPsPeP°P·P°P»Ps, C%Ps P·P°CṽC,PSCṽCṽPIP°PSPSC¶ PrPμC¶PePëC...
PiCḤPsPiPμCṽC,P°PiPμPSC-PI PjPsP¶Pμ P±CṽC,Pë PiPsPiḤḤ™ C¶P·P°PSPμ P·
PiC-PrPIPëC%PμPSPëPj CḤPëP·PëPePsPj PiC-PiPsCṽPiP°PrC-C—. PḤP»Pμ PsCṽPeC-P»CHbPePë
PrPs C†CHbPsPiPs C‡P°CṽCṽ C†Pμ PSPμ P±CṽP»Ps PiC-PrC,PIPμCḤPrP¶PμPSPs PI C-PSCḤPëC...
PrPsCṽP»C-PrP¶PμPSPSC¶C..., PSPμ PjPsP¶PSP° PsCṽC,P°C,PsC‡PSPs PIPëP·PSP°C‡PëC,PëCṽC¶
C%PsPrPs CḤPsP»C- PiCḤPsPiPμCṽC,P°PiPμPSC-PI Cṽ CḤPsP·PIPëC,PeCṛ
PiC-PiPsCṽPiP°PrC-C—. PḤP»C-PSC-C‡PSC- PrPsCṽP»C-PrP¶PμPSPSC¶, PI C¶PePëC...
PsP±PjPμP¶PμPSP° PeC-P»CHbPeC-CṽC,CH P¶C-PSPsPe P»C-PeCṽPIP°P»PëCṽC¶
PrPëPrCḤPsPiPμCṽC,PμCḤPsPSPsPj PSP° CḤP°PSPSC-C... C,PμCḤPjC-PSP°C...

PIP°PiC-C,PSPsCÍC,C-, PSPµ PİPsPeP°P·P°P»Pë PİC-PrPIPëC%PµPSPSCİ ÇĤPëP·PëPeCf.
PĳC-CİPİPePëC... C-PSCëPëC... PµPİC-PrPµPjC-PsP»PsPiC-C‡PSPëC... PrP°PSPëC... PrPsCÍC-
PSPµPjP°C”.

Pj PrPsPeP»C-PSC-C‡PSPëC... PrPsCÍP»C-PrP¶PµPSPSCİC...
PµPjP±CĤC-PsC,,PµC,P°P»CHBPSPsPiPs C,P° PİPsCÍC,PSP°C,P°P»CHBPSPsPiPs ÇĤPsP·PIPëC,PeCf
PµC,,PµPeC,Pë PIC-PrPİPsPIC-PrP°P»Pë C,,P°CĤPjP°PePsP»PsPiC-C‡PSPsPjCf PİCĤPsC,,C-P»CĤ.
PĳPµCÍPİCĤPëCİC,P»PëPIC- PµC,,PµPeC,Pë PIPëPSPëPeP°P»Pë P»PëCëPµ C,PsPrC-, PePsP»Pë
PIPİP»PëPI PİCĤPµPİP°CĤP°C,Cf P·PSP°C‡PSPs PİPµCĤPµPIPëC%CfPIP°PI
PjP°PeCÍPëPjP°P»CHBPSCf PµPeCÍPİPsP·PëC†C-CĤ PrP»Cİ P»CĤPrPëPSPë.

P”PëPrCĤPsPiPµCÍC,PµCĤPsPS PjPsP¶PSP° P·P°CÍC,PsCÍPsPICfPIP°C,Pë PİCĤPsC,CİPİPsPj
PIP°PiC-C,PSPsCÍC,C- P·P° C‡C-C,PePëPjPë PİPsPeP°P·P°PSPSCİPjPë.

PµPµCĤC-PsPr PİPsPrCfPIP°PSPSCİ PİCĤCfPrPrCĤ

PĳPµPjP°C” PrP°PSPëC... PİCĤPs PİCĤPsPSPëPePSPµPSPSCİ PrPëPrCĤPsPiPµCÍC,PµCĤPsPSCf
Cf PİCĤCfPrPSPµ PjPsP»PsPePs. P”PsCÍP»C-PrP¶PµPSCĤ C%PsPrPs
PİCĤPsPSPëPePSPµPSPSCİ PrPëPrCĤPsPiPµCÍC,PµCĤPsPSCf Cf PİCĤCfPrPSPµ PjPsP»PsPePs
PSPµ PİCĤPsPiPsPrPëP»Pë.

P”PsCÍPIC-Pr P·P°CÍC,PsCÍCfPIP°PSPSCİ C-PSCëPëC... PİCĤPsPiPµCÍC,P°PiPµPSC-PI
PIPeP°P·CfC”, C%Ps PİCĤPsPiPµCÍC,P°PiPµPSPë C,P° C—C... PjPµC,P°P±PsP»C-C,Pë
PİCĤPsPSPëPeP°CĤC,CH Cf PİCĤCfPrPSPµ PjPsP»PsPePs PI PjP°P»PëC...
PeC-P»CHPePsCÍC,CİC.... PĳPµPIC-PrPsPjPs, C‡Pë C-CÍPSCfC” ÇĤPëP·PëPe PrP»Cİ
PrPëC,PëPSPë, C,PsPjCf PrPëPrCĤPsPiPµCÍC,PµCĤPsPS PSPµ CÍP»C-Pr
P·P°CÍC,PsCÍPsPICfPIP°C,Pë Cf PİPµCĤC-PsPr PİPsPrCfPIP°PSPSCİ PİCĤCfPrPrCĤ.

PµPµCĤC,PëP»CHBPSC-CÍC,CH

PĳPµPjP°C” PrPsPeP°P·C-PI, C%Ps PrPëPrCĤPsPiPµCÍC,PµCĤPsPS Cf
C,PµCĤP°PİPµPIC,PëC‡PSPëC... PrPsP·P°C... P·PSPëP¶CfC” C,,PµCĤC,PëP»CHBPSC-CÍC,CH.

*P—PrP°C,PSC-CÍC,CH PIPİP»PëPIP°C,Pë PSP° CëPIPëPrPeC-CÍC,CH ÇĤPµP°PeC†C-C—
PİCĤPë PePµCĤC¿PIP°PSPSC- P°PIC,PsC,ÇĤP°PSCÍPİPsCĤC,PsPj P°P±Ps C-PSCëPëPjPë
PjPµC...P°PSC-P·PjP°PjPë.*

P”CfC,,P°CÍC,PsPS^{B®} PjP°C” PSPµC-CÍC,PsC,PSPëPµ PIPİP»PëPI PSP° P·PrP°C,PSC-CÍC,CH
PePµCĤCfPIP°C,Pë P°PIC,PsPjPsP±C-P»PµPj C- PİCĤP°C†CĤPIP°C,Pë P· PjP°CëPëPSP°PjPë C-
PjPµC...P°PSC-P·PjP°PjPë.

PĳPµC‡P°CÍC,Ps PrPëPrCĤPsPiPµCÍC,PµCĤPsPS PjPsP¶Pµ CÍPİCĤPëC‡PëPSCİC,Pë
PSPµPIPµP»PëPeCf CÍPsPSP»PëPIC-CÍC,CH C,P°/P°P±Ps P·P°PİP°PjPsCĤPsC‡PµPSPSCİ,
PsCÍPsP±P»PëPIPs Cf PİPµCĤCëC- PeC-P»CHPeP° PİPsPrPëPS PİC-CÍP»Cİ PİCĤPëPµPsPjCf.
PÿPsPjCf PePµCĤCfPIP°C,Pë P°PIC,PsPjPsP±C-P»PµPj P°P±Ps PİCĤP°C†CĤPIP°C,Pë P·
PjPµC...P°PSC-P·PjP°PjPë PSPµPsP±C...C-PrPSPs P· PsP±PµCĤPµP¶PSC-CÍC,CH.

PÿPİPsCÍC-P± P·P°CÍC,PsCÍC¿PIP°PSPSCİ C,P° PrPsP·Pë.

P—P°PiC₇PsP·P° PIPëPεPëPrPSCU

PrPsC†P°C,PePsPIP° PrPsP·P°: 4 C,P°P±P»PμC,PePë P"CrC,,P°CÍC,PsPS^{B®} PsPrCḡP°P·Cr,
PiPsC,C-Pj PiPs 1 C,P°P±P»PμC,C†C- P"CrC,,P°CÍC,PsPS^{B®} PePsP¶PSC- 8 PiPsPrPëPS. P"PsP·Pë,
PeCḡP°C,PSC- 10 PjPi PSP° PrPsP±Cr, CÍP»C-Pr CḡC-PIPSPrPjC-CḡPSPs
CḡPsP·PiPsPrC-P»PëC,Pë PiCḡPsC,C†PiPsPj PrPsP±Pë. P PμPePsPjPμPSPPrCrC"C,ChCÍC†C†
PiCḡPëP·PSP°C†PëC,Pë PSP°PNëPIPëC%oCr PrPsP·Cr PSP° PiPsC†P°C,PePsPIPsPjCr PμC,P°PiC-
P»C-PeCrPIP°PSPSC†C.

PiPeC%oPs CÍPëPjPiC,PsPjPë PSPμ P·PSPëPeP°CḡC,Ch P°P±Ps P·PSPsPICr
P·bḡ™ C†PIP»C†CḡC,ChCÍC†C† PiC-Pr C†P°CÍ P»C-PeCrPIP°PSPSC†C, PrPsP·Cr
PSPμPsP±C...C-PrPSPs P·P±C-P»ChCëPëC,Pë PSP° 1 C,P°P±P»PμC,PeCr P"CrC,,P°CÍC,PsPS^{B®}
PePsP¶PSC- 8 PiPsPrPëPS.

PμC-CÍP»C†C C,PsPiPs, C†Pe CÍPëPjPiC,PsPjPë P·PSPëPeP°CḡC,Ch, PμC,,PμPeC,PëPIPSCr
PrPsP·Cr PSPμPsP±C...C-PrPSPs P·P±PμCḡPμPiC,Pë PiCḡPsC,C†PiPsPj PsPrPSPsPiPs
C,PëP¶PSC†C, PiC-CÍP»C†C C†PsPiPs C—C— PjPsP¶PSP° PiPsCÍC,CrPiPsPIPs P·PjPμPSCëPëC,Pë.
PiPeC%oPs CÍPëPjPiC,PsPjPë P·bḡ™ C†PIP»C†CḡC,ChCÍC†C† P·PSPsPICr, P»C-PeCrPIP°PSPSC†C
PjP°C" P±CrC,Pë PSPμPiP°PNëPSPs PIC-PrPSPsPIP»PμPSPμ P· PrPsP·CrPIP°PSPSC†C†C, C†PePμ
PIPëC†PIPëP»PsCÍC†C PμC,,PμPeC,PëPIPSPëPj.

P—PIPëC†PSPëPNë PIPëPePëPrPμPSCḡ

P»C-PeCrPIP°PSPSC†C PSPμPsP±C...C-PrPSPs CḡPsP·PiPsC†P°C,Pë PrPs P·P°C†P°C,C,C†C. 1
C,P°P±P»PμC,PeP° P"CrC,,P°CÍC,PsPS^{B®} PSP° PrPsP±Cr PrPs 20-PiPs C,PëP¶PSC†C
PIP°PiC-C,PSPsCÍC,C-, PiC-CÍP»C†C C†PsPiPs PjPsP¶PSP° PiPsCÍC,CrPiPsPIPs
P·PSPëP¶CrPIP°C,Pë PrPsP·Cr.

PiPeC%oPs CÍPëPjPiC,PsPjPë P·P°PiCḡPsP·Pë PiPμCḡPμCḡPëPIP°PSPSC†C PIP°PiC-C,PSPsCÍC,C-
P·bḡ™ C†PIP»C†CḡC,ChCÍC†C† PiC-Pr C†P°CÍ P»C-PeCrPIP°PSPSC†C, P»C-PeCrPIP°PSPSC†C
CÍP»C-Pr PiCḡPsPrPsPIP¶PëC,Pë, C†Pe C†Pμ PsPiPëCÍP°PSPs Cr PIPëPiP°PrPeCr P·P°PiCḡPsP·Pë
PIPëPePëPrPSC†C.

P"PëCÍC,,CrPSPeC†C-PNëPSP° PjP°C,PePsPIP° PeCḡPsPIPsC,PμC†P°

P"P»C†C P·CrPiPëPSPμPSPSC†C PeCḡPsPIPsC,PμC†C- PiCḡPëP·PSP°C†P°CḡC,Ch 2
C,P°P±P»PμC,PePë PiCḡPμPiP°CḡP°C,Cr P"CrC,,P°CÍC,PsPS^{B®} PSP° PrPsP±Cr PiCḡPsC,C†PiPsPj
5bḡ"7 PrPSC-PI. P'C,CḡP°C,P° PeCḡPsPIC- P·PSP°C†PSPs P·PjPμPSCëCrC"C,ChCÍC†C†
PIPiCḡPsPrPsPIP¶ PrPμPeC-P»ChPePsC... PrPSC-PI. P§PμCḡPμP· PeC-P»ChPeP° PrPSC-PI
PiC-CÍP»C†C P·P°PeC-PSC†PμPSPSC†C C,P°PePsPiPs P»C-PeCrPIP°PSPSC†C
P·bḡ™ C†PIPëC,ChCÍC†C† PeCḡPsPIPsC,PμC†P° PIC-PrPjC-PSPë, PiCḡPs C%oPs
PiP°C†C-C"PSC,PeP° PiPsPIPëPSPSP° P±CrC,Pë PiPsPiPμCḡPμPrP¶PμPSP°.

P— PjPμC,PsCḡ PiCḡPsC,,C-P»P°PeC,PëPePë PiPsPrP°P»ChCëPsPiPs PIPëPSPëPePSPμPSPSC†C
CḡC†CÍPSPSc— PjP°C,PePsPIPsC— PeCḡPsPIPsC,PμC†C- P"CrC,,P°CÍC,PsPS^{B®}
PiCḡPëP·PSP°C†P°C,Pë PiPs 1 C,P°P±P»PμC,C†C- PSP° PrPsP±Cr P· 11-PiPs PiPs 25-PNë
PrPμPSCḡ C†PëPeP»Cr, C†PeC%oPs PSPμPsP±C...C-PrPSPs bḡ" Cr PePsPjP±C-PSP°C†C-C— P·
PμCÍC,CḡPsPiPμPSPsPj CrPiCḡPsPrPsPIP¶ 2bḡ"3 C†PëPeP»C-PI. PμC-CÍP»C†C C†ChPsPiPs
P»C-PeCrPIP°PSPSC†C PjPsP¶PSP° PiCḡPëPiPëPSPëC,Pë P· PjPμC,PsCḡ PiPμCḡPμPIC-CḡPePë
PSPsCḡPjP°P»C-P·P°C†C-C— C†PëPeP»Cr Cr PiP°C†C-C"PSC,PePë.

P'C,PsCḡPëPSPSP° P°PjPμPSPsCḡPμC†C

P'C-Pr 1 PrPs 2 C,P°P±P»PμC,PsPe PiCḡPμPiP°CḡP°C,Cr P"CrC,,P°CÍC,PsPS^{B®} PSP° PrPμPSCḡ P·

11-PiPs PīPs 25-PN₂ PrP_μPSCH C†PēPeP»C₁ PrP»C₁ P·P°P±P_μP·PīP_μC†P_μPSPSC₁
PsPīC,PēPjP°P»CH₂PSPsC— C₁P_μPeC₇P_μC,PsC₇PSPsC— C,C₇P°PSC₁C,,PsC₇PjP°C†C-C—
P_μPSP₁PsPjP_μC,C₇C-C₁, P°PrP_μPePIP°C,PSPs C₁C,PēPjC₁P»CH₂PsPIP°PSPsPiPs
P_μPSP₁PsPiP_μPSPSPēPj P°P±Ps P_μPeP·PsPiP_μPSPSPēPj P_μC₁C,C₇PsPiP_μPSPsPj.

P°P»C₁ PīPsPiP_μC₇P_μPrP₁P_μPSPSC₁ PiC-PiP_μC₇PiP»P°P·C-C— P_μPSP₁PsPjP_μC,C₇C-C₁
C₁ PīP_μC₇C-PsPr PjP_μPSPsPiP°C₁P·Pē

P_μC₇PsC,C₁PiPsPj PePsP₁PSPsPiPs 28-PrP_μPSPSPsPiPs C†PēPeP»C₁ C,P_μC₇P°PīC-C—
P_μC₁C,C₇PsPiP_μPSP°PjPē PiC₇PēPN₂PjP°C,Pē P»PēC€P_μ P_μC₁C,C₇PsPiP_μPS PiC₇PsC,C₁PiPsPj
PīP_μC₇C€PēC... 14 PrPSC-PI, C- PīC₇PsC,C₁PiPsPj PSP°C₁C,C₁PīPSPēC... 14 PrPSC-PI
PiC₇PēPN₂PjP°C,Pē 1 P°P±Ps 2 C,P°P±P»P_μC,PePē, C%₀Ps PjC-C₁C,C₁C,CH 10 PjPi
PrPēPrC₇PsPiP_μC₁C,P_μC₇PsPSC₁, PrPsPrP°C,PePsPIPs PrPs C,P_μC₇P°PīC-C—
P_μC₁C,C₇PsPiP_μPSP°PjPē. Pj C₇P°P·C- PrPsP·C₁PIP°PSPSC₁ 10 PjPi
PrPēPrC₇PsPiP_μC₁C,P_μC₇PsPSC₁ 2 C₇P°P·Pē PSP° PrPsP±C₁ PiC₇PēPN₂PsPj C,P°P±P»P_μC,PsPe
C₁P»C-Pr C₇PsP·PiPsPrC-P»PēC,Pē PiC₇PsC,C₁PiPsPj PrPsP±Pē. P_μC₇PsPIPsC,P_μC†P°
PIC-PrPjC-PSPē P·P°P·PIPēC†P°PN₂ PIPēPSPēPeP°C° PīC-Pr C†P°C₁ P·P°C₁C,PsC₁C₁PIP°PSPSC₁
PrPēPrC₇PsPiP_μC₁C,P_μC₇PsPSC₁.

P—P°C₁C,PsC₁C₁PIP°PSPSC₁ PePsPjP±C-PSPsPIP°PSPsC— C,P_μC₇P°PīC-C—
P_μC₁C,C₇PsPiP_μPSPsPj C,P° PiC₇PsPiP_μC₁C,P°PiP_μPSPsPj C₁ P₁C-PSPsPe C₁
PīPsC₁C,PjP_μPSPsPiP°C₁P·C- PSP_μPsP±C...C-PrPSPs PsP±PjP_μP₁PēC,Pē
PjC-PSC-PjP°P»CH₂PSPsC₇ P_μC,,P_μPeC,PēPIPsC₇ PrPsP·PsC₇ C,P° PSP°PN₂PePsC₇PsC,C€PēPj
C,P_μC₇PjC-PSPsPj, C₁PeC- C₁P·PiPsPrP₁C₁C₇C,CHC₁C₁ P· C,P_μC₇P°PīP_μPIC,PēC†PSPēPjPē
C†C-P»C₁PjPē C,P° C₇PēP·PēPeP°PjPē PrP»C₁ PePsP₁PSPsC— P₁C-PSPePē, P° C,P°PePsP₁
PīP_μC₇C-PsPrPēC†PSPs C₁P»C-Pr PīP_μC₇P_μPiP»C₁PrP°C,Pē PrPsC†C-P»CH₂PSC-C₁C,CH
C,P°PePsPiPs P»C-PeC₁PIP°PSPSC₁ (PrPēPI. B«PhC₁PsP±P»PēPIPsC₁C,C-
P·P°C₁C,PsC₁C₁PIP°PSPSC₁B»).

PŸPiPsC₁C-P± P·P°C₁C,PsC₁C₁PIP°PSPSC₁

P°P»C₁ PīP_μC₇PsC₇P°P»CH₂PSPsPiPs PiC₇PēPN₂PsPjC₁.

P_μC₇Pē P·P°C₁C,PsC₁C₁PIP°PSPSC- PIPēC%₀PēC... PrPsP· C,P°P±P»P_μC,PePē PjP°C₇C,CH
P±C₁C,Pē C₇C-PIPsPjC-C₇PSPs C₇PsP·PiPsPrC-P»P_μPSC- PrP»C₁ PiC₇PēPN₂PsPjC₁
PiC₇PsC,C₁PiPsPj PrPsP±Pē.

P°C-C,Pē.

P°PēPrC₇PsPiP_μC₁C,P_μC₇PsPS PSP_μ P·P°C₁C,PsC₁PsPIC₁C₇C,CH PrPs PīPsC†P°C,PeC₁
PjP_μPSC₁C,C₇C₁P°C†C-PN₂. P°P_μP·PīP_μPeP° C,P° P_μC,,P_μPeC,PēPIPsC-C₁C,CH
P·P°C₁C,PsC₁C₁PIP°PSPSC₁ PrPēPrC₇PsPiP_μC₁C,P_μC₇PsPSC₁ PiC-PrP»C-C,PeP°Pj PIC-PePsPj
PIC-Pr 12 PrPs 18 C₇PsPeC-PI PSP_μ PIC₁C,P°PSPsPIP»P_μPSC-.

P_μP_μC₇P_μPrPsP·C₂PIP°PSPSC₁.

PŸPēPjPiC,PsPjPē.

P°PēPrC₇PsPiP_μC₁C,P_μC₇PsPS C° PiC₇P_μPiP°C₇P°C,PsPj P· PrC₁P₁P_μ PSPēP·CH₂PePsC₇

C,PsPeCfPëC+PSC-CfC,Ch. PŸPëPjPïC,PsPjPë, CŸPeC- C,PµPsCŸPµC,PëC+PSPs PjPsP¶CfC,Ch PIPëPSPëPePSCfC,Pë Cr CŸP°P·C- PïPµCŸPµPrPsP·CfPIP°PSPSCŸ вŸ“ PSCfPrPsC,P°, P±P»CŸPIP°PSPSCŸ, CfPsPSP»PëPIC-CfC,Ch C- P·P°PïP°PjPsCŸPsC+PµPSPSCŸ. PkPµPIC-PrPsPjC- PIPëPïP°PrPePë, PePsP»Pë PïPµCŸPµPrPsP·CfPIP°PSPSCŸ PrPëPrCŸPsPiPµCfC,PµCŸPsPSCf PïCŸPëP·PIPµP»Ps PrPs CëPeC-PrP»PëPIPëC... PSP°CfP»C-PrPeC-PI (PjP°PeCfPëPjP°P»ChPSP° PrPµPSPSP° PrPsP·P°, PïCŸPëPNëPSCŸC,P° P»CŸPrPëPSPsCŸ, CfC,P°PSPsPIPëP»P° 360 PjPi).

P>C-PeCzPIP°PSPSCŸ.

PŸPïPµC+PëC,,C-C+PSPµ P»C-PeCfPIP°PSPSCŸ PSPµ PïPsC,CŸC-P±PSPµ. Pj CŸP°P·C- PïPµCŸPµPrPsP·CfPIP°PSPSCŸ PjPsP¶PSP° CŸPsP·PiP»CŸPrP°C,Pë CfPëPjPïC,PsPjP°C,PëC+PSPµ P»C-PeCfPIP°PSPSCŸ.

PµPsP±C-C+PSC- CŸPµP°PeC+C-C—.

PµCŸPë P·P°CfC,PsCfCfPIP°PSPSC- PrPëPrCŸPsPiPµCfC,PµCŸPsPSCf Cr PeP»C-PSC-C+PSPëC... PrPsCfP»C-PrP¶PµPSPSCŸC... P·P° PïPsPeP°P·P°PSPSCŸPjPë P±PµP· P»C-PeCfPIP°PSPSCŸ PµCfC,CŸPsPiPµPSP°PjPë PSP°PNëC+P°CfC,C-CëPµ PïPsPIC-PrPsPjP»CŸP»PsCfCŸ PïCŸPs C,P°PeC- PïPsP±C-C+PSC- CŸPµP°PeC+C-C—: PIP°PiC-PSP°P»ChPSP° PeCŸPsPiPsC,PµC+P°, PjC-PiCŸPµPSCŸ/PiPsP»PsPiPSPëPNë P±C-P»Ch, PSCfPrPsC,P°, P±P»CŸPIP°PSPSCŸ, P±C-P»Ch Cr P¶PëPiPsC,C-, PjPµPSCfC,CŸCfP°P»ChPSC- CŸPsP·P»P°PrPë C,P° P±C-P»Ch/C+CfC,P»PëPIC-CfC,Ch PjPsP»PsC+PSPëC... P·P°P»PsP·.

P—P°P·PSP°C+PµPSC- PSPëP¶C+Pµ PïPsP±C-C+PSC- CŸPµP°PeC+C-C— CfPiPsCfC,PµCŸC-PiP°P»PëCfCŸ P· PSPëP¶C+PµPSP°PiPµPrPµPSPsCŸ C+P°CfC,PsC,PsCŸ Cr PeP»C-PSC-C+PSPëC... PrPsCfP»C-PrP¶PµPSPSCŸC... P·P°CfC,PsCfCfPIP°PSPSCŸ PrPëPrCŸPsPiPµCfC,PµCŸPsPSCf (n=3483) P·P° PïPsPeP°P·P°PSPSCŸPjPë P±PµP· P»C-PeCfPIP°PSPSCŸ PµCfC,CŸPsPiPµPSP°PjPë, Cr PrPiPsC... CfPiPsPSCfPsCŸPsPiP°PSPëC... PePsPjPïP°PSC-C”CŸ C-PSC,PµCŸPiPµPSC+C-PNëPSPëC... PeP»C-PSC-C+PSPëC... PrPsCfP»C-PrP¶PµPSPSCŸC... C%PsPrPs PïC-PrC,CŸPëPjPePë P»CŸC,PµC—PSPsPiPsC— C,,P°P·Pë PïCŸPë P·P°CfC,PsCfCfPIP°PSPSC- PrPsPiPsPjC-P¶PSPëC... CŸPµPïCŸPsPrCfPeC,PëPiPSPëC... C,PµC...PSPsP»PsPiC-PNë (P”P PŸ) C-P· P·P°CfC,PsCfCfPIP°PSPSCŸPj PrPëPrCŸPsPiPµCfC,PµCŸPsPSCf (n=1036) C,P° P·P° CfPiPsPSC,P°PSPSPëPjPë PïPsPIC-PrPsPjP»PµPSPSCŸPjPë. P’PëP·PSP°C+PµPSPSCŸ C+P°CfC,PsC,Pë PIPëPSPëPePSPµPSPSCŸ PïPsP±C-C+PSPëC... CŸPµP°PeC+C-PNë T’CŸCfPSC,CfC”C,ChCfCŸ PSP° PSP°PNëP±C-P»ChCë PePsPSCfPµCŸPIP°C,PëPiPSPsPjCf PïC-PrC...PsPrC-: PrCfP¶Pµ C+P°CfC,Ps (≥1/10); C+P°CfC,Ps (≥1/100, <1/10); PSPµC+P°CfC,Ps (≥1/1000, <1/100); CŸC-PrPePs (≥1/10000, <1/1000).

PkPsPiPsCfC,PIPsCŸPµPSPSCŸ PrPsP±CŸPsCŸPeC-CfPSC-, P·P»PsCŸPeC-CfPSC- C,P° PSPµPIPëP·PSP°C+PµPSC- (PIPeP»CŸC+P°CŸC+Pë PeC-CfC,Pë C,P° PïPsP»C-PiPë):

P C-PrPePs: P·P±C-P»ChCëPµPSPSCŸ Cr CŸPsP·PjC-CŸP°C... PïCŸPsPiPµCfC,P°PiPµPSP·P°P»PµP¶PSPëC... PSPsPiPsCfC,PIPsCŸPµPSCŸ (PSP°PïCŸPëPeP»P°Pr PjPµPSC-PSPiC-PsPjPë)*.

PŸCŸPsPi C- P»C-PjC,,P°C,PëC+PSP° CfPëCfC,PµPjP°

P C-PrPePs: PiPµPjPsP»C-C,PëC+PSP° P°PSPµPjC-CŸ*.

P_μC[†]PëC...C-C[†]PSC- C_ηPsP·P»P°PrPë

P_κP_μC[†]P°C[†]C,Ps: PrP_μPiC_ηP_μC[†]PëPIPSPëPN_ε PSP°C[†]C,C_ηC-PN_ε.

P[†]PjC[†]PSPSP° C[†]PëC[†]C,P_μPjP°

P C-PrPePs: C_ηP_μP°PeC[†]C-C— PiC-PiP_μC_ηC[†]C[†]C,P»PëPIPsC[†]C,C-.

P_κP_μC_ηPIPsPIP° C[†]PëC[†]C,P_μPjP°

P§P°C[†]C,Ps: PiPsP»PsPIPSPëPN_ε P±C-P»CH C- PjC-PiC_ηP_μPSCH.

P_κP_μC[†]P°C[†]C,Ps: P·P°PiP°PjPsC_ηPsC[†]P_μPSPSC_Π.

P C-PrPePs: C[†]PsPSP»PëPIC-C[†]C,CH.

P_γC_ηP°PIPSPëPN_ε C,C_ηP°PeC.

P§P°C[†]C,Ps: PSC[†]PrPsC,P°, P±P»CHPIP°PSPSC_Π, P±C-P»CH C[†] P_¶PëPIPsC,C-.

P°P_μPiP°C,PsP±C-P»C-P°C_ηPSP° C[†]PëC[†]C,P_μPjP°

P_κP_μC[†]P°C[†]C,Ps: PiPsC_ηC[†]C€P_μPSPSC_Π C,,C[†]PSPeC[†]C-C— PiP_μC[†]C-PSPePë, C%_oPs C[†]C[†]PiC_ηPsPIPsPrP_¶C[†]C_η,CHC[†]C_Π C[†]P»P°P±PeC-C[†]C,C_η P°P±Ps PSP_μP·PrC[†]P_¶P°PSPSC_ΠPj, P_¶PsPIC,C_ΠPSPëC[†]P_μC_η C,P° P±PsP»P_μPj C[†] P_¶PëPIPsC,C-.

PëPeC-C_ηP° C- PiC-PrC€PeC-C_ηPSC- C,PeP°PSPëPSPë

P_κP_μC[†]P°C[†]C,Ps: P°P»P_μC_ηPiC-C[†]PSPëPN_ε PrP_μC_ηPjP°C,PëC, (PSP°PiC_ηPëPeP»P°Pr PIPëC[†]PëPiP°PSPSC_Π, C[†]PIP_μC_ηP±C-P_¶ C- PeC_ηPsPiPëPi_β[™] C_ΠPSPëP°).

P C-PrPePs: P°PSPiC-PsPSP_μPiC_ηPsC,PëC[†]PSPëPN_ε PSP°P±C_ηC_ΠPe*.

P P_μPiC_ηPsPrC[†]PeC,PëPIPSP° C[†]PëC[†]C,P_μPjP° C- PjPsP»PsC[†]PSC- P·P°P»PsP·Pë

P°C[†]P_¶P_μ C[†]P°C[†]C,Ps: PIP°PiC-PSPP°P»CHPSP° PeC_ηPsPIPsC,P_μC[†]P°.

P§P°C[†]C,Ps: PjP_μPSC[†]C,C_ηC[†]P°P»CHPSC- C_ηPsP·P»P°PrPë (C[†] C,PsPjC[†] C[†]PëC[†]P»C- PjP_μC,C_ηPsC_ηP°PiC-C_Π, PjP_μPSPsC_ηP°PiC-C_Π, PsP»C-PiPs-/P°PjP_μPSPsC_ηP_μC_Π, PrPëC[†]PjP_μPSPsC_ηP_μC_Π C,P° PSP_μC_ηP_μPiC[†]P»C_ΠC_ηPSC- PjP_μPSC[†]C,C_ηC[†]P°C[†]C-C—), P±C-P»CH C[†] PjPsP»PsC[†]PSPëC... P·P°P»PsP·P°C.../C[†]C[†]C,P»PëPIC-C[†]C,CH PjPsP»PsC[†]PSPëC... P·P°P»PsP·.

P C-PrPePs: PiC_ηPëPiC[†]C...P»C-C[†]C,CH PjPsP»PsC[†]PSPëC... P·P°P»PsP·.

P—P°PiP°P»CHPSC- C_ηPsP·P»P°PrPë C- PjC-C[†]C[†]P_μPIC- C_ηP_μP°PeC[†]C-C—

P C-PrPePs: PSP°P±C_ηC_ΠPePë.

P_hP±C[†]C,P_μP_¶P_μPSPSC_Π

P_κP_μC[†]P°C[†]C,Ps: P·P±C-P»CHC€P_μPSPSC_Π PjP°C[†]Pë C,C-P»P°.

*P_μPsP±C-C[†]PSC- C_ηP_μP°PeC[†]C-C— P·C- C[†]PiPsPSC,P°PSPSPëC... PiPsPIC-PrPsPjP»P_μPSCH, C%_oPs PSP_μ C[†]PiPsC[†]C,P_μC_ηC-PiP°P»PëC[†]C_Π C[†] PeP»C-PSC-C[†]PSPëC...

PrPsCfP»C-PrP¶PµPSPSC¶C..., P±CfP»Pë PIPSPµCfPµPSC- PrPs C‡P°CfC,PsC,Pë
B«CfC-PrPePsB» PSP° PsCfPSPsPIC- C,PsPiPs, C%Ps PIPµCfC...PSC¶ PjPµP¶P° 95 %
PrPsPIC-CfC‡PsPiPs C-PSC,PµCfPIP°P»Cf PsC‡C-PeCfPIP°PSPsC— C‡P°CfC,PsC,Pë
PsC‡C-PSCfC”C,ChCfC¶ PSPµ PIPëC%Pµ 3/C..., PrPµ C...=3483 (P·P°PiP°P»ChPSPµ
C‡PëCfP»Ps CfCfP±B¶ C”PeC,C-PI CfPiPsCfC,PµCfPµP¶PµPSPSC¶ Cf PeP»C-PSC-C‡PSPëC...
PrPsCfP»C-PrP¶PµPSPSC¶C...).B

PµPsP±C-C‡PSC- CfPµP°PeC‡C-C—, P°CfPsC‡C-PNëPsPIP°PSC- P· PµCfC,CfPsPiPµPS-
PiCfPsPiPµCfC,P°PiPµPSPsPIPëPj P»C-PeC‡PIP°PSPSC¶Pj (PrPëPI. C,P°PePsP¶ CfPsP·PrC-P»
B«PhCfPsP±P»PëPIPsCfC,C- P·P°CfC,PsCfC‡PIP°PSPSC¶IB» C,P° C-PSCfC,CfC‡PeC‡C-C—
PrP»C¶ PjPµPrPëC‡PSPsPiPs P·P°CfC,PsCfC‡PIP°PSPSC¶ PiCfPµPiP°CfP°C,C-PI
PµCfC,CfPsPiPµPSC-PI):

- CfP°Pe PjPsP»PsC‡PSPsC— P·P°P»PsP·Pë, PiC-PiPµCfPiP»P°P·C-C¶ C,P°
PeP°CfC‡PëPSPsPjP° PµPSPPrPsPjPµC,CfC-C¶, CfP°Pe C¶C”C‡PSPëPeC-PI**;
- PIPµPSPsP·PSP° C,CfPsPjP±PsPµPjP±PsP»C-C¶;
- C-PSC,,P°CfPeC, PjC-PsPeP°CfPrP°, C-C¶PµPjC-C‡PSP° C...PIPsCfPsP±P° CfPµCfC‡C¶,
C-C¶PµPjC-C‡PSPëPNë C-PSCfCfP»ChC,.

** P—P°CfC,PsCfCfPIP°PSPSC¶ PjPsPSPsC,PµCfP°PiC-C— PµCfC,CfPsPiPµPSPsPj P°P±Ps
PePsPjP±C-PSPsPIP°PSPsC— PµCfC,CfPsPiPµPS-PiCfPsPiPµCfC,P°PiPµPSPsPiPsC—
P·P°PjC-CfPSPsC— PiPsCfPjPsPSP°P»ChPSPsC— C,PµCfP°PiC-C— (P—P”Pÿ) P±CfP»Ps
P°CfPsC‡C-PNëPsPIP°PSPµ C-P· PrPµC%Ps PiC-PrPIPëC%PµPSPëPj CfPëP·PëPePsPj
PrC-P°PiPSPsCfC,CfPIP°PSPSC¶ CfP°PeCf C¶C”C‡PSPëPeC-PI (PrPëPI.
B«PhCfPsP±P»PëPIPsCfC,C- P·P°CfC,PsCfCfPIP°PSPSC¶IB»). PµPµC,P°P°PSP°P»C-P· 52
PµPiC-PrPµPjC-PsP»PsPiC-C‡PSPëC... PrPsCfP»C-PrP¶PµPSCf PiPsPeP°P·P°PI
PiC-PrPIPëC%PµPSPëPNë CfPëP·PëPe CfP°PeCf C¶C”C‡PSPëPeC-PI Cf P¶C-PSPsPe, C¶PeC-
P·P°CfC,PsCfPsPICfPIP°P»Pë P—P”Pÿ, PiPsCfC-PIPS¶PSPs P· P¶C-PSPeP°PjPë, C¶PeC-
PSC-PePsP»Pë PSPµ P·P°CfC,PsCfPsPICfPIP°P»Pë P—P”Pÿ (RR 1,43; 95 % CI 1,31-1,56). Pj
P¶C-PSPsPe PIC-PePsPj 50-54 CfPsPePë, C¶PeC- P·P°CfC,PsCfPsPICfPIP°P»Pë P—P”Pÿ
CfPiCfPsPrPsPIP¶ 5 CfPsPeC-PI, CfPµP·CfP»ChC,P°C, PiPsPeP°P·P°PI PsPrPëPS
PrPsPrP°C,PePsPIPëPNë PIPëPiP°PrPsPe PSP° 2000 PiP°C‡C-C”PSC,C-PI. Pj P±P»PëP·ChPePs 2
C-P· 2000 P¶C-PSPsPe PIC-PePsPj 50-54 CfPsPePë, C¶PeC- PSPµ P·P°CfC,PsCfPsPICfPIP°P»Pë
P—P”Pÿ, P±CfPI PrC-P°PiPSPsCfC,PsPIP°PSPëPNë CfP°Pe C¶C”C‡PSPëPeC-PI P·P° 5-
CfC-C‡PSPëPNë PiPµCfC-PsPr.

PÿPµCfPjC-PS PiCfPëPrP°C,PSPsCfC,C-. 5 CfPsPeC-PI.

PjPjPsPIPë P·P±PµCfC-PiP°PSPSC¶. PkPµ PiPsC,CfPµP±CfC” PsCfPsP±P»PëPIPëC...
CfPjPsPi P·P±PµCfC-PiP°PSPSC¶. P—P±PµCfC-PiP°C,Pë Cf PSPµPrPsCfC,CfPiPSPsPjCf PrP»C¶
PrC-C,PµPNë PjC-CfC‡C-.

PjPiP°PePsPIPëP°. PµPs 14 P°P±Ps 20, P°P±Ps 28 C,P°P±P»PµC,PsPe Cf P±P»C-CfC,PµCfC-;
PiPs 1 P±P»C-CfC,PµCfCf PI PeP°CfC,PsPSPSC-PNë PePsCfPsP±C‡C-.

РЉР°С,РµРiРsСҒС-СҒ PIC-РrРiСrСiРeСr. Р—Р° СҒРµРµС†РµРiС,РsРj.

Р'РёСҒРsР±РSPёРe. РґР±Р±РsС,С, Р'С-РsР»РsРrРҒС-РeР°Р»Р· Р'.Р',
РкС-РrРµСҒР»Р°РSPrРё/Abbott Biologicals B.V., The Netherlands.

**РҖС-СiС†РµР·РSP°С...РsРrРҒРµРSPSCҒ РiРёСҒРsР±РSPёРeР° С,Р° Р°РrСҒРµСiР°
РjС-СiС†СҒ РiСҒРsРiР°РrРҒРµРSPSCҒ РN°РsРiРs РrС-СҒР»СҒРSPsСiС,С-.B**
Р'РµС"СҒРiРµРi 12, 8121 РґРґ РґР»»СҒСiС,, РкС-РrРµСҒР»Р»РёРё/Veerweg 12, 8121 AA Olst,
The Netherlands.